4th European Congress of Chemotherapy and Infection Abstracts

Brief oral presentations

Following State-Of-The-Art Lectures

SoA1

The effect of chlorotetracycline treatment on enteric bacteria in pigs SoA1.3

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*Purpose:* There are concerns within the medical profession that antimicrobial agents used in livestock production contribute to the increased antibiotic resistance observed in zoonotic bacterial pathogens. To minimise this risk, evidence-based control strategies need to be implemented. We investigated the effect of chlorotetracycline treatment on a tetracycline resistant population of Salmonella typhimurium DT104 and the commensal Escherichia coli population in pigs.

*Results:* Our results show that pigs treated with chlorotetracycline consistently shed higher numbers of resistant S. typhimurium DT104 than untreated pigs for up to 6 weeks post-treatment. We also identified a 30% increase in E. coli with a chlorotetracycline MIC \(>16\) mg/l and a 10% increase in E. coli with an MIC \(>50\) mg/l. These effects persisted for up to 2 weeks post-treatment. The tetracycline resistance gene was characterised by gene probing and PCR. The level of chlorotetracycline in the pig faeces, as measured by HPLC, fell below our detection limit 5 days after treatment.

*Conclusion:* This study provides direct evidence that oral administration of chlorotetracycline to pigs significantly increases the proportion of resistant enteric bacteria, and this shift in resistance outlasts any residual chlorotetracycline in the pig faeces.

SoA4

Analysis of Helicobacter pylori resistance to antimicrobial agents in Polish children SoA4.2

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*Background:* Helicobacter pylori resistance to antimicrobial agents is an important factor compromising the efficacy of therapy. Since initial treatment for H. pylori infection is often empirical, therefore it is very important to monitor the local resistance pattern. *Objectives:* The aims of our study were: to determine the prevalence of H. pylori resistance to clarithromycin, metronidazole and amoxicillin in children prior to eradication therapy, and to detect mutations responsible for clarithromycin resistance. *Material and methods:* During 2000–2001, 57 H. pylori strains were isolated from gastric biopsies. Susceptibility to antimicrobials was determined by the E-test. Mutations in the 23S rRNA gene associated with clarithromycin resistance were analysed by PCR-RFLP and direct sequencing. *Results:* Overall, 24 strains (42%) were resistant to metronidazole, 25 strains (44%) were resistant to clarithromycin, and 14 strains (25%) were simultaneously resistant to both drugs. All cultured isolates were sensitive to amoxicillin. Primary resistance to clarithromycin was mainly associated with an A2143G mutation in the 23S rRNA gene of H. pylori. However, isolates containing an A2142G mutation had higher MICs of clarithromycin. *Conclusion:* Our results show the high prevalence of H. pylori resistance to clarithromycin in Polish children, which implies a need for pretreatment susceptibility testing.

23S rRNA genotype in Helicobacter pylori strains resistant to clarithromycin in children SoA4.3

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*Objectives:* To study the primary resistance to clarithromycin (CLA) in children, to analyse the point mutations associated with CLA resistance and to compare these data with the resistance obtained from adults.

*Methods:* Thirty-six resistant strains from children and 30 from adults were obtained from gastric biopsies. In vitro susceptibility to CLA was determined by an agar dilution method. DNA from the isolates was extracted by the Ge and Taylor method. A2142G and A2143G mutations were determined by PCR-RFLP (Versalovic, 1996). A 1.4 kpb of the 23S rRNA gene was amplified and digested with BsaI or MboII.

*Results:* The MICs obtained from children strains were: five with MIC 1.5–2 mg/l; four with MIC 4 mg/l; nine with MIC 8 mg/l; nine with MIC 16 mg/l; six with MIC 32 mg/l and three with MIC 64 mg/l and the MICs obtained from adults were: 12 with MIC 8 mg/l; eight with MIC 16 mg/l; seven with MIC 32 mg/l and three with MIC 64 mg/l/1. The A–G transition mutation at position 2143 was higher in children (80.55%) that in adult patients (46.60%) (P < 0.05); while at position 2142 was higher in adults than in children, 36.66 vs 5.55% (P < 0.05).

*Conclusion:* The prevalence of the A2143G > A2142G mutation in H. pylori population of children showed significant statistical differences respecting to H. pylori isolates of adult patients. A higher level of resistance (16–64 mg/l) in children was observed when A–G mutation in 2143 was detected. However, in adult patient higher MICs were observed when mutation in 2142 (A–G) was detected.
Contribution of *rdxA* and *frxA* mutations to metronidazole resistance in *Helicobacter pylori*: an examination of multiple-isolate patient sets SoA4.4

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Purpose: Mutations in *rdxA* and *frxA* genes, encoding NADPH nitroreductase and NADPH flavin oxidoreductase, respectively, reportedly lead to metronidazole (Mtz) resistance in *Helicobacter pylori*. As no single mutation type has been identified that directly correlates with resistance acquisition, we examined *rdxA* and *frxA* in paired Mtz sensitive (S) and resistant (R) isolates and in mixed Mtz-S/R strain populations. Isolates from nine dyspeptic patients that had different Mtz susceptibilities (S and R) before and after therapy and mixed Mtz-S/R subpopulations that were separated were tested. Both *rdxA* and *frxA* from each isolate population was sequenced.

Results: Several different mutations were identified in *rdxA*, but rarely in *frxA*, of Mtz-R strains (post-treatment) that were absent in matched Mtz-S strains (pre-treatment). In contrast, sequences from the post-treatment Mtz-R isolates may therefore be coincidental and not contributing to the Mtz-R phenotype. For most strains, *frxA* mutations were not a factor in Mtz resistance of these isolates. Other mechanisms therefore may contribute to Mtz resistance in *H. pylori*.

Accuracy of 23S ribosomal RNA gene mutation analysis for predicting high level clarithromycin resistance in *Helicobacter pylori* in the United Kingdom SoA4.5

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Pre-treatment resistance of *Helicobacter pylori* to clarithromycin (CLA) and metronidazole (MTZ) is a key factor in eradication therapy failure. Adenine (A) to guanine (G) or A to cytosine (C) mutations at nucleotide 2142, or A to G at 2143 in the 23S rDNA confer in vitro CLA resistance. Our aims were to determine if mutation type and high level CLA resistance was linked and to test for cross-associations with high level MTZ resistance. One thousand one hundred and fifty-one UK isolates from routine endoscopies were tested for susceptibility to CLA and MTZ using E-test. PCR-RFLP identified rDNA mutations in the 92 CLA resistant isolates using *Mbo* I and *Bsa*I, respectively for the A2142G and A2143G mutations, and by PCR assay for the A2142C mutation. Mutation frequency was: A2142G, 22.8%; A2143G, 63.0%; and A2142C, 3.3%. In addition, 3.3% were heterozygous for A2142G and A2143G. No mutation was detected in 7.6% of resistant strains (confirmed by sequencing). High level CLA resistance (MIC > 256 μg/ml) occurred in 43.3% strains representing 17/21 A2142G mutations. Fifty-six isolates were both CLA and MTZ resistant, of these 30 strains had high level CLA resistance and 27 high level MTZ resistance. No single mutation predominated in dual resistant strains. Our findings indicate that an A2142G mutation predicts a 81.4% likelihood of high level CLA resistance. Our mutation assays provide a specific basis to obtain CLA resistance data for treatment and surveillance.

Real-time PCR detection of 23S rDNA mutations conferring clarithromycin resistance in *Helicobacter pylori* using the Roche LightCycler SoA4.6

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*Helicobacter pylori* colonizes the gastric mucosa of ~50% of the worlds human population. In a significant subgroup of infected hosts, *H. pylori* is associated with the aetiology of a number of gastric diseases, most notably gastric and duodenal ulceration. The macrolide antibiotic clarithromycin is a key component of many combination therapies used to eradicate *H. pylori* infection. However, resistance to clarithromycin is an important cause of treatment failure. Clarithromycin resistance is associated with mutations in 23S rRNA nucleotides 2142 and 2143 that inhibit the binding of the drug to the ribosome. A rapid, real-time PCR assay for the detection of 23S rDNA mutations conferring clarithromycin resistance was developed using the Roche LightCycler. The assay utilized a pair of bprobes, one specific for the A2142G mutation and one for the wild type sequence (A2142C and A2143G mutations were detected by characteristic reduction in bprobe Tm). The PCR assay was applied to DNA extracted from 150 selected *H. pylori* isolates from UK patients and identified the 23S rDNA as wild type (45), A2142G (17), A2142C (3), A2143G (70) and heterozygous (15). These results correlated (95%) with those obtained by disk diffusion sensitivity testing and PCR-RFLP based methodologies. The LightCycler assay was successfully applied to DNA extracted from 20 gastric biopsy samples, thus offering the potential to inform patient management without the necessity of culture.

Efficacy and tolerability of different triple macrolide-containing anti-*Helicobacter pylori* treatment regimens in children SoA4.7

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Purpose: Eighty-one patients aged from 9 to 15 years with endoscopically confirmed *H. pylori*-associated (by urease test and PCR) upper gastrointestinal tract disorders were divided into five comparable groups treated with: roxithromycin, metronidazole, ciprofloxacin—RMO-group (15); clarithromycin, metronidazole, ciprofloxacin—CMO-group (18); azithromycin, amoxicillin, ciprofloxacin—MO-group (11); azithromycin, furazolidone, amoxicillin—AMO-group (15); azithromycin, amoxicillin, clindamycin—AMC-group (17). RMO, CMO, AMC regimens were 7 days long; AAmO3—3 days long; AAmO7—7 days long, but azithromycin was given during first 3 days only.

Results: In 6 weeks after completion of treatment *H. pylori* eradication (by urease test and PCR) was achieved in 60 (9/15), 94.4 (17/18), 46.7 (7/15), 75 (12/16) and 88.2% (15/17) in groups RMO, CMO, AAmO3, AFO, AAmO7, respectively. Mild gastrointestinal side effects were recorded in 6.7 (1/15), 11.1 (2/18), 12.5 (2/16), 13.3 (2/15), 17.6% (3/17), in groups RMO, CMO, AAmO3, AFO, AAmO7, respectively without significant difference between groups (P > 0.05) and with no treatment discontinuation.

Conclusion: CMO, AFO and AAmO7 regimens are well-tolerated and more effective (without significant difference between them, P > 0.05).

*Helicobacter pylori* culture and histological susceptibility from pediatric patients with gastrointestinal tract disorders SoA4.8

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Clinical significance of *Helicobacter pylori* detection in gastric juice by polymerase chain reaction in children SoA4.9
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Purpose of the study was to evaluate clinical significance of *Helicobacter pylori* detection in gastric juice by polymerase chain reaction (PCR) in children with upper gastrointestinal tract disorders.

Methods: Two groups of patients aged from 9 to 15 years (mean age 13.5 years) were included. I Group — 20 children with chronic gastritis before anti-*H. pylori* treatment. II Group — 20 children in 6 weeks after the end of anti-*H. pylori* treatment. During endoscopy performed to all children, gastric juice and antral biopsy (I group) or gastric juice, antral and fundal biopsies (II group) for PCR were taken.

Results: In I group *H. pylori* presence in gastric juice was obtained in 80% (16/20) patients and in antral biopsy specimens — in 18/20 (90%) patients; in II group *H. pylori* presence in gastric juice and in antral biopsy specimens was not obtained (0/20), but in fundal biopsy specimens *H. pylori* presence was obtained in 4/20 (20%) patients.

Conclusion: There was no significant difference in PCR susceptibility in gastric juice and in antral biopsies (*P* > 0.05). Thus, gastric juice, which extraction is less traumatic, then biopsy, may be used for *H. pylori* detection, but not for eradication control in children.

SoA5

Distribution of *Streptococcus pyogenes* M types in Spain by sequencing ermM-specific PCR products and its relationship with erythromycin susceptibility SoA5.2
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Introduction: The prevalence of erythromycin resistance (ER-R) in group A streptococci (GAS) has increased in Spain since early 90s with current rates exceeding 40% in some regions. This study determined the ermM-types associated to erythromycin resistance in Spain.

Material and methods: Isolates belonged to the SAUCE* surveillance collection. Rapid sequence analysis of specific PCR products was used to deduce ermM-types corresponding to the majority of the known GAS M serotypes. PCR primers used: GASM1 (5'-TATTGCCTGTAGAAAAATTTAA-3') and GASM2 (5'-GCAAGTTTCTTAGCTGTTTT-3'). Sequencing was done with the Big Dye terminator mix and autosequenator (Applied Biosystems). DNA sequences were subjected to homology searches against the bacterial DNA database.

Results: Overall, 670 GAS isolates (345 ER-R) were analysed. Three M-types (M4, ST1812 and M12) accounted for 66.4% of the ER-R isolates, whereas they just represented a 16.7% of the Ery-S. For ER-R isolates the strongest association was seen with M4 (OR = 12; 95% CI 6.7–22.1), and M75 was second after M4 only in the last temporal period of the study (1998–1999). No homogeneous distribution of ER-R M-types by centres was seen.

Conclusions: Few M-types (leading by M4) are responsible for the ER-R in Spain. But for M4, the remaining ER-R M types (ST1815, M12 and M75) did not show a temporally nor geographically homogeneous distribution.

*SAUCE is an acronym standing for Sensibilidad a los Antimicrobianos Utilizados en la Comunidad en España (Susceptibility to the Antimicrobials Commonly Used in the Community in Spain) and is the Spanish word for the willow tree.*

Using the standard agar dilution method we studied the prevalence of susceptibility to 14, 15, and 16-membered macrolides, and clindamycin in *Streptococcus pyogenes* isolated in Spain in 2001 in 21 laboratories. We also determined the different susceptibility phenotypes. The results were compared with those obtained by the same methodology in 1998 (Alós et al. J Antimicrob Chemother 2000:45:605–609). A total of 529 non-duplicated isolates was used. Throat swab samples provided 383 (72.4%). One hundred and fifty-seven (29.7%) was resistant to erythromycin (MIC breakpoint 1 μg/ml). Resistance to azithromycin, a 15-membered macrolide, was also 29.7%, whereas to moxalactam, a 16-membered macrolide, this was 1.5%. Prevalence of resistance to clindamycin was 1.3%. One hundred and forty-nine (94.9%) of the 157 erythromycin-resistant strains were susceptible to clindamycin and moxalactam, a 16-C membered macrolide (M-phenotype). The remaining eight erythromycin-resistant strains had an MLSA phenotype. If we compared the results obtained in 1998 and 2001 we observed a statistically significant increase in the prevalence of resistance to erythromycin and azithromycin (*P* = 0.02, χ²-test). Our study provides one of the highest erythromycin resistance, clindamycin and moxalactam susceptibility rates for a country in the world for *S. pyogenes*. Strains with the M-phenotype account for the great majority of these isolates, and have significantly increased since 1998.
Macrolide, lincosamide, oxazolidinone and ketolid resistance in *Streptococcus pneumoniae* SoA5.4

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Penicillin resistant *Streptococcus pneumoniae* strains are frequently related to other unrelated antimicrobials and resistance to macrolides is also emerging.

In this study, the in-vitro activities of penicillin, erythromycin, clarithromycin, clindamycin, linezolid and telithromycin were tested against 264 *S. pneumoniae* isolates. Susceptibility testing was carried out by agar dilution, according to NCCLS guidelines. The overall intermediate susceptibility rates, MIC50 and MIC90 (µg/ml) values were as follows, respectively: penicillin 44.7, 0.06, 1%; erythromycin 16.3, 0.125, 4%; clarithromycin 14.1, 0.125, 4%; clindamycin 15.2, 0.125, 16%; telithromycin 1.2, 0.03, 0.125%. For linezolid MIC range was 0.03–16 µg/ml, MIC50 1 µg/ml, MIC90 2 µg/ml. Among the erythromycin resistant 42 isolates, five were susceptible to clarithromycin, 15 susceptible or intermediate to clindamycin, all except one were susceptible to telithromycin.

According to these results telithromycin seems to have the best in-vitro activity against macrolide resistant pneumococci.

SoA6

Addition of fusidic acid in bone cement to systemic teicoplanin treatment of rat osteomyelitis SoA6.3

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This study investigates the effect of local fusidic acid in bone cement besides systemic teicoplanin therapy in rat osteomyelitis model. Meticillin-resistant *Staphylococcus aureus* (MRSA) was given on cortex of tibia of rats, then foreign bodies were placed on cortices. Macroscopic and microbiologic evaluation of infected areas was performed at 21st day. CMW1 bone cements, which contained fusidic acid at 1/10 g ratio, were administered proximal to the area where foreign bodies placed in 15 rats. Other 15 rats were used as the control group. Teicoplanin was given intramuscularly at 20 mg/kg/day doses bid for 14 days in both groups. At the end of treatment, rats were sacrificed and injected tibias were examined macroscopically, microbiologically and histopathologically. Ten rats were excluded because of no growth or polymicrobial growth. Intramedullar polymorphonuclear leukocyte infiltration, granulation tissue at surrounding soft tissues and bone marrow vasculature were evaluated histopathologically.

Statistical analyses were performed using Fisher’s exact test. Recovery rates were 81.8% in teicoplanin 1/fusidic acid group and 53.6% in teicoplanin only group (P = 0.33). There were no significant differences between study and control groups with respect to histopathologic changes. In conclusion, local fusidic acid besides the systemic teicoplanin therapy for osteomyelitis caused by prosthesis has no significant therapeutic effect.

SoA7

Function of the transmembrane domain of VanT serine racemase from vancomycin-resistant *Enterococcus gallinarum* BM4174 SoA7.2

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**Purpose of study:** Investigation of the role of the transmembrane domain of VanT.

**Methods:** *Enterococcus gallinarum* BM4175 (a vancomycin-susceptible derivative with insertional inactivation of the vanC1 gene) was transformed with plasmid constructs pJP1 (containing the genes necessary for resistance, C1-XYc-T) or pJP2 (with a fragment lacking the transmembrane region of VanT-C1-XYc-8T). Minimal inhibitory concentrations and analysis of accumulated peptidoglycan precursors were performed on BM4175, BM4175/pJP1 and BM4175/pJP2 grown in the presence of t-Ser, t-Ser or in the absence of any supplement. Uptake of 0.1 mM [14C]-l-serine was determined in all strains over a 240 s time course.

**Results:** Vancomycin resistance was restored in BM4175 transformed with pJP1(C1-XYc-T). Peptidoglycan precursors were similar to those in BM4174 under all conditions. pJP2(C1-XYc-8T) failed to restore resistance in BM4175. Pentapeptide[L-Ser] was detected only when t-Ser (50 mM) was present in the growth medium. A 40% decrease in uptake of [14C]-l-Ser at 240 s was observed in BM4175 compared to BM4174. pJP1 restored uptake of [14C]-l-Ser at 240 s in BM4175 similar to values obtained with BM4174, whereas pJP2 did not have any effect.

**Conclusions:** The results indicate that the transmembrane domain of VanT is necessary for resistance and that it is likely to function as an L-Ser transporter.

Influence of conjugative plasmids from *Enterococcus faecium* on the outcome of typing methods SoA7.3

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**Purpose:** A variety of methods is used for a molecular typing of *Enterococcus* spp. and related gram-positive bacteria. These include DNA-based methods such as macrorestriction analysis using pulsed-field gel electrophoresis (PFGE), ribotyping, and amplification-based methods such as rapid amplification of polymorphic DNA (RAPD) and amplified fragment length polymorphism (AFLP). We used a homogeneous strain collection of 24 transconjugants resulting from filter-matings with different antibiotic-resistant *E. faecium* and a recipient isolate from our lab. The influence of transferred antibiotic-resistance determinants on the outcome of different typing methods was investigated.

**Results:** Fragment patterns resulting from PFGE indicated minor differences between the transconjugants and the recipient. In respect to different primers used for RAPD, none or only a single fragment shift was detected in the resulting fragment patterns. AFLP clusters of transconjugants into a group of major relatedness, but the result was strongly dependent on the mathematical method used for cluster analysis. Fragment patterns of digested plasmids showed the possession of different or only widely related plasmids in the transconjugants. **Conclusions:** The results of this study clearly show that under certain situations typing methods commonly used for enterococci and related gram-positive bacteria come to their limits.

Bacteremia due to vancomycin resistant enterococci in Slovakia - SoA7.4

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Methods: We performed a nation-wide survey of enterococcal bacteremia. All 132 episodes of enterococcal bacteremia between 3 years (1997–1999) in all six University Hospitals were described by a prospective protocol. Enterococci were tested in six laboratories and reconfirmed in National Reference Laboratory of Antibiotic Resistance of the Ministry of Health. National Committee for Clinical and Laboratory Standards (NCCLS) recommended disk diffusion method for testing of antibiotics was used in all local and in the reference laboratory. Strains from blood cultures were isolated through semi-automated system Bactec or Bact-Alert (Becton–Dickinson) and identified with Vitek Jr. system (Bio Me´rieux, Hazelwood, MU, USA). Enterococcus faecium were reconfirmed with API 20 STREP (Bio Mérieux, Mercy Etoile, France). We used univariate analysis to assess risk factors for enterococcal bacteremia.

Results: Among 132 enterococcal bacteremias, VRE appeared in 6.8% and teicoplanin resistance in 5.3% of all enterococcal bloodstream isolates (88.6% E. faecalis, 9.1% E. faecium, 4.3 E. gallinarum). However, vancomycin resistance in E. faecium was 33.3% and teicoplanin resistance 16.7%. Also resistance to chloramphenicol, tetracycline, ampicillin and gentamicin was higher among E. faecium than in E. faecalis.

Conclusion: In conclusion, VRE among enterococci is increasing also in CEE from 0.1 to 6.8%. Our survey showed 6.8% vancomycin resistance and 5.3% teicoplanin resistance among bloodstream isolates.

SoA8

The incidence of the CTX-M-15 extended-spectrum beta-lactamase (ESBL) in Poland - SoA8.2

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CTX-M-15 was recently identified in Enterobacteriaceae isolates in India and demonstrated the increased activity against ceftazidime when compared to other CTX-M enzymes. CTX-M-15 differs by a single amino acid (ABL238 aspartate to glycine) from CTX-M-3, which is widely spread in Poland. In this work, the first CTX-M-15 producers from Polish hospitals were analyzed. Eighteen cefotaxime-resistant, ESBL-producing enterobacterial isolates were collected in 1998 and 2000 in two hospitals in different cities. The majority of them expressed CTX-M-3 but a single Escherichia coli isolate from one center, and two Serratia marcescens isolates from the other produced CTX-M-15. These isolates demonstrated clearly higher ceftazidime MICs than CTX-M-3 producers, which was also observed when the transconjugants were compared. Apart from the coding sequence mutation, the E. coli blaCTX-M-15 gene differed from blaCTX-M-3 only by a single mutation in the upstream region of approximately 350 bp. Although the isolates were discriminated from CTX-M-3-producing E. coli and S. marcescens isolates from the same and other hospitals, they contained plasmids that were related to blaCTX-M-3-carrying molecules. CTX-M-15 probably appeared in the hospitals due to independent events of convergent evolution, which modified CTX-M-3 into an enzyme with a significant ceftazidime-hydrolyzing activity. This data, together with other recent findings, demonstrate the danger of the use of ceftazidime against CTX-M-producing strains.

Antimicrobial resistance and molecular epidemiology of Stenotrophomonas maltophilia - SoA8.3

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Nosocomial colonization and subsequent infection by multiresistant strains of Stenotrophomonas maltophilia have resulted in outbreaks that require epidemiologic characterization. The specific aim of this study was to determine the genetic relatedness between S. maltophilia strains isolated from our paediatric wards to compare these genotypes with the antibiotic susceptibility patterns.

A total of 38 S. maltophilia strains were included to the study. The in-vitro susceptibilities were determined by agar dilution method, according to NCCLS guidelines. The genotypes of the isolates were included by ERIC-PCR.

The rates of resistance, when intermediate concentrations included, were as follows: piperacillin 86.9%, piperacillin/tazobactam 73.7%, ceftazidime 97.4%, ceftazidime 50%, cefepime 81.6%, ciprofloxacin 97.4%, imipenem 97.4%, meropenem 39.5%, amikacin 73.7%, gentamicin 68.4% and trimethoprim/sulfamethoxazole 5.3%. The strains revealed 11 different susceptibility patterns. When these phenotypically similar isolates were genotype, 25 different DNA patterns existed, indicating the presence of many patient-unique strains, but also clustering of infections due to isolates of the same DNA type.

The results suggested possible nosocomial transmission of S. maltophilia, indicating the need to enforce infection control and antimicrobial use policies to limit the spread of S. maltophilia.

Imipenem resistance in infections due to Pseudomonas aeruginosa in Greek hospitals - SoA8.4

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Data from the Greek System for the Surveillance of Antimicrobial Resistance (WHONET, Greece) revealed that imipenem resistant Pseudomonas aeruginosa are isolated all over Greece with increasing frequency (from 4.7% in 1996, up to 12.1% in 2001 [January–June]). In this study the possible contribution of VIM metallo-β-lactamas in the increase of imipenem resistance in P. aeruginosa is investigated. All imipenem resistant strains of P. aeruginosa isolated during a 1-month period (May 2001) in the hospitals of the System were collected and tested for the presence of blaVIM and the respective integron by PCR. VIM (+) strains were typed by Random Amplified Polymorphic DNA (RAPD) analysis. Seventeen laboratories from all over Greece participated in this study and 59 multiresistant P. aeruginosa strains were isolated. Strains resistant to imipenem were always found resistant to meropenem, penicillins/inhibitors and aminoglycosides. Moreover, resistance to ceftazidime, aztreonam and cefepime was detected in most isolates. blaVIM was detected in 36 strains from nine hospitals. Spread of blaVIM was clonal in four hospitals and horizontal through the spread of the same integron in different clones.
in two cases. The spread of type VIM metallo-β-lactamasases seems to be an important mechanism for *P. aeruginosa* resistance in carbapenems in Greece. This fact underlines the necessity and the urgency for developing a strategy for the containment of resistance.

### Survey of extended spectrum β-lactamases in a paediatric oncology unit, first report of a cefotaxime hydrolysing β-lactama... 

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**Purpose of this study:** During a survey investigating the prevalence of extended spectrum β-lactamases (ESBLs) in the Paediatric Oncology Ward in St. James’s University Hospital, Leeds (UK), a clinical isolate of *Klebsiella oxytoca* T6768 was found to harbour an ESBL conferring a higher Minimum Inhibitory Concentration (MIC) to cefotaxime (16 mg/l) than to ceftazidime (2 mg/l).

**Results:** Polymerase Chain Reaction (PCR) revealed the presence of an SHV-type enzyme as well as a cefotaxime hydrolysing β-lactama... 

**Conclusion:** CTX-M-9 β-lactamase has been reported in Spain and China. This is the first report of a CTX-M ESBL in the United Kingdom and thus highlights the continuing global emergence of this new group of class A β-lactamases.

### Three year study on an incidence of extended-spectrum beta-lactamases-producing strains of Enterobacteria at University Hospital in Košice, Slovak... 

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The purpose of the study was to get information on an incidence of extended spectrum β-lactamases (ESBL) in 1125 strains of gram-negative bacteria (870 *Klebsiella* spp., 115 *Escherichia coli*, 60 *Enterobacter* spp., 45 *Serratia* spp. and 35 *Pseudomonas* spp.) isolated from patients of three Intensive Care Units, Clinic of Anesthesiology and Intensive Medicine and Clinic of Radiotherapy and Oncology at University Hospital in Košice, Slovakia. ESBL production was determined based on both phenotype characteristics (double disk synergy test, three dimensional test, and E-test) and the presence of specific bla*SHV* and bla*TEM* gene sequences by PCR in isolated bacteria. The results obtained. Of 870 *Klebsiella* spp. isolates the production of ESBL was detected in 120 strains (13.79%) and five *E. coli* strains. In majority of ESBL producing isolates bla*SHV* sequences were detected. In our collection of strains any *Enterobacter*, *Serratia* and *Pseudomonas* clinical isolate was detected to produce ESBL. In our work we demonstrated that the most important ESBL producers at the University Hospital were *Klebsiella* spp. isolates carrying bla*SHV* genes.

### Nationwide surveillance of antibiotic resistance in Saudi Arabia... 

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The SASSS network aims to set up a national surveillance study to obtain standardized information on antimicrobial susceptibility to various bacterial pathogens. Currently, 25 hospitals are participating in the project from different geographical regions in Saudi Arabia. During the 1st year of the (2001), the SASSS focused on setting up this network.

Overall, high frequencies of resistance to antibiotics to different bacterial pathogens in Saudi Arabia were seen. Geographical variae... 

### Evolution of antibiotic resistance in *Streptococcus pneumoniae* (Sp) in France from 1995 to 1999... 

Roussell Delvallez M, Dupont MP, Fauchère JL, Fosse T, Laberki MF, Lemozy J, Mauguet J, Péchinot A, Ploy MC, Vaucel J, Vergnaud M, Vernet-Garnier V, Weber M, Laurans G, Murray B, Cattier B, Chardon H, Chomarat M, Cotin J, Demail MC, Romaszkow J, Laboratoire de Bactériologie, Hôpital Calmette, Lille, France, 3Laboratoire de Bactériologie, CHU, Besançon, France, 4Laboratoire de Bactériologie, CHU, Pottiers, France, 5Laboratoire de Bactériologie, CHU, Nîmes, France, 6Laboratoire de Bactériologie, CHU, Montpellier, France, 7Laboratoire de Bactériologie, CHU, Toulouse, France, 8Laboratoire de Bactériologie, CHU, Bordeaux, France, 9Laboratoire de Bactériologie, CHU, Dijon, France, 10Laboratoire de Bactériologie, CHU, Limoges, France, 11Laboratoire de Bactériologie, CHU, Saint-Brieuc, France, 12Laboratoire de Bactériologie, CHU, Caen, France, 13Laboratoire de Bactériologie, CHU, Reims, France, 14Laboratoire de Bactériologie, CHU, Amiens, France, 15Institut de Bactériologie, CHU, Strasbourg, France, 16Laboratoire de Bactériologie, CHU, Tours, France

Every 2 years from 1995, Pneumococcal Regional Observatories (PROs) carried out a prospective study on pneumococcal resistance to antibiotics. The studies required a multicenter collecting of strains sent to one of the Regional Coordinating Centers (CCRs). Erythromycin (ERY), tetracycline (TET) and cotrimoxazole (SXT) were tested locally and interpreted according to the CA-SFM criteria. MICs for penicillin G (P), amoxicillin (AMX) and cefotaxime (CTX) were determined locally and confirmed by the CCRs using the agar dilution reference method. All pneumococci with diminished susceptibility to P
Therapeutic failure and drug resistance in invasive pneumococcal infection SoA8.9

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Purpose: Drug resistant pneumococcal infection (DRPI) is a growing problem. Clinical data regarding the association between resistance and the development of invasive infections are limited. We evaluated the incidence of penicillin and macrolide resistance and of unsuccessful antibiotic pretreatment in patients with invasive pneumococcal infections.

Results: Sixty-four hospitalized patients with culture proven pneumococcal infections (pneumonia: n = 56, meningitis: n = 5, pneumonia and meningitis: n = 3) were prospectively enrolled in the study. Susceptibility testing of isolates was performed according to NCCLS. Comorbidities, disease severity, antibiotic treatment and complications were assessed in a standardized manner. Resistance to penicillin was found in 2/64 patients, to macrolides in 4/64 patients, one of them was resistant (R) to P (P MIC 0.19 mg/l, four intermediate (I) to P, 15% AMX < 0.25 mg/l). Mean of number of passages (number of passages 6) of resistance were rare (P < 15%, AMX < 5%, CTX < 0.5%). The study of the results by specimen and by age showed that the evolution of resistance seemed to be constant for invasive strains while a stationary level was reached in 1997 for non-invasive strains. For example, in adults, the percentage of PSDP in blood cultures was 20 in 1995, 29 in 1997 and 37 in 1999; for strains isolated in respiratory samples, the percentages were 23, 44.6 and 41.5.

Penicillin and Fluoroquinolone resistance in Streptococcus pneumoniae: a joint venture? SoA8.10

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The world-wide problem of betalactam resistance (R) in Streptococcus pneumoniae (SP) has been complicated by increasing R to macrolides and some older fluoroquinolones (FQ) (ciprofloxacin CIP). Aim of our study was to evaluate rate of acquisition of resistance to different FQ: CIP, sparfloxacin (SPX) and levofloxacin (LEV) of SP strains with different serotypes and susceptibility to penicillin (P). Fifteen strains of SP were screened for ability to colonize the NP of infant rats better than opaque (O) SP. Opaque SP has proven more virulent than the T form during systemic infection in a mouse model. Aim of this study was to evaluate phase variation in the nasopharynx of children. SP strains were isolated during a winter epidemiology study of NP samples in children from family DCC. MICs determinations were performed by E-test for penicillin (P), amoxicilline (AMX) and ceftriaxone (CRO). Serotypes were performed using the Quellung reaction. Upon oil immersion microscopic examination short chains of six to eight cocci were noted as 0, +, ++, +++ for absence, 1, 2, > 3 chains by field, respectively. Phase variation was detected on catalase Trypticase Soja plates, AMX and CRO MICs and bactericidal activity was determined for 10 pairs of O and T variants with different serotypes and susceptibility to penicillin. Seventy strains of SP were screened for phase variation. Nine out of 42 with chain length 0, + had O variants while 23 out of 28 strains with chain length ++ or +++ showed O variants. Proportion of O variants was predominant when chain length increased. Serotype 23F was prevalent. Bacterial activity of O variants showed a four- to eightfold increase of MBC. O variants may be present in NP of children while T are predominant form for colonization. These virulent variants with lower level of autolysis showed less susceptibility to killing by antibiotics. They may persist in NP and explain the absence of eradication by active molecules.

Antimicrobial resistance among clinical strains of S. pneumoniae isolated from patients with community-acquired respiratory tract infections (CARTI) in Russia SoA8.12

Kozlov RS*, Bogdanovitch TM*, Sivaya OV*, Agapova ED*, Ahmetova LF*, Furletova b, Gudkova LVb, Gugutskide b, Ilina VNb, Marinusa b, Multch IGb, Ortenberg EA, Shtetinin EVb, Shturmina
Purpose: To determine the antimicrobial resistance of pneumococci causing CARTI in different Russian cities. Methods: A total of 142 non-duplicate strains isolated in 14 Russian cities in 2001 were studied. Antimicrobials tested included penicillin (PEN), amoxicillin (AMO), ceftriaxone (CRO), amoxicillin/clavulanate (AMC), cefoperazone (CPO), cefotaxime (CTX), cefuroxime (CFX), cefuroxime axetil (CFAX), aztreonam (AZT), cefuroxime/aztreonam (CFAXT), mezlocillin (MEZ), ticarcillin (TIC), piperacillin (PIL), ticarcillin/clavulanate (TICC), ceftriaxone/ticarcillin (CFXT), cefepime (CFM), imipenem (IMP), meropenem (MRO), ceftazidime (CTZ), cefotaxime, Azlocillin (AZL), cloxacillin (CLO), benzylpenicillin (PENB), piperacillin/tazobactam (PIT), trimethoprim (TMS), gentamicin (GEN), tobramycin (TOB), amikacin (AMK), ciprofloxacin, chloramphenicol, gentamicin, and rifampin was 12.6, 28.8, 7.2, 69.4, 46.8%, respectively. All enterococci were susceptible to linezolid. In summary, linezolid, glycopeptides, and chloramphenicol showed the best activity against all isolates.

Antimicrobial resistance and consumption of antibiotics—the first results of National Resistance Monitoring Network (OPTY) in Poland SoA8.14

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Purpose of the study: OPTY network was established as a ongoing national surveillance system to monitor antimicrobial resistance linked to antibiotic consumption in order to promote prudent use of antifective agents. The network is co-ordinated by National Reference Centre for Antimicrobial Resistance (SVCRL). All laboratories have been using standardized methodology and participated in the National and International Quality Assessment Schemes (POLMI-CRO, UK NEQAS).

Results: A total of 1200 isolates were collected from 20 hospitals with about 400,000 admissions during year 2000. The overall percentage of multi-resistant pathogens were 12% for MRSA, 19% for high level aminoglycoside-resistant Enterococci and 15% Enterobacteriaceae producing ESBLs. Utilisation of microbiology was relatively low with an average of eight tests/hospital bed per year. Antibiotic consumption measured as percentage of total cost for all pharmaceuticals utilised in hospitals varied between 12 and 36%, mean 25%. The consumption measured by daily defined doses revied two major groups of antibiotics used, as cephalosporines and aminopenicillins with beta-lactamases inhibitors.

Conclusions: The incidence of selected resistance mechanisms in participating hospitals was moderate. The consumption of antimicrobial agents in some centres was high and differed from hospitals of the same level of care. Microbiology was underutilised thus most of therapeutic regimens was of empirical character.

Anaerobes: lessons from a french multicentric survey SoA8.15

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Background: This study surveyed the antibiotic susceptibilities of 434 nonduplicate gram negative isolates collected from nine large university hospitals including B. fragilis group species (359), Prevotella spp. (40), Fusobacterium spp. (23).

Methods: The NCCLS-approved M11-A4 was used. Drugs tested were: amoxicillin (AXM), AMX+clavulanic acid (AMC), ticarcillin (TC) TC+clavulanic acid (TCC), cefoxitin (FOX), cefotetan (CIT), imipenem (IMP), clindamycin (CM) and metronidazole (MOL).

Results: Resistance rates within the B. fragilis group were: AMC 5.6%, TIC 33%, TCC 2%, FOX 13%, CIT 44%, CM 33%, IMP 1% and MOL <1%, respectively. Only one strain of B. fragilis was resistant to metronidazole (MIC = 64 µg/ml); nimA gene was present. Resistance to imipenem or metronidazole was only found among the B. fragilis species, whereas B. fragilis was less resistant to the other drugs than the non-fragilis species. 1.2Lactamase production was detected for 2/40 Prevotella and 3/23 Fusobacterium.

Conclusion: Dynamic changes of antimicrobial resistance are occuring within the B. fragilis group: FOX, CIT, CM continues to increase. Further antibiotic surveys are needed as a source of information to guide the empiric therapy of anaerobic infections.
A map of bacterial resistance in a Hungarian region  SoA8.16

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Background: Regional trends of microbial resistance pattern constitute basic data and qualifying criteria for effective infection control.

Purpose: The aim of our study was to establish an internationally compatible regional database in a Hungarian county Hajdú-Bihar.

Methods: Our model is the National Nosocomial Infections Society publications’ format from the U.S. published in 2001. It contains data regarding various ICU types, ambulatory patients and hospitalised patients. The same format is used for antibiotic utilisation data and device related infections’ rates as well. We collected cleaned data of years 2000–2001 from all the microbiological laboratories of our county.

Results:

<table>
<thead>
<tr>
<th>Susceptibilities</th>
<th>Ambulatory</th>
<th>Hospitalised</th>
<th>ICU</th>
<th>Closest NNIS percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA</td>
<td>2.2</td>
<td>4.5</td>
<td>4</td>
<td>10–25</td>
</tr>
<tr>
<td>VRE</td>
<td>0.1</td>
<td>0</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Ciprofloxacin R S aeruginosa</td>
<td>14.6</td>
<td>28.5</td>
<td>23.9</td>
<td>10–75</td>
</tr>
<tr>
<td>Carbapenem R S aeruginosa</td>
<td>13.9</td>
<td>16.9</td>
<td>30.8</td>
<td>75–above 90</td>
</tr>
<tr>
<td>Ceftazidim R S aeruginosa</td>
<td>16.5</td>
<td>14.4</td>
<td>22.8</td>
<td>75–above 90</td>
</tr>
<tr>
<td>Carbapenem Enterobacter spp.</td>
<td>1</td>
<td>1.2</td>
<td>1.3</td>
<td>75–90</td>
</tr>
<tr>
<td>Ceftriaxon R Klebsiella spp</td>
<td>6</td>
<td>1.2</td>
<td>0</td>
<td>50–90</td>
</tr>
<tr>
<td>Ciprofloxacin P E coli</td>
<td>6.8</td>
<td>4.5</td>
<td>9.6</td>
<td>75–above 90</td>
</tr>
</tbody>
</table>

Susceptibilities not significantly different from U.S. data were as follows: MR CNS, Streptococcus pneumoniae/penicillin and 3rd generation cephalosporin, Pseudomonas aeruginosa/piperacillin and Enterobacter spp. and Escherichia coli/ceftriaxion.

Conclusions: This database proved to be a very useful tool for choosing primary wards of active surveillance including places for infectious disease physician’s visit (ICU, rehabilitation unit). Additional analysis is needed at an individual institution’s level for other heavily used (or useable) antibiotics and bacteria as well (aminoglycosides, beta-lactam–beta lactamase inhibitor combinations, 2nd generation cephalosporins, corynebacteria).

SoA9

AIDS-defining diseases (ADD) and HIV-related immunodeficiency in patients developing AIDS during the HAART era: what is changing? - SoA9.2

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To compare epidemiological, clinical, and immunological features of ADD before and after HAART introduction, between the 436 patients (p) diagnosed in 1985–1995, and the 103 p detected since 1997, in a case-control study. Though the mean number of newly diagnosed AIDS p had a sharp drop in the HAART era, from 65 p/year in 1991–1995 to 22 p/year since 1997 (P < 0.001), the distribution of ADD and underlying immunodeficiency showed limited changes. When excluding a greater frequency of tuberculosis (TB) (P < 0.001) and wasting syndrome (P < 0.04), all other ADD did not show a different frequency before and after 1997. A tendency towards a higher mean CD4 count at AIDS disease was noticed: 78 vs 61 cells/μl (P < 0.003), with a significant difference for Candida esophagitis, toxoplasmosis, Kaposi sarcoma and TB (P < 0.002–< 0.03). The limited variation of clinical and immunological presentation are attributable to the poor impact of HAART before AIDS recognition: 88.4% of p detected since 1997 did not receive HAART or had insufficient compliance to antiretrovirals, so that 58.2% of p were AIDS presenters. During the HAART era, an increase of mean age and sexual transmission was found (P < 0.001). Notwithstanding the effects of HAART on the natural history of HIV disease, the consequences on ADD distribution and related immunodeficiency were negligible, since most p could not benefit from HAART before AIDS onset. A high clinical suspicion for ADD should be maintained when facing p with missed or undertreated HIV disease.

Radata — communication internet platform management of resistance analysis guided haart switch for implementation in clinical practice of HIV-infected individuals  SoA9.3

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Purpose: HIV-resistance analyses are indicated to prepare switch of HAART in HIV-infected individuals with failure to ongoing HAART regimen. Specialists at several responsible sites often feel lack of complementary informations if interpretation of resistance analyses is done independent from each other. Clinical benefits from resistance analysis assays are significantly higher for those physicians, who can access external advice from HIV-experts for possible treatment options. The database concept ‘Radata’ (www.radata.de) was developed in Germany to generate expert advice for implementation in HAART switch.

Results: Fifteen HIV-treatment centres, seven laboratories and 15 high ranked authorities in HIV-Medicine contribute to Radata database since it is started in January 2002 in Germany. HIV-infected subjects are eligible to participate at the project after presentation of failure to HAART (viral load > 1000 c/ml). Expert advice is generated after all data are evaluated and based on recommendations of 2–4 external HIV-experts. Observation after therapy switch is scheduled for a period of 12 months.

Conclusions: Radata is a new database concept with features for evaluation of data and availability of complementary information to participating sites. The project is designed to provide its proficiency to patients and centres from Germany and foreign countries. Further information will be provided after the number enclosed subjects have enlarged.

In vitro effects of HIV infection on ABC transporter expression and antiretroviral drug efficacy  SoA9.4

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Background: Intracellular concentrations of anti-HIV drugs are determinant for their efficacy. ABC transporters such as P-glycoprotein (P-gp) and multidrug resistance-associated proteins (MRP) are reported to limit protease inhibitor (IP) and nucleoside reverse transcriptase inhibitor (NRTI) access to their targets. Moreover, HIV may regulate the expression and activity of these host cell factors.
Therefore, we evaluate in primary cultures of human monocyte-derived macrophages (MDM) and lymphocytes, effects: (1) of retroviral infection and HAART on the expression and activity of P-gp and MRP; and (2) of specific inhibitors of these host proteins on antiretroviral activities of NRTI, non-NRTI and IP.

**Results:** On the one hand, we evidenced a transitory increase of P-gp mRNA expression in lymphocytes and MDM in response to in vitro HIV infection. This was correlated to an increased P-gp cell surface expression and activity, and an increased TNF-alpha production and mRNA. In contrast, no significant modulation of MRP was observed. On the other hand, PSC833 and probenecid potentiated in vitro the anti-HIV activity of AZT and indinavir. These effects were accentuated when PSC833 and probenecid were combined.

**Conclusion:** These results showed that: (1) HIV infection by increasing ABC transporter expression could favorize the efflux of antiretroviral drugs and decrease their pharmacological effects; and (2) specific inhibitors of these transporters could reverse these deleterious effects.

**Effects of Interferon alpha plus ribavirine therapy on frequencies of HCV, HIV and CMV specific CD4-T-cell responses in peripheral blood of HIV/HCV coinfected patients after 6 months of treatment**

**SoA9.5**

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**Hospital Pitié-Salpêtrière, Laboratoire de Virologie, Paris, France.**

**Hospital Pitié-Salpêtrière, Service de Maladies Infectieuses, Paris, France.**

**Objectives:** To investigate the consequences of HIV-related immune defects on HCV-specific T-cell responses and the influence of IFN-alpha + ribavirine therapy on these responses.

**Methods:** Two groups of patients with chronic HCV infection were studied: 26 HIV coinfected progressors with antiretroviral therapy and 13 HIV-negative controls. Twelve HCV/HIV and 9 HCV patients have already reached 6 months of IFN-alpha + ribavirine therapy. Virus-specific CD4-T-cells in peripheral blood were analyzed by IFN-gamma-ELISPOT-assays using HIV-p24, one CMV and three HCV (Core, NS3, NS4) antigens.

**Results:** (1) at baseline, HCV-specific CD4-Th1-cells frequencies were significantly lower than HIV- and CMV-specific ones; (2) frequencies of CD4-Th1-cells against HCV as well as against CMV were similar in the two groups; (3) in HCV+/HIV-, HCV specific CD4-T-cell frequencies did not change between baseline and 6th month of anti-HCV treatment, decreased in three and increased in only one case. HIV- and CMV-specific frequencies were decreased in seven patients. Similar results were observed in HIV-negative group.

**Conclusion:** (1) HCV-specific immune responses might be more prone to tissue compartmentalization than HIV-specific ones; (2) immune defects induced by HIV infection might not be responsible for the low level of HCV-specific responses observed in HIV-progressors; (3) IFN-alpha + ribavirine therapy influence on HCV- and HIV-specific CD4-T-cell frequencies after 6 months of treatment will be discussed.

**Frequencies of HIV-1-p24 specific Th1 cells (ELISPOT) are correlated with plasma HIV-1 viral load in a cohort of LT-NP and slow progressors**

**SoA9.6**

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**ALT Study Group.**

**Hôpital Pitié-Salpêtrière, Laboratoire d’Immunologie Cellulaire, Paris, France.**

**Faculté de Médecine Saint-Antoine, INSERM SC4, Paris, France.**

**Hôpital Pitié-Salpêtrière, Laboratoire de Virologie, Paris, France.**

**Background:** HIV-1-specific T helper-1 cell responses have been associated with long-term-non-progression (LT-NP) in HIV infection but the correlation between frequencies of HIV-1-p24-specific Th1 cells and viral load has not yet been studied. We prospectively quantified these frequencies by using an IFN-gamma ELISPOT assay in a cohort of LT-NP.

**Methods:** A cohort of 62 LT-NP and slow progressors (infection > 8 years and CD4 counts > 600/mm³) was analysable. HIV-1-p24-specific T cells were analyzed using: proliferation, IFN-gamma ELISPOT assays and IFN-gamma production in cell supernatants.

**Results:** Wide ranges were observed in the frequencies of HIV-1-p24-specific CD4 Th1 cells as assessed by ELISPOT (0-3770 SFC/106 PBMC) with a median of 70 SFC/106 PBMC. These frequencies were negatively correlated with viral load ($r = -0.304, P = 0.026$) but not with CD4 counts and associated with a low level of T cell activation assessed by CD71 on CD4 cells ($r = -0.266, P = 0.035$). Similar results were obtained with T cell proliferation and IFN-gamma production.

**Conclusion:** Interestingly, the numbers of HIV-1-p24-specific Th1 cells correlate with plasma viral load, independently of CD4 counts indicating that: (1) the defect in HIV-1-specific CD4 Th1 cells does not reflect the global CD4 depletion; and (2) these responses are strongly correlated to the control of virus replication.

**Impact of drug–drug interactions on therapeutic management of active tuberculosis in HIV infected patients**

**SoA9.7**

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**Department of Infectious and Tropical Diseases, Pitié Salpêtrière Hospital, Paris, France.**

**Institut Pasteur, Unité de Génétique Mycobactérienne, Paris, France.**

Since 1996 and the use of HAART, management of HIV patients with active tuberculosis raised the question of drug–drug interactions and therapeutic management of both infections.

**Retrospective cohort study:** Follow-up of 43 HIV patients with active tuberculosis diagnosed between 1996 and 2000. Studied data included evolution of tuberculosis and HIV, CD4 cell counts, plasma HIV viral loads, antituberculosis and antiretroviral regimens. Forty-four percent of patients were treated by quadruple combination antituberculosis drug with rifabutin for five patients. Fourteen patients were treated by double antiretroviral therapy of nucleoside reverse transcriptase inhibitors (NRTIs) and 29 by triple or more drugs (NRTIs and/or nonnucleoside reverse transcriptase inhibitors NNRTIs and/or protease inhibitors PIs). The median follow-up was 24 months. There was no difference on CD4 cell counts and viral loads in the two groups and between the patients treated by NNRTIs and PIs at the diagnosis of tuberculosis, at the time of antituberculosis drug discontinuation and concerning cure rates of tuberculosis. On the other hand, the plasma HIV viral load was significantly better controlled in patients with NNRTIs than with PIs ($P < 0.005$). In HIV patients with active tuberculosis receiving HAART, antiretroviral combination including NNRTIs allows a better control of viral replication than regimen including PIs without impact of the use of rifampin or rifabutin.

**Previous survey to the settlement of pharmacy visit among HIV-infected patients**

**SoA9.8**

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Adherence is essential to the effectiveness of antiretroviral therapy. A pharmacy visit would improve the patient advisement. A survey was carried out over a period of 3 months in the U.M.I.T. A self-report was distributed to 150 patients. Ninety were evaluated. For 66%, information’s given by the clinician were sufficient and for 76% the treatment advice cards were useful. However, 72% of them would like to attend a pharmacy visit. The topics they would prefer to be tackled were drug interactions (51%), side effects (49%) and effect of forgetting (44%).

The treatment was well accepted and tolerated for, respectively 91 and 65% of the patients. The viral load and the CD4 count were well known by, respectively 52 and 46%. However, inaccurate pattern of treatment was frequent (> 50%) and bad adherence was observed: treatment forgotten occasionally (60%), regularly (30%) or inadequate attitude when the treatment was forgotten (76%). Number of pills, dose frequency, length of the treatment would be risk factors of nonadherence. For the majority of patients, a pharmacy visit is necessary and beneficial. The first result shows a better understanding of the treatment, an improvement of the adherence and an enhancement of plasma concentration of antiretroviral drugs.

SoA10

In vivo activity of glycopeptides against S. aureus infection in a rabbit endocarditis model: is MIC predictive for in vivo efficacy? SoA10.3

Assery N, Caillon J, Lemaheque V, Jacqueline C, Batard E, Potel G, Bugnon D. Laboratoire Anti-biothérapie, Faculté de Médecine, Nantes, France

We have studied the in vivo efficacy vancomycin (V) and teicoplanin (T) against five *Staphylococcus aureus* (SA) strains: two methicillin-susceptible (MSSA 1 and 2), two methicillin-resistant (MRSA 3 and 4) and one glycopeptide-intermediate (GISA 5) strain, in a rabbit endocarditis model. MICs of V and T (V/T) were 0.5/0.25, 1/0.5, 1/1, 0.5/0.5, and 4/8, for MSSA 1, MSSA 2, MRSA 3, MRSA 4, and GISA 5, respectively. The animals were randomly infected with one of these strains, then treated for 2 days by V or T. A continuous infusion of V, simulating a 30 mg/kg/24 h human dose was used. T was infused as a continuous infusion allowing simulating a 6 mg/kg human dose, following an initial bolus. These regimens achieved clinically relevant serum steady-state concentrations of glycopeptides (> 20 mg/l). Results were as follows: expressed in log CFU/g of vegetation (mean ± SD, followed in parenthesis by the number of rabbits used).

<table>
<thead>
<tr>
<th></th>
<th>MSSA 1</th>
<th>MSSA 2</th>
<th>MRSA 3</th>
<th>MRSA 4</th>
<th>GISA 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>7.3±1.7 (6)</td>
<td>9.7±0.9 (5)</td>
<td>8.7±0.9 (5)</td>
<td>8.4±1.3 (8)</td>
<td>8.2±1.1 (4)</td>
</tr>
<tr>
<td>(untreated)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>3.0±0.3* (7)</td>
<td>8.3±1.5 (5)</td>
<td>3.0±0.9* (4)</td>
<td>6.6±1.6 (6)</td>
<td>6.7±1.9 (6)</td>
</tr>
<tr>
<td>T</td>
<td>3.0±0.6* (4)</td>
<td>7.5±0.4 (4)</td>
<td>4.5±1.6* (6)</td>
<td>8.2±0.6 (4)</td>
<td>5.7±1.9 (6)</td>
</tr>
</tbody>
</table>

* P < 0.05 vs controls.

Conclusion: In vivo activity of V and T in this model were different from one strain to another, whatever the in vitro susceptibility to glycopeptides could be. Apparent susceptibility measured by MIC could not predict the in vivo therapeutic effect of glycopeptides at the early stage of treatment in severe SA infections.

Comparative investigation of polymerase chain reaction and a conventional methods for detection of methicillin resistant *Staphylococcus amont* clinical isolates SoA10.5

Kantaridjev TV?, Vacheva-Dobrevski RS?, Panajotov SV?, Bachvarova AM?, Velinov TV?, Levtrova VS, ?National Center of Infectious and parasitic Diseases, Microbiology, Sofia, Bulgaria, bMilitary Medical Academy, Clinical Microbiology, Sofia, Bulgaria

Purpose: Identification on methicillin resistant Staphylococci has a great clinical implication and significant impact of antibiotic therapy. The aim of this study is to compare the disc-diffusion test (DDT), oxacillin agar screen test (OAST) and PCR for detection of mec A gene. Fifty selective clinical isolates (41 *Staphylococcus aureus* and nine *S. epidermidis*) determined as methicillin resistant by DDT were enrolled in the study. DDT was performed with oxacillin disk (1 mg/k) on Mueller-Hinton agar (MHA) without NaCl (NCCLS, 2000). OAST was performed on MHA with 4% NaCl, oxacillin 6 mg/ml, T 35 °C. These strains were genotypically characterized for the mec A gene presence by PCR method using the mec A 1-5’-AAA ATC CAT GGT AAA GGT TGG C-3’ and the mec A 2-5’-AGT TCT GCA GTA CCG GAT TTG C-3’ primers (GIBCO, BRL).

Results: In the group of 50 MRS isolates, detected by PCR, positive results were as follow: 23 *S. aureus* and six *S. epidermidis*. For six *S. aureus* isolates DDT and OAST were positive; PCR-negative. For two *S. aureus* and two *S. epidermidis* isolates PCR was positive; phenotypic methods-negative.

Conclusions: Accurate and rapid detection of MRS is a constant challenge for laboratories. The PCR assay (first time in our country) appears to be more reliable than routine susceptibility testing for the rapid diagnosis of MRSA infections at hospitals, particularly due to the heterogeneous resistance of many strains.

Susceptibility to glycopeptides of *Staphylococcus aureus* in Strasbourg University Hospital SoA10.4

De Almeida NO, Hennebelle BP, Heckendorn RA, Klein C, Prevost G, Linger L, Monteil HF, Bientz M, Jehl F, Meunier O. *Hygiene Institute, University Hospital, Strasbourg, France, bBacteriology Institute, University Hospital, Strasbourg, France*

Purpose: To determine the prevalence of the decreased glycopeptides susceptibility among 187 clinical isolates of *Staphylococcus aureus* collected from patients hospitalized in Strasbourg University Hospital between 15/01/2000 and 01/03/2000. The susceptibility to glycopeptides of 38 *S. aureus* isolates collected from hospital environment during approximately the same period was also investigated.

Methods: The susceptibility to glycopeptides was studied among the MRSA isolates, using:
- detection of the decreased susceptibility to glycopeptides using agar plates containing 6 mg/l teicoplanin,
- detection of hetero-VISA strains using agar plates containing 4 mg/l vancomycin,
- determination of the MICs of vancomycin and teicoplanin using the agar dilution and the E-test strips methods.

Results: Thirty-nine percent of *S. aureus* clinical isolates (74 out of 187 strains) are MRSA. No VISA or hetero-VISA strain was detected. Six percent MRSA isolates are teicoplanin intermediate *S. aureus* strains. In the environment, 13% *S. aureus* isolates are methicillin-resistant (five out of 38). The five strains are all susceptible to glycopeptides.

Conclusion: The results regarding vancomycin are reassuring. However, the high rate of MRSA and the presence of teicoplanin intermediate *S. aureus* isolates prove that prevention and control measures need to be improved.
Antimicrobial susceptibility levels of *Escherichia coli* isolates cultured from urine at a tertiary care teaching hospital. Temporal trend and comparison between community-acquired and nosocomial urinary tract infection SoA13.3

Nanetti A, Manfredi R, Valentini R, Calza L, Chiodo F. University of Bologna, Infectious Diseases, Bologna, Italy

In order to assess the local temporal trend of antibiotic sensitivity of the most common urinary tract bacterial pathogen, all urine-cultured *Escherichia coli* isolates were reviewed as to susceptibility profile, and specimen source (community- versus hospital-acquired infection). When evaluating sensitivity levels of 2070 community-acquired pathogens (1999–2001), a significant resistance rise was limited to cotrimoxazole (*P* < 0.01) and nalidixic acid (*P* < 0.02), while a tendency towards increased resistance regarding norfloxacin (*P* = 0.05) (Fig. 1). When 1570 community-acquired *E. coli* isolates were compared with 2687 nosocomial strains (tested in the years 2000–2001), a greater susceptibility of community-acquired *E. coli* isolates was limited to cotrimoxazole versus all other compounds in the year 2000 (*P* < 0.03), while it was extended to amoxicillin, cephalothin, nitrofurantoin and piperacillin in the year 2001 (*P* < 0.0001) (Fig. 2). On the whole, *E. coli* showed an elevated sensitivity rate (>90% of tested strains) to nitrofurantoin, gentamicin, amikacin, and 2nd- and 3rd-generation cephalosporins, while only amoxicillin and piperacillin had a mean resistance rate >30%, regardless of the community or nosocomial origin. A permanent surveillance of sensitivity levels of the most common pathogens responsible for infectious diseases enables to identify local antimicrobial activity and its temporal variations, and plays a key role in starting empiric therapy, pending bacterial identification and in vitro assays.

Treatment of urinary tract infections: a report of 100 cases SoA13.4

Amari AL, Tsouri HT, Kilani BK, Goubontini AG, Zouiten FZ, Kanoun FK, Ben Chaabène TBC. Rabta Hospital, Infectious Diseases, Tunis, Tunisia

**Objectives:** To evaluate the therapeutic management of urinary tract infections (UTI) in adults.

**Patients and methods:** The study is carried out from July 1999 to December 2000. We included all patients that have signs of UTI. The predisposing factors of UTI are noted, as well as the susceptibility profile of the pathogens. Antibiotic treatment, the clinical and bacteriological course are reported.

**Results:** One hundred cases of UTI are observed. Thirty men and 70 women with a mean age of 48.5 years are included. Diabetes is a common predisposing factor for UTI reported in 37% followed by *n* prostatic hyperplasia (40%) and arthritiis (7%). The most prevalent pathogens are *Escherichia coli* (75%), followed by *K. pneumoniae* (9%). Of the *E. coli* isolates, 76% are susceptible to the 1st CG, 100% to the 3rd CG and 45.5% to ampicillin. Moreover, this pathogen is susceptible to ciprofloxacin in 98.6% and to trimethoprim-sulphamethoxazole (TMP–SMZ) in 60%. Cefalotine is used in 40 cases, alone in 6 cases and with gentamicin in 34 cases. Cefotaxim is prescribed in 31 cases. The mean duration of treatment is 5.79 days. The recovery is reported in all cases. Recurrence of UTI in 25% but six patients lost sight 7 months with hindsight.
Conclusion: In UTI, the antimicrobial agents such as 1st CG combined with aminoglycosides are recommended as initial treatment as well as the 3rd cephalosporin generation at monotherapy. In addition, the fluoroquinolones and aminoglycosides are effective in UTI.

Following Symposia

S3

Prevalence of resistance mutations to antiretrovirals and relation to virological failure S3.4

Garcia F, Suarez S, Alvarez M, Martinez NM, Valera B, Pascual J, Hernandez Quero J, Maroto MC. Hospital San Cecilio, Microbiology, Granada, Spain; Hospital Virgen Nieves, Microbiology, Granada, Spain

Purpose: To investigate the prevalence of resistance mutations in the reverse transcriptase (RT) and protease (P) genes of HIV and to relate it with the type of virological failure (VF), we have studied 88 patients (11% native or pregnant women, 31% were first VF, 23% were second VF, 35% more than two VF. Resistance mutations were investigated using Trugene HIV-1 Genotyping Kit (Visible Genetics).

Results: Global prevalence of resistance mutations for RT Inhibitors (RTI) has been > 20% for M41L, D67N, K103N, M184V, L210W, T215YF, and for L10I, M36I, L63P, A71VT, L90M for P Inhibitors (PI). The prevalence of resistance mutations for the naïve patients studied was very low (A98G, V118I for RTI and L10I, M36I, M46I—all n = 1—and L63P n = 4 for PI). For patients on first VF only K103N, M184V, T215YF (RTI) were > 20%, as well as L10I, D30N, L63P (PI); when patients on second VF were studied, then M41L, E44D, K103N, M184V, G190A, L210W, T215YF, K219QE (RTI) and M36I, L63P, A71IT (PI) were > 20% prevalence; finally, when patients with more than two VF were studied, the following resistance mutations were > 20%: M41L, D67N, K70R, K103N, V118I, Y181C, M184V, G190A, L210W, T215YF (RTI), and L10I, M36I, M46IL, L63P, A71IT, L90M (PI).

Conclusions: The prevalence of primary resistance in the population studied is very low; the prevalence of mutations in the reverse transcriptase and protease genes increase in parallel to the type of virological failure.

Genotypic resistance in HIV-1 RNA from patient plasma compared with rapid virus isolation and phenotypic resistance in patient PBMCs S3.5

Stuermer M, Groeschel B, Cinatl J, Doerr HW. Institute for Medical Virology, University Clinic Frankfurt, Frankfurt, Germany

Objective: To compare HIV-1 virus isolation in the presence of antiretroviral drugs with plasma HIV-1 genotyping.

Materials and methods: HIV-1 genotyping was performed using the ViroSeq™ Vers. 2 from Applied Biosystems. Interpretation of genotypic was done according to international standards. CD4-cells were purified from patient plasma and cultivated in microtiter plates coated with anti-CD3 and anti-CD28 antibodies in the presence of different concentrations of antiretroviral drugs. Virus production was measured using a p24 antigen assay. Phenotypic activity was expressed as 50% reduction of p24 concentrations.

Results: Seventeen samples were analyzed. For 11 samples results were obtained from both methods, two samples could not be analysed by phenotyping and four samples not by genotyping. Only 3/11 samples showed total and 2/11 samples partial concordance, 6/11 samples showed discordance between the two assays. In discordant samples the genotype gave a definite interpretation.

Conclusion: HIV-1 virus isolation and phenotyping from PBMCs may overcome the problem of currently used resistance assays, which analyse only the Reverse Transcriptase and the Protease gene of HIV-1. Possible mutations in other regions may influence viral fitness and therefore contribute to the growth of the virus population present. The lack of concordance between the two assays is related to the different blood compartments used. The clinical value of resistance tests using PBMCs is under investigation.

S4

Actinomycin-D as a modulator of resistances due to cell-wall active agents like Bacitracin (Bc) and lysozyme (Lz) S4.7

Chakrabarty AN*, Dasidar SG*, Calcutta University, Medical Microbiology, Calcutta, India; Jadavpur University, Pharmaceutical Technology, Calcutta, India

It was observed that development of Lzr in the Lzr mutants took place at three different levels and was accompanied with unselected, distinctive and elevated levels of Bcr. Similarly, Bcr in Bcr-mutants were also detected at three different levels. Although the levels of Bcr (100/200 µg/ml) in the Bcr mutants could be raised only by persistent efforts, an increase in the levels of Lzr (as cross-resistance) in the same mutants could be easily achieved. A correlation of actinomycin-D
resistance with Lzr and Bcr of the mutant bacteria and the effects of lipase treatment on the same showed a 4–20-fold rise in actinomycin-D resistance of the Lzr and Bcr mutants of Gram-positive bacteria compared with their correspondence wild-types. These findings suggest that Lzr and Bcr are controlled by several genes accounting for reduced cell-wall and cell-membrane permeability and indirectly, by phenotypic alteration of the lipid content of the cell-wall. Thus, the alteration of cell-walls and membranes and a phenotypic extra lipid layer can work in conjunction with the efflux pump mechanisms finally determining the levels of drug-resistance.

Experimental development of drug resistance to non-antibiotics: a role of alteration of membrane fluidity and efflux systems S4.8

Dastidar SG, Mazumdar K, Asok Kumar K, Chakraborty AN.

Drug resistance among clinical strains was studied by selecting mutants resistant to promazine (Pr) and methdilazaine (Md). The results showed that successive step-up mutants of Pr and Md developed cross-resistance to several unrelated drugs, which in subsequent steps had broader resistance spectra with higher levels of resistance. Experiments on the membrane fluidity or permeability of bacterial cells using diphenyl hexatrine (DPH), a fluorescent probe on bacterial cells using diphenyl hexatrine (DPH), a fluorescent probe on membrane fluidity and permeability. When several analogues of the basic phenothiazine structure, e.g. 2-chlor-methyl-phenothiazine structure, e.g. 2-chlor-methyl-phenothiazine, methyl-1-methyl-2-pyrrolidone-4-carboxylate (MMPC), 3-hydroxymethyl-N-methyl-pyrrrolidone (HMP) and Md with final substation were tested for antibacterial function on different strains, highest activity was observed with respect to Md. With anaerobic bacteria the resistance(s) dependent on efflux pumps showed higher levels of resistance even to Md. We have found the non-antibiotic agents triflupromazine, trimepazine and diclofenac sodium have high degree of activity against vibrios, staphylococci and pseudomonads. The explanation of such a phenomenon in terms of possible efflux pumps will be discussed.

S7

CSF, plasma and urine PCR in Lyme neuroborreliosis S7.3

Picha D, Moravecová L, Lášková Š, Marešová V, Žížárský E.

The main reason for high diagnostic value of PCR in neuroborreliosis (NB) is the direct way of spirochete detection. Two sets of primers in nested PCR were used: one for plasmide gene encoding OspC protein and second for chromosomal gene 16S rDNA. So far 25 patients with clinically manifested involvement in NB were enrolled into the prospective designed study (being continued). The main including criterion was positive probe of intrathalacal specific antibody secretion (in 22 patients) and PCR positivity in CSF (in 3). All patients were repeatedly examined by neurologist and samples of CSF, plasma and urine were taken: (1) before treatment; (2) after treatment; (3) after 3 months. Before treatment were 12 patients PCR positive in CSF, six in plasma, and 10 in urine. Five were parallel positive in CSF and plasma and four in all three body fluids. Urine after treatment was positive in seven (28%) cases and completely negative after 3 months.

The PCR has had relative high sensitivity (44%), but does not rich the sensitivity of antibody index (88%). Supported by grant MZCR 6244; 11300003.

S12

Consumption of imipenem correlates with β-lactam resistance in Pseudomonas aeruginosa S12.5

Lepper PM, Högel J, Trautmann M, Grusa E. *Department of Medical Microbiology and Hygiene, University of ULM, ULM, Germany, †Department of Biostatistics, University of ULM, ULM, Germany, ‡Hospital Memmingen, Central Pharmacy, Memmingen, Germany

Purpose: In the present study we investigated the monthly consume of three anti-pseudomonas-active antibiotics, namely imipenem, piperacillin/tazobactam (PT) and ceftazidime during a period of 3 years (1997–2000). The use of these antibiotics was correlated to the rate of resistance in Pseudomonas aeruginosa.

Results: Inspection of the time series for use of imipenem, ceftazidime, and PT, and the corresponding time series for resistance (each available from July 1997 to July 2000) indicates a remarkable coincidence between use of imipenem and resistance against the three antibiotics mentioned. Pearson’s coefficient of correlation for the use of imipenem and the resistance against imipenem was 0.62 (P < 0.001), between imipenem use and PT resistance was 0.57 (P < 0.005), and between imipenem use and ceftazidim resistance 0.56 (P < 0.005). We found positive regression coefficients quantifying an association with imipenem use in the same month (P < 0.01) and with the use during the preceding month (P < 0.05). The same was true when checking dependence of ceftazidime resistance (P < 0.05) and PT resistance (P < 0.01) on imipenem use observed during the same month. Neither the use of ceftazidime nor of PT could be identified as factors creating resistance to one of the three antibiotics under consideration within a reasonable period of time.

Conclusion: There might be a strong pressure towards resistance created by carbapenems. This could limit the use of carbapenems for initial empiric therapy.

Treat hard and fast: short course antibiotic treatment and its relation with patient compliance and effectiveness S12.6

Perez-Gorricho BPG, Ripoll M, Pechere JC. *Niño Jesus Hospital, Infectious Diseases, Madrid, Spain, †INSALUD, Outpatient Consult, Madrid, Spain, ‡University of Geneva, Microbiology, Geneva, Switzerland

‘Treat hard and fast’: Short course antibiotic treatment and its relation with patient compliance and effectiveness. Finding the important implications for the way in which physicians manage patients with mild–moderate respiratory tract infections, and the relation of this management with the perception of antibiotic effectiveness, and the compliance with the antibiotic regimen has been the main purpose of the research. In a pan-European market research study of more than 3000 patients, designed to determine behaviour to the antibiotic management of mild-moderate respiratory tract infections, patient expectations of antibiotic therapy were identified, particularly those aspects that relate to efficacy and compliance. The study identifies three key drivers of patients perceived antibiotic efficacy: length of antibiotic course, time to onset of symptom relief and time to complete resolution of symptoms. The results demonstrate that once daily treatment for short periods is perceived by patients to
be significantly more effective than longer antibiotic courses and thus better meets patient expectations of therapy. In this study, a macrolide, azithromycin, was selected as the drug therapy of shortest course, being the antibiotic with the shortest dosage schedule for common outpatient infections. The perception of efficacy with short course therapy also correlates with overall satisfaction with management by the physician and with patient compliance with antibiotic therapy.

Consequences of the prophylaxis by amoxicillin on the colonization of the gastrointestinal tract of newborns S12.7

Jaureguy E, Carton M, Butel MJ, Panel P, Ghnassia JC, Doucet-Populaire F. 

"Université Paris5, Microbiologie, Paris, France, INSERM, U88, St. Maurice, France, CH Versailles, Gynecologie, Le Chesnay, France, CH Versailles, Microbiologie, Le Chesnay, France"

Purpose of the study: Group B streptococci (GBS) remain a major cause of neonatal infections. Consensus guidelines have recommended an intrapartum anti-bioprophylaxis by amoxicillin, which has reduced the incidence of early-onset neonatal GBS infections. However, an increased incidence of beta-lactam-resistant Gram-negative neonatal sepsis has been reported. The aim of our study was to analyse the consequences of this anti-bioprophylaxis on the intestinal microbial colonization of newborns. A study of the fecal flora was carried out on 50 stools samples from 3 days-old newborns divided into groups: group A intrapartum treated mothers (n = 25); and group B untreated mothers (n = 25). Both groups were matched with regards to known factors affecting intestinal microbial colonization: gestational age, type of delivery and birth weight.

Results: Colonization by enterobacteria and enterococci was not significantly different between groups A and B. However, the colonization by clostridia was significantly more frequent in group B (n = 131/3 and 13/16 in groups A and B, respectively). However, the colonization by clostridia was modified: the number of newborns colonized was significantly less important in group A than in group B (group A: 3/25 and group B: 10/25 P < 0.05).

Conclusion: In our study, intrapartum anti-bioprophylaxis did not affect intestinal colonization by aerobes but significantly colonization by clostridia, potentially anaerobic pathogens.

Impact of an antibiotic policy restricting the use of beta-lactams and macrolides on the incidence of Clostridium difficile associated diarrhoea in general medical, renal and elderly patients S12.8

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"Nottingham City Hospital, Microbiology, Nottingham, UK, Nottingham City Hospital, Pharmacy, Nottingham, UK, Nottingham City Hospital, Infection Control, Nottingham, UK"

The purpose of the study: To investigate the short-term impact of a new antibiotic policy for the treatment of urinary and respiratory infections on the incidence of Clostridium difficile associated diarrhoea (CDAD) in hospitalised medical, elderly care and renal patients.

The results obtained: A policy restricting the use of beta-lactams (except parenteral penicillin), and promoting alternative antibiotics including levofloxacin for pneumonia, and doxycycline for non-pneumonic respiratory infections, was launched in July 2000. As a result there was a significant and sustained reduction in use of aminopenicillins, cefuroxime and macrolides, with a corresponding increase in doxycycline and levofloxacin. The incidence of CDAD was determined during the first 12 months of the new policy and compared to the last 12 months of the old policy. The incidence of CDAD fell from 10.02 to 4.91 per 1000 patients, and from 1.2 to 0.59 per 1000 in-patient days (P < 0.00001). In contrast, there was no change in the incidence of CDAD in other specialties (surgery, oncology etc.) that had not introduced the new policy. There was no change in the incidence of nosocomial bacteraemia with quinolone-resistant coliforms or MRSA, despite the increased use of levofloxacin.

Conclusions: Hospital-wide reduction of beta-lactam and macrolide use in medical patients can result in a significant and immediate reduction in CDAD. Longer follow-up will determine if this effect is sustained.

Use of imipenem/cilastatin i.v. (tienam i.v.) for the treatment of lower respiratory tract infections in intensive care units S12.10

Izzo L, Orsetti R, Boschetto A, BINDA B, Della Casa U, Carmanico L, La Mazza A. "Department of Surgery, Università degli Studi di Roma 'La Sapienza', P. Valdoni', Rome, Italy, S. Camillo-Forlanini, Intensive Care Unit, Rome, Italy"

Ventilator associated pneumonia (VAP) is considered the most frequent infection in the intensive care unit (ICU), occurring in 9–24% of patients intubated for longer than 48 hours besides nosocomial pneumonia is a common complication in critically ill surgical or trauma patients. Inadequate treatment can lead to the complications of acute respiratory distress syndrome (ARDS), empyema, and lung abscess. The most important aetiological agents both in VAP and in pneumonia which arise as complication in surgical or trauma patients are bacteria, without a marked predominance of Staphylococcus aureus and Pseudomonas aeruginosa. The Authors present their experience (30 cases) on the employment of imipenem/cilastatin i.v. (tienam i.v.) as initial empirical monotherapy at the dose of 500 mg × 3/day or 1 g × 3/day for the treatment of the serious lower respiratory tract infection in an ICU. Tienam is a well tolerated broad spectrum antibacterial agent that is effective against the majority of gram-positive and gram-negative aerobic and anaerobic bacteria including most Pseudomonas species. Except one patient deceased for causes related to his very poor general conditions and three cases in which has been necessary the addition of an aminoglycoside, in all the other patients the imipenem/cilastatin (tienam) monotherapy has shown satisfactory clinical and bacteriological responses.

Clinical auditing of the impact of recommendations on antibiotic treatment S12.11

Kinoo J, DAVID-Ouaknine P, Hacquard B, Echar Y, Decazes JM. "Centre Hospitalier Lagny Marne la Vallée, Lagny sur Marne, France, Hospital Saint Louis, Paris, France"

The aim of this study was to assess the impact of curative antibiotic recommendations on suitable prescriptions at Lagny-Marne la Vallée Hospital (general hospital, 714 beds). Two prospective exhaustive audits were made (all complete hospitalizations, excluding psychiatry, February–May 1997 and 2000) of the detailed curative antibiotic prescriptions, before and after distribution of internal recommendations. The same methodology, designed by a multidisciplinary team, was used for both periods. The same antibiotics were available at the pharmacy. The prescriptions were assessed by an infectious diseases specialist and a pharmacist using pre-established criteria: literature recommendations (1997 audit), internal recommendations (2000 audit). Six hundred and fifty-six prescriptions for 498 patients were collected and analysed in 1997, 738 for 497 patients in 2000. Exhaustivity of the recovered prescriptions was over 95%. Patient characteristics, infection sites and microbiological findings were similar for both groups. Suitable prescriptions were significantly increased (47–59%, P < 0.001). Unsuitable prescriptions (economic reasons, too
short or too long course, incorrect administration, or underdosage) were significantly reduced. Prescriptions for incorrect indications were unchanged and necessary combined treatment not being prescribed, increased. Local recommendations improved prescriptions, but efforts have to be done in order to go on the improvement of the practice behaviour.

Cost-effectiveness analysis of antibiotic therapy in hospitalized patients with COPD Exacerbations (AE-COPD) S12.12

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Antibiotics costs represent a high burden of total drug costs for hospital administrations. A scientific approach considering also the economic aspects of each therapeutic decision may gain optimal treatment objectives at pondered costs.

In our study we retrospectively evaluated the clinical effectiveness and costs of antibiotic therapy in patients with AE-COPD. From 1997 to 2001, 1058 patients were treated as follows: 832 patients with oral therapy only: 30.9% with AMC 1 g b.i.d.; 24.4% with CIP 500 mg b.i.d.; 17.4% with DOX 100 mg u.i.d.; 10.2% with LEV 750 mg u.i.d.; 8.5% with CLA 500 mg. b.i.d.; 7.8% miscellaneous. Ninety-four patients with switch therapy: 56.4% with AMC; 37.2% with CLA. Sixty-eight therapy only: 30.9% with AMC 1 g b.i.d; 24.4% with CIP 500 mg b.i.d.;

<table>
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<th>Antibiotic</th>
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<th>Clinical success (%)</th>
<th>Cost/success (€)</th>
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<td>CIP</td>
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<td>CLA</td>
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<td>DOX</td>
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<td>90.6</td>
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<td>1.39 o.s.</td>
<td>38.02</td>
<td>90.6</td>
<td>41.96</td>
</tr>
</tbody>
</table>

Our retrospective study results support previous pharmaco-economic considerations according which in choosing an antibiotic regimen for AE-COPD we must take into consideration the expected clinical and microbiological results without forgetting to consider the economic burden of our decisions.

S20

Significant increase in fungaemia due to Non-Albicans Candida species S20.4

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Until 1996, predominant Candida species in blood cultures was Candida albicans. It accounted for 72.8% of all Candida species cultured from blood. Since then we have observed a gradual increase in number of non-albicans Candida species. From 1999, onwards non-albicans Candida species out-number C. albicans. This observation is especially important as non-albicans Candida species are generally non-susceptible to azole derivatives and empirical use of azoles in suspected Candidaemia should not be recommended. Amphotericin B is uniformly active against almost all Candida species. Echinocandin may be an alternative. See figure below.

A search for newer antifungal chemotherapeutics S20.5

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Fungal infections due to the mucor-rhizopus (M-Z) group present formidable problems due to lack of appropriate and effective drugs against them, as seen in increasing number of clinical situations; death due to mycoromycosis is nearly inevitable. We analysed the biological ‘weak-spots’ of the mucor-rhizopus group and attempted to devise suitable drugs using their weak-spots. We have noted that like many free-living fungi, the M-Z fungi are facultatively chemoautotrophic (can grow on simple sources of carbon and nitrogen and a solution of mineral salts), like the human pathogenic chemoautotrophic nocardioform bacteria. We devised a minimal medium based on that of Davis and Mingioli, supplemented with simple chemical compounds as sole sources of carbon and nitrogen. The key chemical here was diphenylamine with trypan blue (DPA–TB) and other similar sources of C and N. We found that while media free of these chemicals (controls) allowed good growth of different strains of M-Z fungi, a mixture of DPA–TB completely prevented their growth over a wide concentration range. Experiments with immunocompromised mice showed that these drugs at the concentrations used are well tolerated; mice experimentally infected with several clinical isolates of M-Z fungi and receiving these chemicals showed that these fungi could not grow in vivo.

S33

In vitro activity of newer fluoroquinolones against multi-drug resistant Salmonella typhimurium S33.4

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Purpose: Multidrug-resistant Salmonella typhimurium DT 104 has emerged as an important cause of food-poisoning outbreaks, characterized by resistance to ampicillin, tetracyclines, streptomycin, chloramphenicol and sulphonamides. Moreover, increasing fluoroqui-
nolones resistance is being also reported. We have studied the in vitro activity of β-lactams and fluoroquinolones against multi-drug resistant S. typhimurium from human sources. Material and methods: Fifty multi-drug resistant S. typhimurium were tested against ceftazolin, cefuroxime, cefotaxime, cefepime, ofloxacin, levofloxacin, and moxifloxacin, by the agar dilution method according NCCLS guidelines. Results and conclusions: All the strains were resistant to four or more of the following antibiotics: ampicillin, tetracyclines, chloramphenicol, streptomycin, sulphonamides and nalidixic acid. A high proportion of strains were intermediate or resistant to amoxicillin/clavulanate. We found no resistance to cephapirins. Nevertheless, 26% were intermediate to first and/or second gen. cephalosporins. Cefotaxime and cefepime were the most active cephapirins (MIC50: 0.1 mg/l). Though increasing fluoroquinolones resistance has been described among this kind of strains, no resistance to fluoroquinolones was found here. Levofloxacin was the most active fluoroquinolone (MIC90: 0.06 mg/l), followed by ofloxacin (MIC90: 0.1 mg/l) and moxifloxacin (MIC90: 0.2 mg/l).

High rates of resistance to antibiotics by salmonellae from diarrhoeic children in Zliten-Libya S33.5

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Salmonellae are major bacterial cause of diarrhoea in Libya particularly in children. Included in the present study 23 Salmonella species isolated from 169 children with diarrhoea in Zliten city-Libya. The children aged between a few days to 10 years. The organisms were tested for their susceptibility to antibacterial agents using the disc diffusion method. Of the isolates examined, 23 (100%) were resistant to ampicillin, 22 (95.7%) to amoxicillin–clavulanic acid combination, 20 (87%) to cefotaxin, 22 (95.7%) to chloramphenicol, 21 (91.3%) to doxycline, 18 (78.3%) to gentamicin, 1 (4.3%) to nalidixic acid, 1 (4.3%) to trimethoprim–sulphamethoxazole and none (0.0%) were resistant to norfloxacin. A strong relationship was observed between the availability of antibiotics in the pharmacies of the city and resistance of the isolated salmonellae to these drugs. The misuse of the antibiotics by the community may be an important factor (among others) in the emergence of these high rates of resistance by the salmonellae examined.

S34

Effect of ceftriaxone along with probiotics administration on intestinal ecosystem and beta-lactamase activity S34.6

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Oral bacteriotherapy during antibiotic treatment is a much debated topic. Aim: To study whether different probiotics can prevent imbalance of the intestinal ecosystem (dysbiosis) in children during therapy with ceftriaxone (Cx).

Methods: Fifty-one children (mean age 5.1 years) with febrile respiratory tract infections were treated with Cx 50 mg/kg/day IV, alone (therapy 1) and along with the following preparations: Saccharomyces boulardii (2); Enterococcus spp. (3); lactulose (4); L. casei GG (5); L. rhamnosus, L. bifidus and L. acidophilus (6); B. bifidum and L. acidophilus (7); and a mixture of various lactobacilli and bifidobacteria at high concentrations (8). Faecal samples, collected before and after treatment, were analysed for microflora composition, Cx concentration, and beta-lactamase (BL) activity.

Results: Cx causes intestinal dysbiosis. No C. difficile was found. Faecal BL increased after therapy in all treated groups. Cx alone increased BL activity in 60% (3/5) of children (no activity before treatment); a higher incidence (75–80%) was found in groups 2 and 5. After therapies 3, 4, 6, 7, and 8, BL activity was found in 1 or 2 more children. Cx was detected in 36% of faecal samples.

Conclusions: The probiotics administration seems to protect against dysbiosis caused by Cx and to contain the increase in faecal BL activity. The effects differ according to the probiotic administered and are peculiar to certain bacterial species. These preliminary data need further studies.

S37

Comparative study of initial and acquired drug resistance in pulmonary tuberculosis in Iran S37.4

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Purpose: Resistant to anti-tuberculosis agents particularly multiple drug resistant (MDR) is a major obstacle in treatment tuberculosis in the world. Between September 1996 and March 2000 for 273 smear and culture positive pulmonary tuberculosis patients (old = 86, new = 187) pretreatment susceptibility tests of isolated bacilli to INH, RIF, EMB and STM were performed by standard proportional method and the results were attributed to three groups: (I) newly diagnosed without any history of treatment; (II) patients with history of treatment for one course; (III) patients with history of treatment for two or more courses suposed to be MDR cases. The results were collected for each drug individually and different combinations of two, three and four medications.

Results: Resistance to one, two, three and four drugs was significantly increased in group III comparing to groups I and II, also in group II compared to group I. We observed a high rate of primary resistance to INH and STM in groups I and II and a high rate of MDR (INH and RIF) resistance in groups II and III.

Conclusion: The duration of bacilli exposure to antituberculosis agents in the past is a major factor in developing resistance. In contrast to WHO’s guideline, due to high rate of primary resistance especially to STM in our area, we do not recommend addition of STM for treatment of patients whose initial four-drug regimens have been failed (group II).

Cellular immune response to exported protein of Mycobacterium tuberculosis in tuberculosis infected patients and in healthy donors in French Hospitals S37.5


The objectives were to study cellular immune responses to exported antigens of Mycobacterium tuberculosis in TB patients and in healthy
donors, to understand host interactions with this bacteria, to develop new methods of diagnosis and define new vaccine candidates. Nineteen TB patients and seven healthy donors were enrolled in French Hospitals. Cellular immune responses were evaluated by lymphoproliferation and ex-vivo quantification of specific Th1 cells by ELISPOT-IFN-gamma assays. Four recombinant proteins of *M. tuberculosis* were tested: ESAT-6, 85B, Erp and TB B1.3 and compared with tuberculin. We confirmed that 85B (but not ESAT-6 in our study) were tested: ESAT-6, 85B, Erp and TB B1.3 and compared with proliferation and ex-

Renal tuberculosis in district Brcko S37.6

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The incidence of tuberculosis (TB) is increasing worldwide. In recent some years, geographical differences in the incidence of TB in former Yugoslavia have been observed. An important rise in TB cases was registered in the bordering region of Bosnia. It is likely that poorer living conditions, influenced by war and emotional stress, may promote such rising incidence of TB.

Renal tuberculosis was diagnosed in 25 patients (female 21, male 4) from district Brcko in Bosnia, during the period of 2 years, 2000–2001. At the same time none patient had active pulmonary TB lesions, fibrous lesions were noticed in 18 patients, but we did not diagnose any signs of previous pulmonary TB in seven patients. Seven patients developed relapse of renal TB after 1–5 years of previous treatment. Guided by clinical parameters, precisely done renal echonography enabled early suspicion and searching for renal TB, by radiological and other methods. Bacteriological diagnosis was performed by detection *Mycobacterium tuberculosis* on Loewenstein–Jensen medium in 18 patients. PCR as simple, fast and highly sensitive method enabled diagnosis in incipient stadium of disease, so antituberculous therapy could be instituted some months earlier.

Prompt diagnosis of renal tuberculosis (using PCR, besides standard methods) is necessary, otherwise delayed diagnosis may be dangerous.

A study on resistance to first generation anti-tuberculosis drugs in *Mycobacterium kansasii* S37.7

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**Purpose:** This research has been performed to determine antibiotic resistance of atypical mycobacteria especially *Mycobacterium kansasii*. **Results:** Twenty-three pigmented colonies which indicated atypical agents from NRITLD’s mycobacterium culturebank were selected, they then underwent type identification and antibiogram for INH, RIF, ETB, STM. Nine samples were *M. kansasi* and 14 were other non-MTB, 4 was *M. gordonii*, 2 *M. xenopi*, 3 MAC, 1 *M. bovis*, 2 *M. terrera*, 1 *M. ariiatureum*, 1 *M. marinum* and 1. Mean age in *M. kansasi* cases was 34± 1.3 year and in non-kansasi cases 52± 15.6 yean and in whole society NTM was 44.9±16.4. Frequency of resistance in kansasi group were 4 to INH (44%), 4 to RIF (44%) 4 to ETB (44%), 5 to STM (55%) and prevalence of MDR was 4 (44%) and in non-kansasi group frequency of resistance were 13 (92%) to INH, to RIF 9 (64%), to ETM 9 (64%) and to STM was 10 (71%), to MDR was 9 (64%).

**Conclusion:** A significant difference was seen between the age groups of patients who are affected with *M. kansasi* and non-kansasi (*P < 0.01), also in frequency of resistance to first generation anti-TB drugs. *M. kansasi* is detected as the most common atypical mycobacterium agent in pulmonary infections and attention to antibiogram is recommended before treatment.

Combination of Amikacin–Rifampin in experimental chemotherapy of *Mycobacterium ulcerans* S37.8

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Buruli ulcer caused by *Mycobacterium ulcerans*, is the third most common mycobacterial after tuberculosis and leprosy in west Africa. Nowadays, the only effective treatment is surgery. It consists in a large excision of the lesions, often followed by a skin transplant. In this study, the effectiveness of rifampin, amikacin and their combination were estimated in the treatment of mice, which were infected experimentally by *M. ulcerans*. After 15 weeks of treatment with rifampin, amikacin or their combination, no more viable bacilli were found in infected tissues. The animals were kept for 3 other months. Among the mice treated with rifampin alone, two mice out of 30 relapsed. The minimal inhibitory concentration of these isolated strains went from 0.5 to 8 µg/ml. The DNA sequence, obtained from a 93-pb of the rpoB gene from these strains, showed a missense mutations, which affect a Ser-415 replaced by a phenylalanine. This modification on the gene leads to an important inefficacy of treatment when rifampin was used alone. This study showed that rifampin and amikacin have a bactericidal action on *M. ulcerans* and that a combination of these antibiotics is necessary to avoid the selection of resistant mutants.

Slide Sessions

Cases for discussion

Histopathologic and electron microscopy studies of a severe isolated HIV enteropathy detected in an AIDS presenter. Favorable response to HAART introduction OR1.1

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Advanced HIV infection was detected in a heterosexual female with a 1-year history of chronic diarrhea and severe wasting, as expressed by a body weight of 39 kg, a CD4+ count of 64 cells/µl, and a plasma viremia of 2.5 million copies/ml. A malabsorption syndrome was confirmed by x-ray and test, but repeated pathogen search tested negative at stool examination and light microscopy, scanning electron microscopy (EM), and transmission EM study of enteric mucosa. EM
assays detected an ultrastructural modification of duodenal mucosa never reported to date: an extensive thinning of enterocyte microvilli, disappearance of glyocalyx, and large vacuolization of the enterocyte cytoplasm. Two weeks after starting an indinavir-based HAART, diarrhea disappeared and our patient significantly gained body weight: 6 kg after 4 months, 15 kg after 8, and 18 kg after 1 year, paralleling a CD4+ increase to 299 cells/µl and undetectable HIV viremia. The subsequent 3-year follow-up confirmed absence of gut disturbances, a stable body weight, a CD4+ count of 350–480 cells/µl, and HIV viremia persistently < 50 copies/ml. Repeated endoscopy and related histopathologic and EM assays documented a notable improvement of mucosal damage, with complete cure reached after 2 years of HAART. A direct intestinal localization of HIV may be responsible for severe diarrhea, malabsorption, and wasting, though the morphological features of HIV enteropathy are still unclear. HAART acts favourably also against isolated HIV-related enteropathy.

Kaposi’s sarcoma in a non-HIV immunocompetent adult: relapsing due to the development of a squamous cell carcinoma

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A 26-year-old heterosexual HIV negative girl was diagnosed with cutaneous Kaposi’s sarcoma. The disease was started 2 years earlier with the appearance of lesions on the left feet and on the right knee. Absolute number of CD4 and CD8 were 1200 and 486 cells/dl, respectively with a decreased lymphocyte proliferation. Human herpes virus type 8 had been detected in biopsy specimens and she placed on recombinant interferon alpha-2b. Follow up few months later the patient readmitted because of a mass on the left sternal region. The mass biopsy demonstrated mediastinal well defined soft tissue infiltration associated with mucosal damage, with complete cure reached after 2 years of treatment with IFN. The condition subsided medically and thoracic imaging showed gradual resolution of his fungal lesions. This is the first reported use of the new echinocandin, caspofungin, in the management of disseminated A. terreus infection.

Longterm-treatment with linezolid in a patient with mediastinitis caused by small variant MRSA

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A 58-year-old male patient with insulin-dependent diabetes underwent cardiac surgery for aortocoronary bypass 2 years ago. Two weeks after surgery he developed mediastinitis and sternal osteomyelitis caused by methicillin-resistant Staphylococcus aureus (MRSA). Twice, revisions and plastic surgery for sternal osteomyelits were performed. The patient received initially treatment with vancomycin. Then the patient received intravenous outpatient treatment with teicoplanin for 6 weeks followed by treatment with fusidic acid and then trimethoprin/sulfametrol. The fistula was closed. Four months later he presented again with substernal pain and purulent discharge. The culture revealed the growth of staphylococci which were first mistaken for coagulase-negative staphylococci. After closer investigation these staphylococci were identified as small variant MRSA. Computer tomography (CT) revealed multiple mediastinal abscesses. The patient was treated with intravenous linezolid 600 mg bid for 10 days and then switched to oral linezolid 600 mg bid. The oral therapy was pursued for 16 weeks under close surveillance. The patient improved substantially, the purulent discharge disappeared. The mediastinal abscesses were not detected any longer by CT at the end of treatment. The treatment with linezolid was well tolerated. Platelets decreased initially but rose to normal values without treatment modification.

Nosocomial pneumonia due to Stenotrophomonas maltophilia in a profound granulocytopenic patient hospitalized for community-acquired Staphylococcus aureus severe sepsis

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A 57-year-old engineer, of Indian origin, was diagnosed and the conditions that evolved in it were paronychia in a patient with chronic leukemia having prolonged and profound granulocytopenia due to aggressive treatment with IFN. The condition at admission was critical due to trombocytopenia (< 2000 platelets/µl) and hemorrhage syndrome. The evolution was favorable under

Disseminated Aspergillus Terreus infection treated with caspofungin

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A 57-year-old, of Indian origin, was diagnosed with multiple myeloma in 1996. He received autologous peripheral blood stem cell transplants in May 1997 and August 2001. The second transplant was complicated by prolonged profound neutropenia (> 100 days). During this period he developed a necrotic lesion on the palm of his right hand, which resembled erythema gangrenosum. However, repeated blood cultures yielded Alcaligenes xylosoxidans. The wound was extensively debrided and a small splinter was identified in the palmar fascia. Unexpectedly, intraoperative deep tissue samples demonstrated fungal hyphae on histology, and subsequently Aspergil-
antimicrobial treatment (imipenem), blood and platelet transfusion, intravenous immunoglobulins, granulocyte colony-stimulating factor, antifungal prophylaxis and supportive care. Blood and pus cultures revealed MSSA. In the 6th day of hospitalization she developed bronchopneumonia and respiratory failure. The sputum culture was positive for Stenotrophomonas maltophilia susceptible to ceftazidime, fluoroquinolones. Treatment was unsatisfactory until introducing ticarcillin–clavulanate and ciprofloxacin. She had uneventful recovery despite remaining granulocyto-trombocytopenic.

Conclusions: Treatment of infections with emerging agents in immunocompromised patients is difficult, guidance by results of susceptibility testing being misleading with a poor correlation between the tests and treatment outcome.

**Early disseminated listeriosis in a liver transplant recipient (LTR): a rare case due to an in vitro multiresistant strain** OR1.6


A LTR receiving cyclosporin, azathioprine and steroids, developed an extraordinary episode of sepsis and pleural effusion due to a multiresistant Listeria monocytogenes (Lm) isolate. A Lm strain serov. 4 showing the same, extensive resistance pattern (all penicillins and 1st- and 2nd-generation cephalosporins), was isolated from multiple blood cultures and pleural fluid 2 weeks after surgery, while stool exam was negative. Our p spent her life in countryside and bred some animals, but denied consumption of uncontrolled food. I.

**Problems for discussion**

**HBV–HCV and liver carcinogenesis: where does the viral influence end?** OR2.2

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Hepatocellular carcinoma (HCC) is a major clinical problem worldwide, usually evolving over a long-standing liver pathology, in the latter stages in the form of cirrhosis. HBV and HCV chronic infection is a common etiology of cirrhosis, and hence, HCC. A number of studies have attempted to clarify the role of these viruses into the progression towards HCC. Does their end in the stage of cirrhosis? Is progression towards HCC independent of the etiology of cirrhosis (since alcoholic cirrhosis also proceeds to HCC)? Do the trials with interferon alfa for patients with HBV or HCV cirrhosis exhibit a favorable result due to the antiviral properties of interferon, or is interferon exhibiting anti-oncogenic potential?, and is HCC cytokine and hormone sensitive (view ongoing trials with somatostatin analogues versus HCC)? (hence, if we treat alcoholic cirrhosis patients with interferon could we have a favorable response?). Which patients with HBV or HCV cirrhosis are eligible for interferon treatment?: interferon treatment is a potential hazard for those with thrombocytopenia. How ethical is it to conduct a randomised trial where one leg of cirrhotic patients is left without antiviral therapy? And on the basis of which classification system should the two legs of such a trial be separated? Moreover, do viral proteins with oncogenic potential exist (the controversy over the recently discovered HBV protein is still, unresolved)? A major topic awaiting for a major debate.

**The behavior of Campylobacter spp. intestinal and systemic disease is significantly modified by both underlying HIV infection and antiretroviral treatment** OR2.3

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To assess the role of HIV-associated campylobacteriosis (C) according to HAART availability, 17 patients with positive culture were identified since 1991. Compared with the ~1000 HIV-infected P followed in the last decade, no epidemiological differences were shown, save a greater sexual exposure to HIV (P < 0.005). The introduction of HAART caused a drop of frequency of C (from 1.8 to 0.9 episodes per 1000 P-year; P < 0.0001), and modified clinical features, with disappearance of dissemination and mortality, reported in 7 and 2 patients before 1996 (P < 0.03). HIV-related immunodeficiency and disease stage were significantly related to C features before and after HAART availability: P < 0.0001 for CD4 and neutrophil count, P < 0.007 for AIDS diagnosis. Most cases (15) were community-acquired, but alimentary or environmental risk factors were never found. Ten patients received cotrimoxazole prophylaxis (nine before 1996; P < 0.03), while no relationship occurred with steroid or antibiotic use, caused 14 cases out of 17. A 100% sensitivity was found to quinolones, followed by cephalosporins (82.5%), gentamicin (76.5%), macrolides (64.7%), and cotrimoxazole (47.1%). A 8–18-day antimicrobial therapy cured 16 P, but relapses caused by similar strains occurred in 6 patients within 2–8 weeks, all in the pre-HAART era (P < 0.05). C still occurs in the HAART era, probably due to its varied mode of transmission. The frequency of C is greater in HIV-infected patients, but less frequent visceralization, recurrences, and mortality characterized the HAART era.

**Human Coronavirus-related outbreaks in a neonatal and pediatric intensive care** OR2.4

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Objective: To determine the incidence and risk factors for nosocomial viral respiratory infections (NRVI) and involvement of Human Coronavirus (HCoV) in a neonatal and pediatric intensive care unit.

Methods: Prospective observational study. Nasal samples were obtained by cytological brush at admission and weekly thereafter for all hospitalized infants. Nasal samples were taken monthly from staff. Virological studies were performed, using immunofluorescence for Respiratory Syncitial Virus (RSV), Influenza viruses, paramyxoviruses, and adenoviruses; both immunofluorescence and RT-PCR were used for HCoV detection.

Results: During 1998, 42 HCoV-related NRVI were detected in 152 NN and six in 92 children. Three HCoV-related outbreaks were
observed (February, August and December), associated with a high prevalence of infection in staff. During August outbreak, 18 HCoV-infected NRVI were detected over 23 hospitalized infants. Seventy-five of hospitalized preterm NN with gestational age under 32 weeks and 52.4% of staff members were infected. Risk factors for NRVI in NN were birth weight, gestational age, ventilation, oxygenation and hospitalization length. Ninety-two percent of infected preterm NN were symptomatic, mainly with bradycardia and respiratory worsening.

Conclusions: These data provide additional evidence for a significant role of HCoV in NRVI occurring in hospitalized preterm NN.

Strain typing and screening of 8 DNA targets to assess Echinococcus sp transmission in new and old geographic endemic foci

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Purpose: Cystic echinococcosis is due to Echinococcus granulosus. Parasite cycles depending on the main intermediate host species involved in different foci have been described promoting mixed infection in the same definitive host. Strain typing is a tool to identify the main intermediate host involved via the dogs in the human infection route and to focus the control measures. Many DNA targets have been used to compare samples and to access the parasite cycle in the different countries. But no study has compared the infection route and to focus the control measures. Many DNA targets have been tested in Mauritania where echinococcosis is an emergent disease, and in Algeria where strain typing has never been done. Thirty-five cyst samples from human, ovine, camel and bovine have been tested with six nuclear and two mitochondrial targets.

Results: The two mitochondrial targets and four out the six nuclear targets have allowed to discriminate the different foci. Two strains have been found infectious to human: the ‘sheep’ strain in Algeria and the ‘camel’ strain in Mauritania.

Conclusion: Although overlapping geographically sometimes, this raises the question of the respective genetic evolution of the different strains and of their involving in human infection.

Alveolar echinococcosis in France: an update


Introduction: The highest prevalence rate for alveolar echinococcosis (AE) in Europe has been found in France. In 1997, a French observatory of human AE was done in order to get data that could be used to evaluate presentation, evolution and management of AE.

Material-Methods: French cases were collected for the period 1982–2002. Registration of every case was performed with the subject’s agreement. A questionnaire was filled in by referring to the patients’ medical files or to practitioners or to patients themselves. Completeness of the collection of cases was ensured by multiplying the sources of information.

Results: Two hundred and sixty nine French patients were registered. Sex ratio averaged 1. Mean age at diagnostic was 54.8 years. 12.5% of diagnosis was performed in ‘echinococcosis free’ French areas. Symptoms, but not always specific liver symptoms, were present at diagnosis in 76.4% of cases. The liver was the main location of lesions in 93.6% of cases. A wide spectrum of management of the patients was observed, accounting for regional differences.

Conclusion: This French observatory of human EA will facilitate a better management of the disease at the national level. It shows new epidemiological trends, and especially an extension of the endemic area.

Can coins and paper currency transmit Bacillus anthracis? OR2.7

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Anthrax is an often fatal bacterial infection caused by Bacillus anthracis. Recent events that began in September 2001 in US has gained the organism worldwide attention and heightened awareness of and concern about anthrax. Many cases of anthrax with a number of deaths have been reported as a result of contact with envelopes, sent through postal mail, containing B. anthracis endospores. A number of studies have shown that currency is colonized with bacterial organisms, that include enteropathogens (e.g. Shigella sp.), other enteric flora (e.g. Escherichia coli) and potential pathogens (e.g. Staphylococcus sp., Pseudomonas sp. and Bacillus sp.). Furthermore, methicillin-resistant S. aureus (MRSA) isolates that produced enterotoxin (SEB) and toxic shock syndrome toxin-1 also been reported. All of these studies do agree on that currency may be considered as a method of spreading potentially pathogenic and pathogenic bacteria in the community. Therefore, currency could also be a vehicle for spreading other highly pathogenic organisms that include B. anthracis. In addition, the introduction of the ‘euro’ could also allow such bacteria greater freedom to travel across the euro zone. The threat of using currency, particularly paper notes, in spreading lethal organisms should be investigated and proper measures to prevent the use of such a method by terrorists should be implemented.

Salvage of temporary femoral catheters for haemodialysis using antibiotics in ambulatory patients OR2.8

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The stay of femoral catheters (FC) for haemodialysis is typically short-term for several days. We used FC as a temporary vascular access (VA) for a longer period of time in outpatients going on regular ambulatory haemodialysis, who had a problem with their permanent access. We analysed 43 patients who were discharged from hospital with FC. Duration time of FC was between 13 and 183 days (average 44.2 days) with cumulative total of 1989 days. The incidence of bacteremia was 2.51 episodes/1000 catheter days. In six patients we had signs of infection, so according to our protocol we took blood with FC. Duration time of FC was between 13 and 183 days (a range of time). We used FC as a temporary vehicle for spreading other highly pathogenic organisms that include B. anthracis. In addition, the introduction of the ‘euro’ could allow such bacteria greater freedom to travel across the euro zone. The threat of using currency, particularly paper notes, in spreading lethal organisms should be investigated and proper measures to prevent the use of such a method by terrorists should be implemented.
cultural therapy with negative blood culture from peripheral vein.

Advances in meningitis education OR2.9

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Background: Meningitis remains an important cause of death worldwide despite improvements in diagnosis, treatment and prevention. Clinical and lay awareness of the disease relies on education, however educational delivery has changed and the introduction of material suitable for computer and internet application is now necessary. We have developed educational material on CDROM and on the internet applicable both at tertiary university and secondary school level.

Application: A computer-aided learning program on CDROM, covering all aspects of meningitis has been produced. It is suitable for undergraduate teaching of healthcare professionals from student nurses and doctors to pharmacists. In order to reach school children in a form acceptable to both pupils and teachers, we have developed a curriculum-linked website. These applications are simple to use and can be incorporated into existing courses of study, so that issues raised can be discussed with tutors and group peers.

Comment: The introduction of new methods of teaching and learning mean that compatible educational material must be produced. We believe that these applications, focusing on meningitis, are the first of their kind and that they offer tutors the opportunity to progress their teaching of the disease both in methodology and content.

Antiviral therapy

Brivudin compared to famciclovir for improved therapy of herpes zoster: effects on acute disease and postherpetic neuralgia OR3.1

Wassilew SW, Stubsinski BM, Koch P, Schumacher K, Capriati A. *Klinikum Krefeld, Department of Dermatology, Krefeld, Germany, 1Berlin-Chemie/Menarini Group, Clinical Research, Berlin, Germany, 2Berlin-Chemie/Menarini Group, Clinical Research, Berlin, Germany, 3Menarini Group, Menarini Ricerche, Florence, Italy

Objective: Comparison of efficacy and safety of brivudin 1 × 125 mg and famciclovir 3 × 250 mg, both for 7 days, in the treatment of herpes zoster. Methods: Randomised, double-blind study on 2027 immunocompetent patients ≥ 50 years (brivudin: n = 1019, famciclovir: n = 1008). Primary endpoint was the prevalence of postherpetic neuralgia (PHN), defined as at least moderate zoster-associated pain ≥ 3 months after start of treatment. Results: Prevalence of PHN under brivudin (11.1%) and famciclovir (9.2%) did not differ significantly (OR (ITT): 1.23 [0.92 – 1.65]; P = 0.17). Prevalence of zoster-associated pain, regardless of intensity, was 21.2% under brivudin and 19.3% under famciclovir. Median duration of PHN was 47.0 days with brivudin and 54.0 days with famciclovir (RR (ITT): 1.05 [0.76 – 1.45]; P = 0.77). Median duration of vesicle formation was identical (32 h) under brivudin and famciclovir (RR (ITT): 1.01 [0.90 – 1.12]; P = 0.91). Potentially treatment-related adverse events occurred in 11.8% of the brivudin recipients and in 10.1% of the famciclovir recipients (P = 0.26).

Conclusions: In zoster patients ≥ 50 years, brivudin 1 × 125 mg and famciclovir 3 × 250 mg showed equivalent effects on prevalence and duration of PHN. Brivudin is as effective as famciclovir in stopping viral replication in acute herpes zoster. Brivudin offers the advantage of a once daily dosage regimen while being as well tolerated as famciclovir.

Activity of complexes of Pt(II) and Pd(II) with pyridine-2-carbaldehyde thiosemicarbazone (HfOTsc) against Herpes simplex virus infection OR3.2

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Our previously published data have shown that [Pt(HfOTsc)2]Cl2 inhibited HSV 1, strain Victoria, infection in cultured cells (Acta Virol., 2001, 45, 87) with selectivity index (SI) 1.5 times higher than that of acyclovir (ACV). In order to evaluate virus specific response and structure–activity relationships we continue our investigations with three Pt(II) and three Pd(II) complexes. The activity was evaluated against sensitive to ACV HSV 2 (strain Bja) and resistant strains R-100 (HSV 1) and PU (HSV 2) and compared to that obtained against strain Victoria (HSV 1) infection. SI was indicative for activity. The virus specific response was demonstrated by the fact that viruses sensitive to ACV were also sensitive to Pt(HfOTsc)2Cl2, while ACV resistant viruses were sensitive to [PtCl(FOtsc)]. The structure–activity relationship was proved by the fact that the less active against HSV infection was [Pd(FOTsc)].

Influenza diagnosis, treatment, and the impact of new antivirals on current treatment behaviours during influenza outbreaks OR3.3

Schaetz L, Sessa A, Hoffman-La Roche F. Basel, Switzerland, 1Italian College of General Practitioners, Italy

Introduction: Annual influenza epidemics severely affect individuals, families, health care systems and society. The availability of new and specific antivirals provides an opportunity for better management of influenza.

Methods: During the 1999/2000 and 2000/2001 influenza seasons, physicians (~ 100/country) and public (~ 1000/country) in the USA and Europe were interviewed to determine perceptions of influenza and behaviours for its treatment.

Results: Patients recognize influenza illness as severe and identify it by symptoms of fever, muscle aches/pains and cough. Physicians use these symptoms to diagnose influenza clinically (93% fever, 78% muscle aches/pains, 47% cough); their main treatment objective being to reduce complications. Antibiotics for influenza treatment are broadly recommended/prescribed by about 30% of European physicians, whereas currently available antivirals are only recommended by 10%. The recommendation of antivirals by US physicians increased from 47% (season 99/00) to 62% (00/01) and markedly decreased antibiotic use (from 25 to 11%). Experience from the two influenza seasons shows that influenza antivirals are only used while the virus is circulating and that the volume of use is proportional to the size of the outbreaks.

Conclusions: Experiences in the USA show that with prompt outbreak information antivirals can be used appropriately in times of influenza activity.

Influenza treatment with oseltamivir: costs and benefits for the individual as well as for society OR3.4

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Objective: To evaluate the effects of treatment of influenza with antivirals (oseltamivir) on health outcomes and costs to patients and society.

Methods: Based on clinical trial data and data from the literature a simulation model has been developed. The underlying clinical pathway covers morbidity and mortality due to influenza and its specified complications. Health outcome data and costs were attached to events in the model. The model compares various scenarios, which are defined by treatment schemes within defined populations and other parameters. Application of the model is shown using UK unit cost data simulating an otherwise healthy adult population comparing oseltamivir with usual care.

Results: Early treatment results in reduced morbidity, which translates into faster recovery and return to normal activities (1.93 days). Lower morbidity and mortality make this a cost-effective intervention from a societal perspective. The analysis covers more than 10 different scenarios and the incremental cost effectiveness ratios will be discussed.

Conclusion: Antiviral treatment appears to be effective in terms of health outcome and cost for otherwise healthy adults from the perspectives of both the individual patient and society. However, this effect is very sensitive to time when treatment is started and the accuracy of the diagnosis of influenza.

Oseltamivir is well tolerated by all patient groups OR3.5

Introduction: Oral oseltamivir, the ethyl ester pro-drug of a potent inhibitor of influenza virus neuraminidase, is licensed for the treatment and prophylaxis of influenza in the USA.

Patients and Methods: Safety data [adverse events, laboratory safety evaluations] derived from clinical trials involving >12,000 subjects (including ~1000 children and ~1200 high-risk adults) and 400 healthy volunteers in a large study investigating ECG parameters. Spontaneous event reports from MEDWATCH or yellow-card reports following use by ~20000 individuals worldwide. An observational case-control study of >10,000 subjects with influenza-like illness treated with oseltamivir.

Results: Oseltamivir was well tolerated in clinical trials; drug-related side-effects were limited to transient GI effects occurring in ≤1:10 exposed individuals. These resolved spontaneously and caused drop out in <1% of treated subjects. No effects on ECG parameters were noted at doses ≥sixfold above the licensed regimen. Oseltamivir had no adverse effects on pulmonary function. No additional effects were identified among high-risk adults or children, or following prolonged dosing for prophylaxis. Occasional reports of liver dysfunction have been documented post-marketing but causal association has not been established.

Conclusions: Oral oseltamivir is an effective and safe antiviral suitable for influenza management in all patient groups.

Selection of active antiviral substances on Vaccinia virus uracil DNA glycosylase OR3.6

Scaramozzino N, Crane JM, Drillien RB, Dideberg O, Garin D. aCRSSA, Unité virologie, La Tronche, France, bINSERM 99-08, Biologie, Strasbourg, France, cIBS, Cristalloigraphie Macromoleculaire, Grenoble, France

The decision to stop the vaccination against smallpox and the loss of specific immunity of a high proportion of the population made apocalyptic the perspective of a natural or provoked re-emergence of smallpox. Therefore, it is important to improve the current capacities to prevent or to treat the orthopoxvirus infections. Uracil DNA glycosylase (UDG) is one viral enzyme indispensable to the replication of poxviruses. UDG of the Copenhagen strain of Vaccinia virus (VV) was characterized with the aim of defining specific inhibitors susceptible to be used as a new class of active antiviral substances on the viruses of the Orthopoxvirus genus. The activity of this enzyme was analysed in real time, in an original method, on a PCR quantitative instrument by digestion of amplified DNA revealed by fluorescent intercalated molecules. This technique was used to screen and select several active antiviral substances on UDG. Moreover, the antiviral activity was estimated by the cytopathic effect of the VV on infected vero cells. The cytotoxicity was determined by inhibition of Trypan Blue exclusion. The specificity of action of each tested compound was estimated by the selective index (50% cytotoxic dose/50% effective dose). Two antiviral compounds were selected for their inhibitory effect on UDG activity and on VV replication in Vero cell culture: (+)-5-iodo-2'-deoxyuridine and 4-chlorouracil. These compounds are candidates for the chemotherpay of poxvirus infections.

Russian antiviral drugs for immunocompromised patients OR3.7

Novik D, Kaplina E, Nossik N, Ladigina A. aThe D.I.Ivanovsky Institute of Virology Russian Acad. Med., Laboratory of Immunodeficiency Viruses, Moscow, Russian Federation, bTechnomeederevice Company, Research, Moscow, Russian Federation. aThe D.I.Ivanovsky Institute of Virology Russian Acad. Med., Laboratory of virus ontogenesis, Moscow, Russian Federation

Abstracts

Objective: To study the efficacy and tolerance of Russian antiviral drugs produced from DNA in a limited resources context.

Results: The drug Derinat was produced from salmons' milt. Mn of DNA was 270–500 kDa, hyperchrome effect >37%, protein content <0.5%. The conjugation of the DNA with Fe3+ resulted in a new drug named Ferrovir which influences DNA and RNA synthesis during early stages of HIV-1 replication by blocking the virus' action on cells' metabolism and reduces cytomegalovirus titre in fibroblast cells for 1.5–2.0 Ig TCID50. A protective effect of ferrovir against fatal herpes encephalitis mice was found. The drugs are not toxic. IC50 >4000 mg/ml. EC90 of ferrovir against HIV-1 was 800 mg/ml. In limited clinical trials patients received 75 mg of drugs twice daily (7–14 days). Administration was well tolerated and no side effects were observed. Derinat in 88.1% cases of herpesvirus infection (42 patients) improved the healing and shortened duration of illness. HIV-infected patients (34) treated with ferrovir showed sustained, elevated CD4+ counts and a significant reduction in HIV-1 viral load (median 1.8 Ig). The apparent remission was found in patients with concomitant HIV and Herpes Virus infection.

Conclusions: Antivirals show good antiviral potency against RNA- and DNA-viruses; are well tolerated by patients and are useful in case of mixed infections; low price makes them accessible to populations with low financial resources.

Ortho Total HCV core antigen assay can aid early prediction of response in patients treated with Interferon/Ribavirin OR3.8

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Objectives: To evaluate the predictive value of Total HCV Core Antigen Assay and viral kinetics in patients with chronic HCV.

Methods: One hundred and twenty two patients infected by genotype 1, 4, 5 or pretreatment viral load (bDNA 2.0, Chiron) >3
Lamivudine in the treatment of acute hepatitis B OR3.9
Vincenti A, Meini M, Luchi S, De Gennaro M, Ricciardi L, Moneta S, Scasso A. Infectious Diseases Department, Infectious Diseases, Lucca, Italy

Acute hepatitis B is a self-limiting infection, but in some cases its course may be particularly severe. We report a case of a 77-years-old woman affected by acute hepatitis B treated with lamivudine. On admission in the hospital the alanine-aminotransferase was 1060 UI/l, the aspartate-aminotransferase 1017 U/l, bilirubin 10,2 mg/dl, HBsAg, HBcAg and HBeAg were positive, HBV DNA was 300,000 copies/ml. During the following days, the levels of AST and ALT gradually rose; on the 14th day prothrombine time was 39%, bilirubin 30 mg/dl and the aspartate-aminotransferase 1017 U/l, bilirubin 10,2 mg/dl, HBsAg, HBcAg, and HBeAg were positive, HBV DNA was 300,000 copies/ml. During the following days, the levels of AST and ALT gradually rose; on the 14th day prothrombine time was 39%, bilirubin 30 mg/dl and the patient developed signs of encephalopathy. Four plasmapheresis were practiced without benefit, so the patient was treated with lamivudine, 100 mg/day. After 24 days of therapy, lamivudine was discontinued because of the appearance of diffuse maculopapular rash. At this time the results of liver function tests were normal; after four months HBsAg and HBV DNA were no longer detectable. In our patient lamivudine prevented an acute hepatic failure. Our experience suggests a promising role of lamivudine in the treatment of acute hepatitis B, but how long such therapy have to be practiced and in which patients? Prospective, controlled, clinical studies using lamivudine in patients with acute-hepatitis B are necessary.

The cost-effectiveness of amantadine versus symptomatic care in the treatment of influenza OR3.10
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\textit{Aim:} To assess the cost-effectiveness of amantadine versus best symptomatic care in the treatment of influenza in the UK.

\textit{Methods:} We constructed an economic model populated with parameters from the published literature. The model structure is the same as that used in the economic evaluation of zanamivir published by the National Institute for Clinical Excellence in the UK. We conducted a cost-utility analysis (incremental cost per QALY gained) of amantadine versus best symptomatic care. The analyses are conducted for all adults (average-risk group) and the at-risk population (high-risk group), based on the prevalence of influenza over an average season and when the virus is circulating. The perspective is that of the NHS.

\textit{Results:} In the average-risk group the incremental cost per QALY gained of amantadine relative to best symptomatic care is £30,488 during an average influenza season and £12,538 when the virus is circulating. For high-risk individuals the figures are £35,278 and £14,526, respectively. The results are sensitive to the hospitalisation rate.

\textit{Conclusions:} If the threshold for cost-effectiveness is £20,000 per QALY gained amantadine represents value for money in the treatment of influenza in a variety of scenarios, including the baseline for both average-risk and high-risk groups when the virus is circulating.

Posters
Sunday, 5 May 2002

Quinoline posters

Susceptibility of currently used antibiotics including newer fluoroquinolones in penicillin—resistant \textit{Streptococcus pneumoniae} PS101

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\textit{Background:} Surveillance studies all over the world have revealed an extraordinary increase in the prevalence of penicillin resistant \textit{Streptococcus pneumoniae}. The newer quinolones are believed to have broad activity against \textit{S. pneumoniae}.

\textit{Methods:} A total of 87 penicillin resistant clinical strains isolated from patients at Hacettepe Children’s Hospital, Ankara, Turkey between 1999 and 2001 were tested for their in vitro susceptibility to various antibiotics that are commonly used in the treatment of respiratory tract infections. The minimum inhibitory concentrations (MICs) of the penicillin, amoxicillin/clavulanic acid, doxycycline, azithromycin, clarithromycin, ceftriaxone, ciprofloxacin, levofloxacin, moxifloxacin and gemifloxacin were determined using the NCCLS recommended procedure for \textit{E}-test.

\textit{Results:} The range of MICs, MIC50 and MIC90 values for all agents tested against the strains are shown in the Table. Gemifloxacin and moxifloxacin had the highest in-vitro activity among the quinolones tested. All strains tested were susceptible to $< 0.2 \mu g/ml$ gemifloxacin, $< 1 \mu g/ml$ moxifloxacin and $2 \mu g/ml$ levofloxacin.

\textit{Conclusions:} There is some degree of resistance to all the drugs except the newer quinolones which were active against all isolates studied. Table 1 MICs of the tested antibiotics against penicillin resistant isolates of \textit{S. pneumoniae}.

\begin{table} [H]
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
Antimicrobial & \multicolumn{2}{c|}{MIC50} & \multicolumn{2}{c|}{MIC90} & \multicolumn{1}{c|}{Range} \\
 & (mg/ml) & (mg/ml) & (mg/ml) & (mg/ml) \\
\hline
Amoxicillin/clavulanate & 0.38 & 1.5 & 0.016–4 \\
Ceftriaxone & 0.25 & 16 & 0.064–24 \\
Doxycycline & 1.5 & 256 & 0.38–>256 \\
Azithromycin & 0.125 & 256 & 0.047–>256 \\
Clarithromycin & 0.75 & 1.5 & 0.25–2 \\
Ciprofloxacin & 0.38 & 1.5 & 0.06–1.5 \\
Levofloxacin & 0.125 & 0.19 & 0.047–0.64 \\
Moxifloxacin & 0.023 & 0.032 & 0.006–0.064 \\
Gemifloxacin & 0.023 & 0.032 & 0.006–0.064 \\
\hline
\end{tabular}
\end{table}
Abstracts

Comparative activity of quinolones against nosocomial Staphylococcus aureus: the results of multicentre study in Russia  

PS102

Kretchikov VA, Dekhnich AV, Stratchounski LS. Institute of Anti-microbial Chemotherapy, Smolensk, Russian Federation

Objectives: To compare in vitro activity of ciprofloxacin (CIP), levofloxacin (LEV) and moxifloxacin (MOX) against nosocomial strains of Staphylococcus aureus isolated in different regions of Russia.

Methods: A total of 879 S. aureus isolates obtained from patients hospitalised in 17 medical institutions in different regions of Russia: 4 in Central region (Moscow, Ryazan, Smolensk), 2 in North-Western region (St.-Petersburg), 3 in Southern region (Krasnodar, Stavropol), 2 in Volga region (N. Novgorod, Kazan), 3 in Ural region (Ekaterinburg, Ufa) and 3 in Siberia (Krasnoyarsk, Novosibirsk, Tomsk) were included. Antimicrobial susceptibility testing was performed by agar dilution method in accordance with the NCCLS recommendations (2001).

Results: Against all strains MOX was the most active agent with MIC90 = 0.25 mg/l, compared to 4 mg/l for CIP and 1 mg/l for LEV. The MIC50, MIC90 and MICs ranges are shown in the table. Against ciprofloxacin-susceptible MRSA (N = 199) the following MIC90 were found: 0.5 for CIP, 0.25 for LEV and 0.06 for MOX. Against non-susceptible to CIP MRSA strains (N = 96) MIC90 were: 16 for LEV and 2 for MOX.

Conclusions: According to the above data MOX is more active than CIP and LEV against both MSSA and MRSA strains. However, MOX and LEV have a reduced activity against non-susceptible to CIP MRSA isolates.

<table>
<thead>
<tr>
<th>Antimicrobials</th>
<th>MIC50 (mg/l)</th>
<th>MIC90 (mg/l)</th>
<th>MIC range (mg/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSSA (N = 584)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIP</td>
<td>0.5</td>
<td>1</td>
<td>0.125 – 32</td>
</tr>
<tr>
<td>LEV</td>
<td>0.25</td>
<td>0.5</td>
<td>0.06 – 16</td>
</tr>
<tr>
<td>MOX</td>
<td>0.06</td>
<td>0.125</td>
<td>0.015 – 4</td>
</tr>
<tr>
<td>MRSA (N = 295)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIP</td>
<td>0.5</td>
<td>32</td>
<td>0.125 – 64</td>
</tr>
<tr>
<td>LEV</td>
<td>0.25</td>
<td>8</td>
<td>0.125 – 16</td>
</tr>
<tr>
<td>MOX</td>
<td>0.06</td>
<td>2</td>
<td>0.015 – 8</td>
</tr>
</tbody>
</table>

Fluoroquinolones resistance and topoisomerases mutations in Stenotrophomonas maltophilia  

PS103

Trigo-Daporta M, Alonso-Manzanares MA, Munoz Criado S, Munoz-Bellido JL, Garcia-Rodriguez JA. 1Department of Microbiology, Hospital Universitario de Salamanca, Salamanca, Spain, 2Department of Microbiology, Hospital Virgen de la Concha, Zamora, Spain

Purpose: Stenotrophomonas maltophilia prevalence is growing, mainly in some hospital areas. S. maltophilia is frequently multi-drug resistant. Fluoroquinolone (FQ) resistance varies from one to another study, but in whole resistance is moderate to high. GyrA and parC QRDR partial codes have been recently described. We have studied correlations between FQ-resistance and mutations in these sequences in S. maltophilia clinical strains.

Material and methods: gyrA and parC QRDR regions from six FQ-resistant and two FQ-susceptible S. maltophilia clinical strains were amplified and sequenced. MICs of ciprofloxacin (CFX), gatifloxacin (GFX) and clinafloxacin (CNFX) were determined by the agar dilution method, according guidelines defined by NCCLS for P. aeruginosa.

Results and conclusions: MICs ranges of CFX, GFX and CNFX for resistant strains were 8 – 32, 1 – 32 and 0.5 – 8 mg/l. Susceptible strains had MICs of CFX, GFX and CNFX of 1, 0.2 and 0.06 – 0.1 mg/l, respectively. Most susceptible and resistant strains had no significant mutations in the fragments sequenced. Only one resistant strain (MIC of CFX 16 mg/l) and one susceptible strain (MIC of CFX 1 mg/l) had a significant gyrA mutation, the same in both strains (Ile112→Val). Thus, FQ resistance in S. maltophilia shall derive from changes in other areas in the topoisomerases or probably from other mechanisms of resistance, such as efflux pumps.

Fluoroquinolone resistance in genetically characterized Corynebacterium urealyticum clinical strains  

PS104

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Purpose: Corynebacterium urealyticum is the cause of encrusted cystitis and other insecpecific UTIs and systemic infections. It is frequently multi-drug resistant, with a high rate of resistance to fluoroquinolones (FQ). The mechanisms of resistance to FQs have not been described in C. urealyticum. We describe the C. urealyticum parC gene QRDR region and its relationship with quinolone resistance.

Materials and methods: The activity of ciprofloxacin (CFX), levofloxacin (LFX), gatifloxacin (GFX), clinafloxacin (CNFX) and moxifloxacin (MFX) against 30 C. urealyticum clinical strains was determined following NCCLS guidelines for enterococci. We amplified and sequenced their parC QRDR by standard methods.

Results and conclusions: Five strains (16.6%) were CFX-susceptible (MIC 0.1 – 0.5 mg/l), 5 had MICs 1 – 2 mg/l and 20 (66.7%) were high-level CFX-resistant (MIC 32 – 128 mg/l). CNFX was 64-fold more active than CFX. MFX and GFX had MICs of 4 and 8 mg/l. All the strains, including the type strain, showed a C to T change at the 2614 position referred to wild type S. aureus parC gene, leading to a Ser-80-Phe change, described as the main parC change in FQ-resistant S. aureus. This finding suggest that this mutan sequence, as compared with parC sequences from other Gramapositives, might be the wild-type for this species, and might explain in part its high resistance rate, and its apparent lightness to development of high-level resistance.

Ciprofloxacin-resistant Streptococcus pneumoniae isolated by Birmingham Public Health Laboratory between 1997 and 2001  

PS105

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Purpose: During routine surveillance, we identified 32 ciprofloxacin-resistant (MIC > 8 mg/l) pneumococcal isolates and compared clinical details and resistance patterns.

Results: They were isolated from spits (29) and blood cultures (3) from adults, most with heart or lung disease. Hospital admissions were common; half had been inpatients in the previous 3 months. Nineteen patients received quinolones in the preceding 3 months, in part reflecting the local policy (introduced in 1997) of penicillin and oxacillin for first line treatment of pneumonia. Thirteen patients had radiological signs of pneumonia and 10 were pyrexial with raised
inflammatory markers. Agar dilution MICs for quinolones, including norfloxacin with and without reserpine, penicillin and erythromycin were performed. An increase in norfloxacin MICs was noted over the period 1997 (16–64 mg/l) to 2001 (256 mg/l). Fluoroquinolone efflux was suggested in three isolates. Resistance to moxifloxacin (MIC 8–16 mg/l) was noted from 1998 onwards. All isolates were serotype 9V and resistant to penicillin (MIC > 0.5 mg/l). Thirty-one were resistant to erythromycin (MIC > 1 mg/l).

Conclusion: The 1997 policy of using quinolines may have contributed to the development of quinoline resistance and this cluster of isolates. The increasing levels of quinoline resistance observed raise concerns about the future use of newer quinolones for the treatment of respiratory infections.

Susceptibility of 78 strains of *S. maltophilia* to quinolones: comparison of results at 18, 24 and 48 h. of incubation time with different methods, temperatures and atmospheres  PS106

Sevillano D, Fuentes F, Valero E, Amores R, Garcia R, Prieto J, Department of Microbiology, Universidad Complutense, School of Medicine, Madrid, Spain

*S. maltophilia* has emerged in the last years as an important nosocomial pathogen, inherently resistant to most of the antimicrobial agents. New quinolones has been proposed as a treatment of choice because their enhanced activity, but several parameters (T*, atmosphere, method) can affect the results of MICs.

Methods: We have performed MICs using two different methods (agar dilution and microdilution) and different conditions: 35 and 30 °C of temperature; atmosphere of O2 and CO2 and incubation times of 18, 24 and 48 h. A total of 78 strains were assayed with nine quinolones following standard NCCLS. Comparisons were made between results with 18–24 and 24–48 h using the z2-test (z = 0.05).

Results: No differences were found between 18–24 and 24–48 h results with agar dilution, except with 3 ATBs in the case of MICs at 30 °C CO2. On the contrary, almost all the ATBs showed significant differences in the results of 24 and 48 h using microdilution method, at any condition of T or atmosphere.

Comparison of MICs (P values, significance level = 95%) with incubation times of 24 and 48 h at different procedure conditions.

<table>
<thead>
<tr>
<th>ATB</th>
<th>Agar Microdilution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>35 °C</td>
</tr>
<tr>
<td></td>
<td>O2</td>
</tr>
<tr>
<td>Orlo</td>
<td>0.2957</td>
</tr>
<tr>
<td>Norf</td>
<td>0.8386</td>
</tr>
<tr>
<td>Cipro</td>
<td>0.8456</td>
</tr>
<tr>
<td>Oflo</td>
<td>0.2076</td>
</tr>
<tr>
<td>Levo</td>
<td>0.7224</td>
</tr>
<tr>
<td>Mozl</td>
<td>0.3957</td>
</tr>
<tr>
<td>Reva</td>
<td>0.8536</td>
</tr>
<tr>
<td>Torna</td>
<td>0.1097</td>
</tr>
<tr>
<td>Clina</td>
<td>0.6901</td>
</tr>
</tbody>
</table>

Conclusions: The incubation time is a parameter that seems to affect significantly the results of MICs of quinolones when microdilution method is used, whereas only few differences can be encountered with the agar dilution method.

Comparative activity of quinolones against the *Burkholderia cepacia* complex  PS107

Mihaylova SAM, Georgieva-Sredkova MGS, Higher Medical Institute, Microbiology, Pleven, Bulgaria

Objective: To compare the in vitro activity of five quinolones against 135 *B. cepacia* complex isolates.

Materials and methods: A total of 135 *B. cepacia* complex isolates from 115 patients were tested. They were collected from a variety of clinical and environmental sources between 1996 and 2001. MICs of nalidixic acid (NAL), cinoxacin (CIN), norfloxacin (NOR), pefloxacin (PEF), and ciprofloxacin (CIP) were determined by the agar dilution method according to NCCLS guidelines.

Results: MIC90s for CIP, PEF, NOR, NAL, and CIN were 1, 4, 8, 16, and 64 mg/l, respectively. MIC50s were equal to (for CIP, NOR, and NAL) or one dilution lower than the MIC90s (for PEF and CIN). Results are shown below:

<table>
<thead>
<tr>
<th>Quinolones</th>
<th>MIC (mg/l)</th>
<th>Number of isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>50%</td>
</tr>
<tr>
<td>NAL</td>
<td>16 16 16</td>
<td>135</td>
</tr>
<tr>
<td>CIN</td>
<td>32 64 64 0</td>
<td>86</td>
</tr>
<tr>
<td>NOR</td>
<td>4 8 8 19</td>
<td>116</td>
</tr>
<tr>
<td>PEF</td>
<td>2 4 4 4 *</td>
<td>*</td>
</tr>
<tr>
<td>CIP</td>
<td>0.5–1 1 1 135</td>
<td>0</td>
</tr>
</tbody>
</table>

*No available data for susceptible, intermediate, and resistant.

Conclusions: CIP is the most active agent against the *B. cepacia* complex followed by PEF. NAL and NOR have lower activity. CIN exhibits the lowest in vitro activity against this organism.

Comparative antibacterial activity of five fluoroquinolones against Romanian *Streptococcus pneumoniae* strains involved in respiratory infections  PS108

Pana M, Ghita M, Dorobat O, Papageorghe R, Popescu NJ, Ungureanu V, Andrei M, Andries D, Blana D, Iacob S, Cantacuzino Institute, National Reference Center for Streptococcus, Bucharest, Romania, *Victor Babes* Hospital, Clinical Laboratory, Bucharest, Romania, *Coltea Hospital*, Clinical Laboratory, Bucharest, Romania, *Emergency Hospital*, Clinical Laboratory, Bucharest, Romania, Cantacuzino Hospital, Clinical Laboratory, Bucharest, Romania, Maria Sklodowska-Curie, Clinical Laboratory, Bucharest, Romania, Matei Bals Institute, Infectious diseases, Bucharest, Romania

The purpose of the study was to analyse the antimicrobial activity of five fluoroquinolones (FQ) against pneumococci resistant to penicillin, erythromycin and trimethoprim/sulfamethoxazole.

Methods: Two hundred and twenty-nine clinical samples of *S. pneumoniae* coming from blood (N = 55), sputum (N = 97), tracheal aspirate (N = 54), and sinus (N = 23) were recovered from adult hospitalized patients with community-acquired pneumonia, acute exacerbation of chronic bronchitis and acute sinusitis, from February 1999 to November 2000. The isolates were analysed for susceptibility (MICs) to penicillin (PC), erythromycin (EM) and trimethoprim/sulfamethoxazole (SXT) by agar standard dilution MIC testing and to five fluoroquinolones–ciprofloxacin (CIP), levo-
Gatifloxacin (LVX), ofloxacin (OFX), trovafloxacin (TVX) and grepafloxacin (GRX) by E-test according to the manufacturers specifications.

Results: Breakpoints were used as proposed by NCCLS 1999. During the study period the pneumococci resistance was noted as follows: 65% to PC, 39% to EM and 73% to SXT. The rank order of activity of the five FQs against multi-drug resistant pneumococci was: CIP (MIC 90.2 mg/l), OFX (MIC 90.2 mg/l), LVX (MIC 90.1 mg/l), GRX (MIC 90.0.25 mg/l), TVX (MIC 90.025 mg/l).

Conclusions: In Romania, fluoroquinolones represent alternative treatment to beta-lactams and macrolides for first-line empirical treatment for respiratory tract infections caused by pneumococci but, continued vigilance for emerging resistance to FQs is further indicated.

Activity of six quinolones against clinical isolates of Streptococcus pneumoniae with reduced susceptibility to ciprofloxacin in Spain PS109

García-Rodríguez JA, Cercenado E, Perea E, García-Rey C, Aguilar L, García-de-Lomas J, and the Spanish Surveillance Group for Respiratory Pathogens1. Microbiology Department, Hospital Clínico Universitario, Salamanca, Spain; 2 Microbiology Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain; 3Microbiology Department, Hospital Virgen de la Macarena, Sevilla, Spain; 4GlaxoSmithKline, Medical Department, Tres Cantos, Madrid, Spain; 5Instituto Valenciano de Microbiología, Valencia, Spain, 6Spain

Introduction and Material/methods: Susceptibility testing (semiautomated broth microdilution method, Sensititre, Trek Diagnostics, USA, following NCCLS recommendations) was performed with six different quinolones to 817 Streptococcus pneumoniae isolates with a ciprofloxacin-CIP—MIC ≥ 2 mg/l collected in two consecutive SAUCE† surveillances in Spain (1996–97/1998–99). NCCLS resistance (R) breakpoints were used (≥ 8 for ofloxacin-OFL and levofloxacin-LEV; ≥ 2 for sparflaxin-SPA; ≥ 4 for gatifloxacin-GAT—and moxifloxacin-MOX), but for gatifloxacin-GEM—where ≥ 1 was used. Results were as follows.

CIP MIC (n)  MIC90/ %R

<table>
<thead>
<tr>
<th></th>
<th>OLF</th>
<th>LEV</th>
<th>SPA</th>
<th>GAT</th>
<th>MOX</th>
<th>GEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 2 (817)</td>
<td>4/5.3</td>
<td>2/1.8</td>
<td>0.5/2.1</td>
<td>0.5/1.0</td>
<td>0.50/2.0</td>
<td>0.120</td>
</tr>
<tr>
<td>≥ 4 (179)</td>
<td>16/23</td>
<td>4/8.4</td>
<td>1/9.5</td>
<td>1/4.5</td>
<td>1/1.1</td>
<td>0.250</td>
</tr>
<tr>
<td>≥ 8 (43)</td>
<td>32/55.8</td>
<td>16/32.6</td>
<td>8/37.2</td>
<td>4/18.6</td>
<td>2/4.7</td>
<td>0.250</td>
</tr>
</tbody>
</table>

Conclusions: For CIP-R isolates GEM and MOX were the most active agents. GEM was the only agent not influenced by CIP MIC increase regarding prevalence of R, with 0% resistance for strains with CIP MIC ≥ 8 mg/l.

†SAUCE is an acronym standing for ‘Sensibilidad a los Antimicrobianos Utilizados en la Comunidad en España’ (Susceptibility to the Antimicrobials Commonly Used in the Community in Spain) and is the Spanish word for the willow tree.

In vitro activity of gatifloxacin and seven other antibiotics against respiratory and urinary tract pathogens from the community. First results of the BASIC—study PS110

Grimm H, on behalf of a European Multicenter Study Group, Institute for Med. Microbiology, 88250 Weingarten, Germany

A total of 24 centers in Austria, France, Germany, Italy, Portugal, Spain and Switzerland are involved in the BASIC study (Bacterial Annual Susceptibility Information Collection). The MICs of gatifloxacin (Gati), ciprofloxacin (Cipro), clarithromycin (Clari), benzylpenicillin G (Pen), amoxicillin (Amox), amoxicillin/clavulanic acid (Augm), cefuroxime (Cur) and cefixime (Cix) were determined using the microdilution method. Each center is requested to investigate 30 strains each of the following species: S. pneumoniae (Spn), S. pyogenes (Spy), S. aureus (Sau), E. faecalis (Efa), M. catarrhalis (Mca), H. influenzae (Hin), E. coli (Eco), K. pneumoniae (Kpn), P. mirabilis (Pmi) and P. aeruginosa (Pae).

So far approximately 1400 strains are enrolled. Some important MIC90/percentage resistance were as follows:

<table>
<thead>
<tr>
<th></th>
<th>Gati</th>
<th>Cipro</th>
<th>Clari</th>
<th>Augm</th>
<th>Cur-axetil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spn</td>
<td>106</td>
<td>0.50/0</td>
<td>2/—*</td>
<td>16/19.8</td>
<td>0.030/0</td>
</tr>
<tr>
<td>Hin</td>
<td>129</td>
<td>0.03/0</td>
<td>0.03/0</td>
<td>8/1.6</td>
<td>1/1.6</td>
</tr>
<tr>
<td>Mca</td>
<td>69</td>
<td>0.06/0</td>
<td>0.06/0</td>
<td>0.25/1.4</td>
<td>0.25/0.0</td>
</tr>
<tr>
<td>Eco</td>
<td>157</td>
<td>0.25/1.3</td>
<td>0.13/3.8</td>
<td>&gt;32/—*</td>
<td>&gt;8/—**</td>
</tr>
<tr>
<td>Pmi</td>
<td>109</td>
<td>2/3.72</td>
<td>&gt;0.5/5</td>
<td>&gt;32/—*</td>
<td>&gt;8/—**</td>
</tr>
<tr>
<td>Pae</td>
<td>122</td>
<td>8/13.9</td>
<td>&gt;2/9.0</td>
<td>&gt;32/—*</td>
<td>&gt;8/—*</td>
</tr>
</tbody>
</table>

* NCCLS breakpoints not available; ** breakpoints out of MIC range tested.

From the oral antibiotics tested gatifloxacin has the highest activity and broadest spectrum against all relevant respiratory and urinary tract pathogens. Gatifloxacin is a promising alternative for therapy of respiratory tract bacterial infections.

In vitro activity of gatifloxacin against Bordetella pertussis in comparison with erythromycin, ciprofloxacin and levofloxacin PS111

Bourgeois N, Pangon B, Gnassia JC, Doucet-Populaire F, de Versailles CH. Microbiologie, Le Chesnay, France

Purpose of the study: Bordetella pertussis infections are far more common in adults and adolescents than is generally estimated. However, they are often not recognised. Infected or colonised adults can act as a reservoir of infection, passing it to children. Fluoroquinolones are currently recommended for the treatment of respiratory tract infection in adult patients, which is usually empirical. Gatifloxacin is a novel 8-methoxyquinolone, with a potent activity against both Gram-negative and -positive bacteria. The in vitro activity of gatifloxacin was compared with those of erythromycin, the drug of choice for both treatment and prophylaxis of pertussis, ciprofloxacin and levofloxacin, against 52 clinical isolates strains of B. pertussis including 12 erythromycin resistant strains.

Results: We used the agar dilution method on Mueller–Hinton medium supplemented with 10% horse blood to determine the MIC of each antibiotic. Gatifloxacin (MIC90, 0.125mg/l) was as active as ciprofloxacin and levofloxacin (MIC90, 0.06mg/l) against both sensitive erythromycin (MIC90, 0.015 mg/l) and resistant erythromycin (MIC90, > 512 mg/l) strains.

Conclusion: Gatifloxacin may be an effective drug in the treatment or prophylaxis of adults with suspected or confirmed pertussis.

Ex vivo serum activity (killing rates) after gemifloxacin 320 mg versus trovafloxacin 200 mg single doses against ciprofloxacin-susceptible and -resistant Streptococcus pneumoniae PS112

Serum bactericidal activity was measured ex vivo after single dose administration of gemifloxacin (GEM) 320 mg and trovafloxacin (TRO) 200 mg to 12 healthy volunteers in a randomized, cross-over phase 1 trial. Blood samples were collected 1 h (Cmax) after dosing and serum killing rates were determined against a serotype 3 penicillin (PEN)–ciprofloxacin (CIP) susceptible strain (S3) (MICs of 0.03, 1, 0.015 and 0.06 mg/l for PEN, CIP, GEM and TRO) and a serotype 9 PEN–CIP resistant strain (S9) (MICs of 2, 4, 0.03 and 0.25 mg/l for PEN, CIP, GEM and TRO). Tubes with 1.6 ml of serum sample and 0.4 ml broth (50% Todd–Hewitt + 50% HBSS) were incubated over 3 h at 35\(^\circ\)C. Final inocula was 10\(^2\) cfu/ml. Mean colony counts for samples and controls (K) are shown in the figure:

GEM exhibited higher colony counting decrease of the initial inocula, versus TRO, for both strains. After 3 h incubation, the initial inocula decrease obtained with TRO and the CIP susceptible strain was similar to that obtained with GEM and the resistant strain, showing a lower influence of CIP MIC increase in the ex vivo bactericidal activity of GEM versus TRO.

Urine bactericidal activity after administration of gemifloxacin and trovafloxacin single doses in a phase 1 study  PS113

Garcia-Calvo G\(^b\), Parra A\(^a\), Gimenez MJ\(^b\), Ponte Ca, Aguilar L\(^b\), Soriano F\(^b\), Fundacion Jimenez Diaz, Medical Microbiology, Madrid, Spain, \(^b\)GlaxoSmithKline, Medical, Madrid, Spain

Urine bactericidal activity after o.d. administration of gemifloxacin (GEM) 320 mg and trovafloxacin (TRO) 200 mg, was assessed in six adult males in a cross-over phase 1 trial. Urine killing rates (UKR) of bacterial logarithmic growth were added to 2 ml sample, giving a final inoculum of 107 cfu/ml. Colony counting was performed after 1, 2, 3 and 4 h incubation. Percentages of initial inoculation reduction (IIR) were calculated. Mean urine concentrations measured by bioassay were (mg/l): 28.4, 14.7 and 0.5 for GEM, and 3.6, 3.0 and 0.1 for TRO. Against E. coli, an IIR of 99.9% was obtained after 2 h incubation with all samples except with TRO at 60–72 h. Against S. saprophyticus an IIR of 90% was obtained after 3 h incubation with all samples except with TRO at 60–72 h, where bacterial regrowth was found. The maintenance over 72 h of GEM urine antibacterial activity suggests its efficacy in the treatment of uncomplicated cystitis.

Influence of the decreased susceptibility to ciprofloxacin on gemifloxacin versus levofloxacin efficacy in experimental pneumococcal pneumonia in guinea pigs  PS114

Garcia-Oltmos M\(^a\), Parra A\(^a\), Gimenez MJ\(^b\), Garcia-Calvo G\(^b\), Ponte Ca, Aguilar L\(^b\), Soriano F\(^b\), Fundacion Jimenez Diaz, Medical Microbiology, Madrid, Spain, \(^b\)GlaxoSmithKline, Medical, Madrid, Spain

The efficacy of ciprofloxacin (CIP), levofloxacin (LEV) and gemifloxacin (GEM) in the treatment of pneumococcal pneumonia was assessed in a guinea pig model using three strains (S) with MICs (mg/l) of 2, 2 and 0.03 (S1), 32, 4 and 0.25 (S2) and 64, 32 and 1 (S3) for CIP, LEV and GEM, respectively. Intraperitoneal treatments started 1 h after S. pneumoniae intratracheal inoculation, and continued t.i.d up to four doses. Ten animals were included in each group. Doses (mg/kg) used were 20, 16 and 6 for CIP, LEV and GEM, respectively, in order to mimic AU0-C4 by H and Cmax obtained in humans after standard doses. Animals that survived 48 h after inoculation were sacrificed and colony counts were performed in lungs (Table: mean log10 cfu/g).

<table>
<thead>
<tr>
<th>Group</th>
<th>Strain</th>
<th>Strain</th>
<th>Strain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>7.65</td>
<td>6.61</td>
<td>6.76</td>
</tr>
<tr>
<td>CIP</td>
<td>3.40*</td>
<td>6.29</td>
<td>6.98</td>
</tr>
<tr>
<td>LEV</td>
<td>2.29*</td>
<td>3.94*</td>
<td>6.37</td>
</tr>
<tr>
<td>GEM</td>
<td>1.38*</td>
<td>3.56*</td>
<td>4.25*</td>
</tr>
</tbody>
</table>

\(\* P \leq 0.05 \) versus placebo. All treatments against S1 and LEV and GEM against S2 produced \(\geq 99.9\%\) reductions in cfu/g versus placebo while GEM against S3 obtained a 99.69\% reduction in spite of administering only four shots. Further studies with this model and strains with high CIP MIC are needed to evaluate GEM capability in overcoming CIP resistance in S. pneumoniae.

Pharmacokinetic–pharmacodynamic relationships of levofloxacin 500 mg bid in patients with ventilator-associated pneumonia  PS115

Pea F\(^a\), Di Qual E\(^b\), Cusenza A\(^b\), Brollo L\(^a\), Baldassarre M\(^b\), Furlanut M\(^b\),  
Institute of Clinical Pharmacology and Toxicology, DPMSC, University of Udine, Udine, Italy, \(^b\)1st Department of Anaesthesia, SM Misericordia Hospital, Udine, Italy

The purpose of the study Levofloxacin (LFX) is a fluoroquinolone whose activity against both Gram-negative bacilli and Gram-positive cocci enables its use in monotherapy for the treatment of nosocomial pneumonia. Our aim was to study the pharmacokinetic–pharmacodynamic appropriateness of LFX 500mg iv bid in the treatment of six inpatients with ventilator-associated pneumonia (VAP) (45±25 years; 4M-2F; 74±9 kg). Blood and urine samples were collected in steady-state conditions at appropriate intervals. LFX concentrations were analysed by HPLC. The aetiological agent was identified in all the cases and its in vitro sensitivity to LFX was always assessed. The results obtained mean values (±SD) of the major pharmacokinetic parameters were: Cmax, 8.78±2.05 μg/ml; Vdss, 1.25±0.36 l/kg; t1/2β, 4.69±0.87 h; Cl, 3.65±1.01 ml/min/kg; AUCO-t, 32.47±12.80 μg/ml h. Cumulative urinary excretion was 82.89±10.23%, confirming that LFX clearance is mainly renal. Clinical cure and microbiological eradication were obtained in all the patients after a 7–13 day therapy.
A suprainfection due to *Acinetobacter anitratus* insensitive to LFX occurred in 1 case. The major pharmacodynamic parameters of fluoroquinolone efficacy were significantly higher than the proposed threshold \((\text{Cmax/MIC} > 10; \text{AUC/MIC} > 125)\) in all the cases. The conclusion reached The findings suggest that LFX 500 mg bid iv may be considered effective in the treatment of VAP caused by sensitive bacteria.

**Comparative pharmacokinetics of levofloxacin in patients with lower respiratory tract infections (LRTI) being treated with sequential therapy** PS116

Pea F\(^{a}\), Brollo L\(^{a}\), Lugati E\(^{b}\), Di Qual E\(^{a}\), Dolcet F\(^{b}\), Talmassons G\(^{b}\), Furlanet M\(^{b}\), \(^{a}\)Institute of Clinical Pharmacology and Toxicology, DPMSC, University of Udine, Udine, Italy, \(^{b}\)Division of Pneumology, SM Misericordia Hospital, Udine, Italy

The purpose of the study Levofloxacin (LFX) is a fluoroquinolone whose activity against both Gram-negative bacilli and Gram-positive cocci enables its use in monotherapy for the treatment of LRTI. Our aim was to study the pharmacokinetic–pharmacodynamic appropriateness of a standard switch LFX iv/os regimen (500 mg iv od for 5–7 days followed by 500 mg os od for 4–10 days) in the treatment of seven inpatients with LRTI (70 ± 17 years; 6M–1F; 76 ± 15 kg). Blood samples were collected in steady-state conditions at appropriate intervals. LFX plasma concentrations were analysed by HPLC. The aetiological agent was identified in 27 cases and its in vitro sensitivity to LFX was assessed. The results obtained Absolute oral bioavailability was 1.07±0.19, with a Cmax of 10.89 ± 3.39 vs 8.36±3.90 µg/ml after iv and oral administration, respectively. No significant difference in the main pharmacokinetic parameters was observed between the two routes. The major pharmacodynamic parameters of fluoroquinolone efficacy were significantly higher than the proposed threshold \((\text{Cmax/MIC} > 10; \text{AUC/MIC} > 125)\) in the two assessable cases. All the patients were clinically cured after a 9–15 day therapy. The conclusion reached The ad interim findings show that LFX 500 mg od may guarantee per os an exposure similar to that achieved after iv administration, suggesting that sequential therapy may be considered effective in the treatment of LRTI.

**Levofloxacin in the exacerbations of copd due to Pseudomonas ae PS117**

Micheletto C, Tognella S, Pomari C, Dal Negro R, Ospedale Orlandi, Div. Pneumologia, Bussolengo, Italy

Development of antibiotic resistance in bacteria is a problem of great concern. Gram-negative bacteria, including multirug-resistant (MDR) *Pseudomonas aeruginosa* (Ps), are responsible for a significant proportion of episodes of COPD exacerbations, particularly in elderly (1). Aim was to check the susceptibility to common antimicrobial treatments against Ps strains isolated from bronchial secretions in patients with severe exacerbations of COPD.

**Methods:** Microbial investigations were conducted on 290 specimens: spontaneous purulent sputum (88.4%), and tracheobronchial aspirates (11.6%, collected with a protected specimen brush).

**Results:** Fifty-seven Ps pathogen strains (106 CFU) were identified (19.6%) and tested over a 6-month period: Ps. aeruginosa 91.2%; Ps. Putida 3.5%; Ps. fluorescens 3.5%, and Burkholderia cepacia 1.8%. The assessed susceptibility to most common antibiotics was: levofloxacin (90%), ciprofloxacin (84%), ipenem cil. (88%), ceftazidime (84%); amikacin (84%), and Piperacillin + tazobactam (74%). A much lower susceptibility was found for ticarcillin–clavulanic acid (58%), gentamicin (48%), and netilmicin (40%).

**Conclusion:** (1) At present, Levofloxacin proves the most effective antimicrobial option for treating COPD exacerbations due to Ps infection; (2) a much more efficient policy of antibiotic prescribing should be promoted in order to prevent the selection of resistant strains in these cases. Ref. (1) Infect Med., 1999; 16: 54–60.

**‘In vitro’ activity of levofloxacin against nosocomial Gram-negative pathogens PS118**

Santini L, Cianflone M, LanzaFame A, Mattina R, University of Milan, Institute of microbiology, Milan, Italy

**Aim:** to evaluate the ‘in vitro’ activity of levofloxacin in comparison with some β-lactams, meropenem, ciprofloxacin and netilmicin against 600 Gram-negative nosocomial rods, isolated during the year 2000, MICs, MBCs, and Killing curves, were determined by the broth microdilution method according to the NCCLS procedures. We also evaluated the MBC e Killing curves of levofloxacin and ciprofloxacin against 73 ESBL producing strains. Susceptibility results are showed in Fig. 1:

<table>
<thead>
<tr>
<th></th>
<th>Levo (%)</th>
<th>Cip (%)</th>
<th>Caz (%)</th>
<th>Cre (%)</th>
<th>Net (%)</th>
<th>Mero (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P. mirabilis</td>
<td>85.2</td>
<td>77.8</td>
<td>100</td>
<td>96.3</td>
<td>79.6</td>
<td>100</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>74.6</td>
<td>74.6</td>
<td>73.2</td>
<td>5.3</td>
<td>82.1</td>
<td>85.7</td>
</tr>
<tr>
<td>M. morganii</td>
<td>91.2</td>
<td>88.9</td>
<td>77.8</td>
<td>87.5</td>
<td>86.1</td>
<td>100</td>
</tr>
<tr>
<td>S. marcescens</td>
<td>94.7</td>
<td>92.1</td>
<td>73.7</td>
<td>65.8</td>
<td>63.2</td>
<td>100</td>
</tr>
<tr>
<td>C. freundii</td>
<td>97.7</td>
<td>97.7</td>
<td>72.7</td>
<td>72.7</td>
<td>88.6</td>
<td>100</td>
</tr>
<tr>
<td>E. coli</td>
<td>83.6</td>
<td>81.8</td>
<td>76.4</td>
<td>81.8</td>
<td>85.5</td>
<td>100</td>
</tr>
<tr>
<td>E. cloacae</td>
<td>88.5</td>
<td>85.5</td>
<td>59.6</td>
<td>57.7</td>
<td>92.4</td>
<td>98</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>91.7</td>
<td>86.1</td>
<td>55.6</td>
<td>63.8</td>
<td>77.8</td>
<td>100</td>
</tr>
<tr>
<td>S. maltophilia</td>
<td>90.6</td>
<td>31.3</td>
<td>53.1</td>
<td>0</td>
<td>20.3</td>
<td>23.4</td>
</tr>
</tbody>
</table>

These results confirm the excellent ‘in vitro’ activity of levofloxacin against nosocomial Gram-negative pathogens, including the ESBL producing strains (90% of *Escherichia coli*, *E. cloacae* and *K. pneumoniae* were inhibited at 0.5 mg/l). Levofloxacin was more rapid than ciprofloxacin to determine a bactericidal effect particularly against *S. maltophilia*. Moreover, considering the favourable PK/PD profile, levofloxacin can represent a valid therapeutic option for the treatment of severe Gram-negative nosocomial infections.

**Efficacy of levofloxacin and rifampicin for Rhodococcus equi treatment in HIV patient PS119**

Moretti F, Quiros-Roldan E, Casari S, Chiodera A, Viale P, Carosi G, University of Brescia, Institute of Infectious and Tropical Diseases, Brescia, Italy

A 34-year-old man, IVDU, HIV positive was admitted in our hospital for fever and toracic pain. A X-chest radiography revealed a round lesion of 5 cm near the lingula with central hyper-diaphan area. Lymphocytes CD4+ count was 21 cells/mm\(^3\) and viral load 91,900 cp/ml. Hospital stay *Rhodococcus equi* was found in cultures of peripheral blood, faecal and sputum specimens. Antibiotic treatment with oral rifampin (600 mg/QD) and with intravenous imipen (500 mg tid) was started. Due to the persisting fever, immediated radiography and negativety for *P. carini*, Mycobacteria and bacteria in BAL cultures, imipenem was substituted by parenteral vancomycin (400 mg bid). After 10 days, because of persisting fever and increase of the diameter of the lung lesion (6 cm) vancomycin was sustituted by oral levofloxacyn (500 mg bid), continuing rifampin. After a 4 days course of levofloxacin therapy the fever remitted. The patient was discharged with levofloxacin (500 mg bid) and rifampin and, after 2 months of...
follow-up, a radiological control pointed out a remarkable resolution in the lung lesion. We may suppose that levofloxacin can be effective for the treatment of *R. equi* infection, even if more studies (particularly controlled studies) are necessary.

**Treatment with levofloxacin in adult patients with enteric fever**  PS120


II Department, Naples, D. Cotugno Hospital, Italy; III Department, Naples, D. Cotugno Hospital, Italy

The increasing prevalence of *Salmonella typhi* strains with reduced susceptibility of chloramphenicol had prompted the search for other antibiotics with the same efficacy. Quinolones are a class of antibiotic with an activity in vitro and in vivo against enteropathogens. We investigated the use of Levofoxacin in two regimens of treatment of typhoid and paratyphoid infection.

**Patients and methods:** Thirty-two adult patients were included in this study from September 1999 to April 2001; 26 patients had positive culture for *S. typhi* and six had positive cultures for *S. paratyphi*. All isolated were fully susceptible to Levofoxacin. We compared treatment with Levofoxacin for 7 days, 500 mg b.i.d. (group 1, 16 patients), with treatment for 10 days, 500 mg b.i.d. (group 2, 16 patients). Clinical cure was defined as defervescence of fever by day 3 of treatment, with an absence of complications and no clinical relapse during the follow-up.

**Results and conclusion:** The clinical cure rate was 87% (14 patients) for group 1 and 94% (15 patients) for group 2; the difference in these rates was not statistically significant. The blood cultures of all patients were sterile by day 2 of treatment and remained so until the 6th month of follow-up, no subjects had clinical or microbiological relapse and all stool cultures remained negative, also.

The two regimens of treatment was good tolerated and no adverse event was registered; it was concluded that Levofoxacin treatment for 10 days in enteric fever is not necessary the muldrug-resistance of *S. typhi* led to the use of Quinolones as the first-line drug in the treatment of enteric fever.

**Pefloxacin in the treatment of patient with acute infectious diarrhoea**  PS121

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The purpose of the study was to investigate clinical and bacteriological efficiency in 5 and 7 days pefloxacin treatment and to compare it with symptomatic therapy.

The results obtained in 47 patients treated with pefloxacin the therapy was clinically effective already in the third day while in the control group this happened in the 7th day. Bacteriological eradication was noted in 18 patients (95%) of the first and 25 patients (93%) of second group in the 5th days of the treatment. They all had negative cultures 1 and 4 weeks after pefloxacin protocols were completed. Only 22 patients (63%) in control group had negative stool cultures in the 7th day of the treatment and all of them 4 weeks after it ended. There was no statistically significant difference in clinical (P = 0.232) and bacteriological (P = 0.972) efficiency between 5 and 7 days pefloxacin treatment protocols. Both protocols significantly differed in clinical (P < 0.001) and bacteriological (P = 0.017) eradication from the control group.

The conclusion reached is that the efficiency of pefloxacin (quinolones) in the treatment of acute infectious diarrhoea and justifies their use in the more severe forms of the disease.

**Antibacterial activity of moxifloxacin and four comparators in an in vitro model simulating lung and serum drug concentrations**  PS122

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**Background:** The antibacterial activity of moxifloxacin (MXF) was compared to levofloxacin (LEV), amoxicillin (AMX), clarithromycin (CLA) and erythromycin (ERY) in an in vitro model.

**Method:** Pharmacokinetics in bronchial mucosa (BM) and serum (S) following single oral doses of 400 mg MXF or CLA and 500 mg LEV, AMX or ERY were simulated using a one compartment model. Bacteria tested Staphylococcus aureus (Nos. 133, 25895), *Streptococcus pneumoniae* (Nos. 4241, 672). Aliquots were taken (0–8 h) and plated on to Brain Heart Infusion agar for enumeration.

**Results:** *S. pneumoniae* 4241 was eliminated by all agents studied. Significant differences were apparent with *S. pneumoniae* 672 and the *S. aureus* strains.

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<th>Antibiotic</th>
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*nK* = no. 99.9% kill.

**Conclusions:** Although quinolones and macrolides are concentrated in BM, higher focal concentrations of MXF only translated into increased bactericidal activity. MXF eliminated all four test strains most rapidly from the in vitro model.

**Efficacy and safety of oral moxifloxacin vs. intravenous ceftriaxone in the treatment of community—acquired pneumonia (CAP) in patients with HIV infection**  PS123

Mastroianni A, G.B. Morgagni General Hospital, Division of Infectious Diseases, Forlì, Italy

**Objective:** To compare the safety and efficacy of once-daily moxifloxacin with once-daily ceftriaxone in the treatment of CAP in HIV-infected patients (pts).

**Methods and Results:** In a retrospective survey, oral moxifloxacin (400 mg daily × 12–15 days) was compared to standard regimen of i.v. ceftriaxone (2 g daily × 10–12 days) for treatment of CAP in HIV-pts. Adults pts with clinical signs and symptoms of CAP and consistent chest X-ray findings were included. Pts had a median age of 39 years (range 29–529 and 70% were male). Demographic characteristics were similar in both treatment groups; 15 pts received moxifloxacin and 25 pts ceftriaxone. Clinical success rates were 94% for moxifloxacin and 96% for ceftriaxone. At a post-study evaluation approximately 8 weeks later, 2 moxifloxacin-treated pts and 3 ceftriaxone-treated pts had relapsed. The adverse events reported were comparable for both
Abstracts

S31
treatment groups. There were four-related adverse events (3 GI, 1 headache) for moxifloxacin-treated and 7 (4GI, 3 skin) for ceftriaxone-treated pts.

Conclusion: The results of this study show that moxifloxacin as oral therapy is as effective and well tolerated as i.v. ceftriaxone in the treatment of HIV+ pts with CAP. Therapy with moxifloxacin was not associated with any significant clinical or laboratory abnormalities. These data suggest that once-daily oral administration of moxifloxacin is potentially convenient and cost-effective alternative therapy for CAP in pts with HIV infection.

Moxifloxacin in the treatment of acute maxillary sinusitis after first-line therapy failure or acute sinusitis with high risk of complications PS124

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The efficacy and safety of moxifloxacin (MXF) 400 mg once daily for 7 days was evaluated in the treatment of acute maxillary sinusitis after first-line therapy failure or acute sinusitis with high risk of complications. In this prospective, multicenter study, a total of 216 patients with acute bacterial sinusitis confirmed by sinus X-ray were valid for efficacy analysis: one hundred and seventy five patients (81.0%) had an acute maxillary sinusitis which failed to respond to a previous antibiotic therapy given for a mean duration of 7.2 days, and 41 (19.0%) had an acute sinusitis with high risk of complications (frontal: 24, pan-sinusitis: 15 and sphenoid: 2). Ninety two patients (42.6%) were microbiologically valid. Clinical cure and continued clinical cure rates at 7–10 and 28–35 days post-therapy were 92.6 and 99.0%, respectively. Clinical cure rates at 7–10 days post-therapy were 94.9 and 82.9% in sinusitis after first-line therapy failure and in sinusitis with high risk of complications, respectively. Bacteriological eradication rate during therapy (Day 3–4) was 95.7%. At 7–10 days post-therapy, Bacteriological success rates were 97.1% in patients who failed to respond to a previous antibiotic and 95.4% of patients who had sinusitis with high risk of complications. 12.2% of patients experienced drug-related adverse events, abdominal pain (2.4%), nausea (2.4%) being the most frequently reported events. MXF was rapidly effective and a well-tolerated treatment for this kind of infection.

Neisseria gonorrhoeae with decreased susceptibility to penicillin and ciprofloxacin: novel mutation patterns in the gyrA and parC genes of ciprofloxacin resistant isolates and plasmid profile of penicillin resistant isolates of N. gonorrhoeae in India (Delhi) PS125

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Commercial sex workers (CSWs) serve as the most important reservoir of gonorrhoea. Periodic monitoring of the antimicrobial susceptibility profile of Neisseria gonorrhoeae in a high-risk population provides essential clues regarding the rapidly changing pattern of antimicrobial susceptibilities. In India, such a surveillance of the in vitro antimicrobial susceptibility of N. gonorrhoeae was established in 1997. Significant increasing trend of penicillin and ciprofloxacin resistance with high MIC of 2–16 and 1–32 μg/ml, respectively were found over the years (1997–2001). The molecular basis of ciprofloxacin resistance, i.e. mutations in the gyrA and the parC genes of 170 isolates, were analyzed. Four isolates (with an MIC of 32 μg/ml for ciprofloxacin) harbored triple mutations (Ser-91 to Phe, Asp-95 to Asn and Val-120 to Leu) in the gyrA gene. The third mutation of Val-120 to Leu, lies downstream of the quinolone resistance determining region of the gyrA and has not been described before in gonococcus. In addition, these isolates had an Phe-100 to Tyr substitution in the parC, a hitherto unknown mutation. The alterations in the parC gene were seen in these isolates only in the presence of changes in the gyrA gene and comprised amino acid changes at codons 91, 100, 104, 109, and 131. The presence of β-lactamase plasmid among the penicillin-resistant isolates was determined by their plasmid profiles and further confirmation was carried out by a PCR based protocol. Our findings suggest that emergence of penicillin and ciprofloxacin resistance in N. gonorrhoeae isolates from a major STD center in India, indicates the need for the increased awareness and prudent use of antimicrobials.

New agents

In vitro activity of newer antibiotics against methicillin-resistant Staphylococcus aureus PS126

Gutierrez Zufiaurre MN, Sanchez Hernandez J, Munoz-Bellido JL, Garcia-Rodriguez JA. Hospital Universitario de Salamanca, Microbiologia, Salamanca, Spain

Purpose: MRSA are frequently co-resistant to a number of structurally unrelated antibiotics. More than 70% MRSA are resistant to gentamicin, ciprofloxacin, macrolides and clindamycin. Newer antibiotics active against multi-drug resistant Gram-positives have been developed. We have tested the in vitro activity of newer antibiotics against genetically-characterized, high level ciprofloxacin resistant MRSA.

Material and methods: Thirty-six ciprofloxacin-resistant, gyrA/parC mutant MRSA clinical strains were tested against levofloxacin (LFX), ciprofloxacin (CFX), moxifloxacin (MFX), gatifloxacin (GFX), erythromycin (ER), telithromycin (TL), linezolid (LIN), synergic (SYN) and vancomycin (VA). MICs were determined by the agar dilution method, according NCCLS guidelines.

Results and conclusions: All the strains were resistant to CFX, 55.5% were LFX-susceptible and 63.9% were GFX-susceptible. Vancomycin was significantly its activity against all the strains. They showed a very homogeneous behaviour against all the strains that were included in a range of 1–4 mg/l of LIN and VA and 0.5–1 mg/l.

In vitro activity of newer antimicrobial agents against multi-drug resistant Corynebacterium urealyticum PS127

Sanchez Hernandez J, Gutierrez Zufiaurre MN, Munoz-Bellido JL, Garcia-Rodriguez JA. Hospital Universitario de Salamanca, Microbiologia, Salamanca, Spain

Purpose: Corynebacterium urealyticum is the etiologic agent of encrusted cystitis and inespecific UTIs, and can be also involved in systemic infections. C. urealyticum is frequently multi-drug resistant, so only glycopeptide antibiotics and tetracyclines have high susceptibility rates, while fluoroquinolones resistance rates vary significantly. We have tested the in vitro activity of linezolid, telithromycin, synergic and newer fluoroquinolones against multi-drug resistant C. urealyticum clinical strains.

Material and methods: Sixty-four C. urealyticum clinical strains were
tested against levofloxacin (LFX), ciprofloxacin (CFX), moxifloxacin (MFX), erythromycin (ER), telithromycin (TL), linezolid (LIN), synergic (SYN) and vancomycin (VA). MICs were determined by the agar dilution method according guidelines defined by the NCCLS for enterococci.

Results and conclusions: Results confirm the high resistance rate to older fluoroquinolones and macrolides, with >50% CFX resistance and 100% ER-resistance. LFX was more active (MIC90 32 mg/ml). MFX was the most active fluoroquinolones (MIC90 4 mg/ml). TL improve its behaviour in respect to ER (range 0.5–1 mg/ml). VA, LIN and SYN had excellent antimicrobial activity. No resistant strains were found. MIC90 were 1, 0.5 and 1 mg/ml, respectively. MICs were similar for all the strains independently of their resistance to other antibiotics

Plasma concentrations, urinary excretion and bactericidal activity of linezolid (600 mg) versus ciprofloxacin (500 mg) in healthy volunteers after a single oral dose

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Purpose of the study: In a randomized cross-over study 12 volunteers received a single oral dose of 600 mg linezolid versus 500 mg ciprofloxacin to assess plasma concentrations (up to 24 h), urinary excretion (by HPLC), and urinary bactericidal titers (UBT) up to 120 h. The mean maximum plasma concentration of linezolid was 12.1 µg/ml and of ciprofloxacin 2.4 µg/ml. The cumulative renal excretion (mean) of parent drug was 40%/41% for linezolid/ciprofloxacin. UBTs were determined for a reference strain and five Gram-positive clinical uropathogens with the following MICs (µg/ml) for linezolid/ciprofloxacin: S. aureus ATCC 27278 (4/0.25), S. aureus (MSSA) (2/32), S. aureus (MRSA) (2/128), S. saprophyticus (MSSE) (2/0.5), E. faecalis (2/1), E. faecium (2/2). Results: Median UBTs measured within the first 6 h for linezolid were 1.96 for enterococcal strains and 1:128 to 1:256 for the four staphylococcal strains. Median UBTs for ciprofloxacin were 1:64 for the two enterococcal strains, 1:384 to 1:512 for the two ciprofloxacin susceptible, 1:1.5 for the two resistant staphylococcal strains. Areas under the UBT–time-curve showed statistically significant differences only for the two ciprofloxacin resistant staphylococcal strains in favour of linezolid. Conclusion: Linezolid exhibited the same bactericidal activity against ciprofloxacin resistant as susceptible strains. Linezolid should be tested for treatment of complicated UTI due to Gram-positive uropathogens in a clinical trial.

The pharmacokinetic profiles of linezolid and teicoplanin in the critically ill

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Purpose: We performed pharmacokinetics within a double-blind, randomised trial comparing linezolid and teicoplanin in intensive care patients with known or suspected Gram-positive infection. They received either 600 mg linezolid intravenously 12-hourly, or 400 mg teicoplanin 12-hourly for the first three doses and once daily thereafter (or every 3rd day if renally impaired). Blood samples were collected to create serum pharmacokinetic profiles. Linezolid was quantitated by HPLC and teicoplanin by fluorescence polarization immunoassay.

Results: Twenty two patients were studied in the linezolid group (M–F 13:9, mean age 54 years [range 19–90 years]). Median treatment duration was 8.5 days (range 4–18). Eighteen patients were treated with teicoplanin (M–F 13:5, mean age 57 years [range 17–86]) for median 9 days (range 4–17). Steady state peak concentrations (mean ± SD) for linezolid and teicoplanin were 12.8 ± 5.0 and 10.5 ± 4.7 mg/l, respectively. Trough concentrations at day 4 were 4.7 ± 4.3 mg/l for linezolid and 7.9 ± 2.5 mg/l for teicoplanin. Recommended breakpoints of Staphylococcus aureus are 4 mg/l for linezolid and 8 mg/l for teicoplanin. Accumulation occurred in 90-year-old linezolid-treated patient with impaired renal function.

Conclusion: Current recommended dosing regimens for linezolid and teicoplanin are generally appropriate in the critically ill, though a more detailed analysis is required.

Laboratory evaluation of streptogramins and oxazolidinones against methicillin-resistant Staphylococcus aureus clinical isolates

Stamos G, Lebessi E, Ioannidou S, Paleologou N, Kallergi K, Foustoukou M1, ‘P. and A. Kyriakou’ Children’s Hospital, Microbiology, Athens, Greece

The purpose of the study was to investigate the susceptibility of methicillin resistant Staphylococcus aureus (MRSA) isolates from a 500-bed Paediatric Hospital to Quinupristin/Dalfopristin (Q/D, streptogramin combination) and Linezolid (LZD, oxazolidinone).

Material: We performed a retrospective analysis of 85 MRSA strains, isolated from patients hospitalized in miscellaneous medical departments [Neonatal Unit (35), Surgical Wards (15), Orthopaedic Wards (9), Oncology Unit (7), other wards (8) and outpatient clinic (11)], during a 3-year period (1998–2000). The sources of isolation were pus (23), throat (22), nasal (8), bronchial (5), skin (6), stool (6) ear (4) and other (11) specimens. All isolates were sensitive to glycocypeticides, while 22.4% were resistant to gentamicin and 7.1% to erythromycin.

Methods: The sensitivity testing was performed by a disk diffusion method (BBL, sensitivity disks, Becton Dickinson), according to NCCLS guidelines. The breakpoint zone diameters for LZD and Q/D were ≥ 21 and ≥ 19 mm for susceptibility and ≤ 17 and ≤ 15 mm for resistance, respectively.

Results: All isolates were proved to be susceptible to both antibiotics. The mean inhibition zones were 29.1 mm for LZD and 26 mm for Q/D.

Conclusions: LZD and Q/D are very promising antimicrobial agents, showing excellent activity against MRSA clinical isolates. The prudent therapeutic use is strongly recommended to avoid the emergence of resistance.

In vitro activity of streptogramins and oxazolidinones against Streptococcus pneumoniae clinical isolates

Stamos G, Lebessi E, Paleologou N, Psatha M, Sanida P, Zaphiropoulou A, Foustoukou M1, ‘P. and A. Kyriakou’ Children’s Hospital, Microbiology, Athens, Greece

The purpose of this study was to evaluate the in vitro activity of Linezolid (LZD), a member of oxazolidinones and the streptogramin combination Quinupristin/Dalfopristin (Q/D) against clinical isolates of Streptococcus pneumoniae from a tertiary care Paediatric Hospital.

Material: A total of 53 pneumococcal isolates exhibiting reduced susceptibility to common antibiotics were included in the study. The strains were isolated from middle ear fluid (34), eye (4), nasal (5) blood (6) and other (4) cultures during the last 4 years. The percentages of the isolates that were resistant to penicillin, erythromycin, cotrimoxazole
and clindamycin were 67.9, 67.9, 67.9 and 26.4%, respectively. 

Methods: The susceptibility testing was performed by a standard disk diffusion method (BBL sensitivity disks, Becton Dickinson). In case of marginal results or intermediate susceptibility to Quinupristin/Dalfopristin, the MIC was determined using the E-test method (AB Biodisk).

Results: All isolates were found to be sensitive to LZD. Q/D was very active as well, except for two isolates that exhibited intermediate susceptibility, showing cross-resistance to macrolides and clindamycin, as well.

Conclusions: The new antimicrobial agents show excellent activity against resistant to common antimicrobials pneumococcal isolates, but the clinical use is not suggested, unless no other therapeutic solutions are available.

In vitro susceptibility of Gram-positive cocci to linezolid and teicoplanin:
use of linezolid for Gram-positive infections in ICU  

PS132

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Linezolid is a new oxazolidinone with excellent activity against Gram-positive organisms including glycopeptide-resistant strains of staphylococci and enterococci. In ICU linezolid has been used for the treatment of severe Gram-positive infections in a control trial. The susceptibility pattern of all Gram-positive isolates from ICU patients has been studied.

Methods: A total of 2427 specimens from ICU patients were processed, 767 were from patients enrolled in the antibiotic trial. All methicillin-resistant Staphylococcus aureus (MRSA), coagulase-negative staphylococci (CoNS), Enterococcus sp and methicillin-sensitive Staphylococcus aureus (MSSA) were tested. The break point for linezolid was 4 mg/l and for teicoplanin 8 mg/l. Isolates were tested for susceptibility by E-test.

Results: Linezolid (1063 isolates) MIC 50/90 (mg/l) were as follows: MRSA (N = 541) 0.62, CoNS (N = 143) 0.9/1.4, Enterococcus sp (N = 39) 0.7/0.8, MSSA (N = 340) 0.8/1. Teicoplanin (782 isolates) MIC 50/90 (mg/l) MRSA (N = 415) 1.9/3.5, CoNS (N = 100) 4/7.4, Enterococcus sp (N = 24) 0.9/1.4, MSSA (N = 243) 2.2/2.6. All Gram-positive isolates were inhibited by concentrations of linezolid below the breakpoint including eight strains of staphylococci resistant to teicoplanin.

Conclusions: Linezolid was highly active against Gram-positive isolates. Resistance to teicoplanin was similar to other reported series. There was no emergence of resistance to linezolid.

Methicillin-resistant Staphylococcus aureus clearance during treatment with Linezolid  

PS133

Cepeda JA a, Whitehouse T b, Singer M b, Bellingan G b, Kibbler C c, Shaw S b, Wilson APR c. aUniversity College London Hospitals, Clinical Microbiology, London, UK  bUniversity College London Hospitals, Intensive Care, London, UK  cRoyal Free Hospital, Medical Microbiology, London, UK  *Royal Free Hospital, Intensive Care, London, UK

MRSA colonization is often a limiting factor for discharge from ICU. Clearance of MRSA is seldom achieved with conventional glycopeptide treatment. The oxazolidinone, linezolid, has excellent soft tissue and respiratory tract penetration and might be expected to eradicate carriage in some patients. We recently performed a double-blind randomized trial in 204 ICU patients with known/suspected Gram positive infection. 100 received intravenous linezolid, 600 mg b.d., and 104 patients received teicoplanin 400 mg o.d. MRSA clearance was assessed at End of Treatment (EOT), at 7- and 21-days follow-up.

Results: In the linezolid and teicoplanin groups, 45 and 43 were known to be colonized with MRSA at study entry, respectively, while 39 and 40 were not. Detection of clearance of MRSA colonization at EOT was 51% for linezolid vs 19% for teicoplanin group (χ² P < 0.005), at 7 days it was 35% vs 14% (χ² P < 0.1), and at 21 days 19% vs 33% (ns).

Conclusion: Short-term MRSA clearance can be achieved in significantly more patients treated with linezolid however this was not maintained at 21 days, either because of incomplete initial eradication or recolonization. Further analysis will follow when molecular typing of the isolates is completed.

Penetration of linezolid into bone, fat and muscle during hip arthroplasty  

PS134

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There are limited data describing the concentrations and penetration of linezolid (LZD) into tissues, such as bone, that can be used to guide therapy for non-vascular infections. Here we report the concentrations and penetration of LZD for bone, fat and muscle in comparison with cefamandole (CMD). Twelve patients received 600 mg LZD as a 20 min infusion and 1000 mg CMD as a bolus injection immediately before hip arthroplasty. Bone, fat, muscle and blood samples were collected at timed intervals after the infusion and assayed by a validated HPLC method. For bone, peak levels of both agents occurred 10 min after administration with mean levels of LZD 9.1 mg/kg versus CMD 17.5 mg/kg, decreasing to LZD 5.7 mg/kg versus CMD 9.7 mg/kg at 30 min. Correction for blood concentrations gave penetration of LZD 51% versus CMD 25% at 10 min and LZD 46% versus CMD 23% at 30 min. For fat and muscle, peak levels occurred 20 min after infusion. Mean levels were LZD 5.2 mg/kg versus CMD 10.9 mg/kg (fat) and LZD 13.4 mg/kg versus CMD 10.9 mg/kg (muscle). Correction for blood concentrations gave penetration of LZD 37% versus CMD 19% (fat) and LZD 95% versus CMD 31% (muscle). We conclude that linezolid exhibits rapid penetration into bone and associated soft tissues achieving levels in excess of the MIC for sensitive organisms; with a similar distribution and penetration profile to agents currently used for treatment of infections in these tissues.

Design, synthesis and in vitro evaluation of XRP2868, a new oral streptogramin  

PS135

Baqué E a, Barrière JC b, Berthaud N b, Desmazeau PB b, Dutruc-Rosset G b, Dutka-Malen S b, Ronan B c. aAventis Pharma, Chemistry, Paris, France  bEntis Pharma, Disease Group, Paris, France

XRP2868 is a new oral streptogramin composed of 2 semi-synthetic synergistic components in a 30/70 (w/w) association: RPR202868 (5β-(1-morpholino)methyl-5,8,9-dehydro pristinamycin Ia) from PIa and RPR132552 [16R]-16-deoxy-16-fluoro pristinamycin Ia] from PIb by original synthetic routes. The association has antibacterial activity against staphylococci including methicillin—MLSB-resistant strains (MIC90 range: 0.12—1 μg/ml), streptococci (MIC90: 0.25 μg/ml), pneumococci including multidrug resistant strains (MIC90: 0.50 μg/ml), enterococci including vancomycin-resistant strains (MIC90: 4 μg/ml), M. catarrhalis and Neisseria spp. (MIC90: 0.12 μg/ml), H. influenzae (MIC90: 1 μg/ml), Legionella spp. (MIC90: 0.06 μg/ml) and anaerobes (MIC range: 0.06—4 μg/ml). XRP2868 is generally
bactericidal at the concentration of 2–4 × the MIC against *S. aureus*, *S. pneumoniae*, *H. influenzae;* it demonstrates consequent PAE (2.1–>5.7 h at 2–4 × MIC, following an exposure of 0.25–2 h). Mutants of *S. aureus* to XRP2868 were isolated at low frequencies (3.6 × 10⁻⁹–9.7 × 10⁻¹⁰) at 2 × and 4 × MIC while no mutant could be isolated at 8 × MIC. These results suggest that XRP2868 (30/70 w/w) is a promising compound for the treatment of community-acquired infections.

**Ex vivo evaluation of RPR202868/RPR132552 (XRP2868), a new oral streptogramin** PS136

Berthaud N, Diallo N. Aventis Pharma SA, Infectious Disease Group, Paris, France

The intra cellular activity of XRP2868, was assessed in J774 murine macrophages containing ingested *Staphylococcus aureus* (three strains) or *L. pneumophila* (one strain). At the concentration of 8 × the MIC, growth of *S. aureus* was strongly inhibited after a 3-h period of incubation (Δ log₁₀ cfu/ml vs T₀ controls range: −2.16–1.24, according to the strain tested). At the concentration of 8 × the MIC, growth of intracellular *L. pneumophila* was inhibited after a 48–72-h period of incubation (Δ log₁₀ cfu/ml vs T₀ controls about −1.30 and −1.48 at 48 and 72 h, respectively). RPR202868 and RPR132552 alone had also inhibiting effect on bacterial growth (Δ log₁₀ cfu/ml vs T₀ controls after 72 h of incubation about −1.54 and −0.87, respectively). The bactericidal activity of XRP2868 was also assessed against slowly growing *S. aureus* under experimental conditions mimicking those observed in patients with an infected indwelling device (first step of infection: adherence to inert support; declared infection: biofilm model). Under the experimental conditions, XRP2868 demonstrated a rapid and potent bactericidal effect against *S. aureus* adherent to an inert support or included in biofilm. This effect was observed at each of the three concentrations tested (5, 10, 50 and 8, 100 and 200 × MIC, respectively).

**In vivo evaluation of XRP2868 (RPR202868/RPR132552), a new oral streptogramin** PS137

Berthaud N, Huet Y, Aventis Pharma SA, Infectious Disease Group, Paris, France

The oral efficacy of XRP2868, was assessed in *Staphylococcus* and pneumococcal murine infections. Mice were challenged ip (× 10, and ×100 times LD₉₀). Abscesses were established by intramuscular injection of about 10⁷ bacteria into the right thigh of mice. Pneumonia was established by intranasal infection of about 10⁷ bacteria. Mice were treated twice a day for 1 (XRP2868 was efficacious in the treatment of experimental infections caused by *S. pneumoniae* (one strain). At the concentration of 8 × MIC, growth of intracellular *S. pneumoniae* (two strains) or 3 days (S. pneumoniae pneumonia). Six to 15 days post infection, for septicaemia and abscess models, respectively. It was also efficacious in the treatment of infections caused by *S. pneumoniae* whatever the serotype and the resistance profile of the strains tested (ED₉₀ range: 28–55 mg/kg/administration in septicemia and abscess models, respectively). This also efficacious in the treatment of infections caused by *S. pneumoniae* whatever the serotype and the resistance profile of the strains tested (ED₉₀ range: 28–55 mg/kg/administration in septicemia, AST: 50 mg/kg/administration). These results suggest that XRP2868 might be effective for the treatment of staphylococcal and pneumococcal community-acquired infections.

**XRP2868 (RPR202868/RPR132552), a new oral streptogramin: bactericidal activity and pharmacokinetics in a model of Streptococcus pneumoniae mouse pneumonia** PS138

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The bactericidal activity against *Streptococcus pneumoniae* of XRP2868, a new oral streptogramin composed of two semi-synthetic synergistic components in a 30/70 (w/w) association (RPR202868, pristinamycin I derivative and RPR132552, pristinamycin II derivative), was assessed in lungs of mice with pneumonia. Mice were inoculated intranasally with about 10⁷ cfu of strain 6254-01 (MLSg-resistant). Eighteen hours later (T₀), animals received RPR2868 (120 mg/kg p.o.). The administration was repeated 6, 24, 30, 48 and 54 h afterwards. To study the influence of varying the ratio of PI to PII component administered on activity and PK parameters, ratios of RPR202868 to RPR132552 ranging from 0/100 to 100/0 were also administered under the same conditions. After an oral unitary administration at 120 mg/kg, XRP2868, as well as ratios of RPR202868 to RPR132552 ranging from 50/50 to 90/10, demonstrated strong and quick bactericidal activity in lungs. Lung levels of XRP2868 and RPR132552 were generally equal or two times higher than blood levels. Resulting RPR202868/RPR132552 ratios in blood and lung, although not in accordance with the initial ratio administered, were synergistic for 3–4 h in blood and for 1–3 h in lungs explaining the activity observed.

**In vitro activity of telithromycin against respiratory tract pathogens isolated in France during 2000–2001** PS139

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One thousand six hundred and ninety-four of adult respiratory tract infection (RTI) isolates were collected from November 2000 to April 2001 in 30 French centers. MICs of telithromycin (TEL), erythromycin (E), penicillin (P), amoxicillin (AMX), amoxiclav (AMC), cefuroxime (CMX) and levofloxacin (LVX) were determined by agar dilution method. MICs 50/90 (mg/l) were the following: *Streptococcus pneumoniae* (SP): Overall SP strains (n = 675): TEL 0.015/0.06; E 0.5/64; AMX 0.06/2; CMX 0.25/4; LVX 1/2. P susceptible strains (n = 331): TEL 0.0075/0.015; E 0.03/0.16; AMX 0.015/0.03; CMX 0.03/0.12; LVX 1/1. P intermediate strains (n = 191): TEL 0.015/0.12; E 32/64; AMX 0.5/1; CMX 2/4; LVX 1/2. P resistant strains (n = 153): TEL 0.015/0.5; E 64/64; AMX 2/4; CMX 4/16; LVX 1/2. E susceptible strains (n = 353): TEL 0.0075/0.015; E 0.03/0.12; AMX 0.03/0.5; CMX 0.03/2; LVX 1/2. E resistant strains (n = 322): TEL 0.015/0.25; E 64/64; AMX 0.5/2; CMX 2/8; LVX 1/2. Four percent of the strains were of high level of resistance (MICs ≥ 4 mg/l) to AMX. *Haemophilus influenzae* (n = 751): TEL 1/2; E 8/16; AMX 0.5/2; CMX 1/4; LVX 0.03/0.03. *Moraxella catarrhalis* (n = 268): TEL 0.06/0.12; E 0.12/0.25; AMX 0.03/0.12; CMX 0.5/1; LVX 0.06/0.06.

**Conclusion:** Based on in vitro data, telithromycin is a good candidate for the treatment of RTI.

**In vitro evaluation of abt-773, telithromycin and azithromycin against Streptococcus pneumoniae, Moraxella catarrhalis, Haemophilus influenzae and methicillin-resistant Staphylococcus aureus** PS140

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Macrolide resistant Streptococcus pneumoniae (SP) is a worldwide concern predominantly because these isolates tend to be multiple drug resistant. New agents with increased activity against these pathogens are clinically important. The ketolide class of antimicrobial agents demonstrate excellent in vitro activity against SP, even those that are macrolide resistant. The in vitro activities of the ketolides ABT-773 (A) and telithromycin (T) were compared to azithromycin (AZ) against clinical isolates of SP, Moraxella catarrhalis (M.cat), Haemophilus influenzae (H.flu) and MRSA. Organisms tested: 51 strains of SP (including 14 AZ resistant), 25 H.flu, 25 MRSA and 10 M.cat.

Microdilution MIC tests were performed following NCCLS recommendations using freshly prepared plates containing Haemophilus Test Medium for H.flu, cation adjusted Mueller-Hinton Broth (CAMHB) with laked horse blood for SP and CAMHB for M.cat and MRSA. The new ketolides, A and T had superior activity against SP including the AZ resistant strains (MIC90s: A = 0.12 mcg/ml, T = 0.25, AZ = 4).

All compounds had excellent activity against M.cat while none demonstrated activity against MRSA. H.flu activity was comparable among A, T and AZ. These new ketolides are not currently approved by the FDA; however T has been approved in Europe.

Medical and economic impact of telithromycin in the outpatient treatment of community-acquired pneumonia (cap) in Argentina PS141

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Objective: We evaluated the impact of the initial treatment failure rate, hospitalisation and costs in outpatient treatment of adult CAP in Argentina comparing amoxicillin, clarithromycin and telithromycin.

Method: A probabilistic model was implemented in outpatient treatment of CAP. We estimated an initial treatment with amoxicillin, clarithromycin or telithromycin. We assumed expected clinical cure at 90.1, 88.5 and 94.6%, respectively. For those patients with failure treatment we evaluated a second-line of antibiotics (amoxicillin followed by clarithromycin and clarithromycin followed by new fluoroquinolone) or hospitalisation. Patients with telithromycin and failure treatment must be hospitalised without a second line of outpatient treatment. Costs of CAP included drug’s costs by 10% if failure treatment must be hospitalised without a second line of treatment. Costs of CAP included drug’s costs by 10% if failure treatment must be hospitalised without a second line of treatment. Costs of CAP included drug’s costs by 10% if failure treatment must be hospitalised without a second line of treatment.

Results: We estimated treatments in 100 patients and first-line drug failure in 10, 11 and 5 patients with amoxicillin, clarithromycin and telithromycin, respectively. Costs in outpatient treatment were: hospitalisation $12,224 and $13,489.4; second-line drug $1039 and $1045; second-line hospitalised $1320.4 and $1232 with amoxicillin and clarithromycin, respectively and hospitalisation with telithromycin $6137.

Conclusions: Telithromycin showed lower clinical failure, hospitalisation and costs in CAP. Some studies suggest shortening CAP telithromycin treatment to 7 days helping adherence to treatment and decreasing costs even more.

The new macrolides—a good alternative of tetracycline in the treatment of Mediterranean Spotted Fever PS142

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Mediterranean Spotted Fever (MSF) caused by Rickettsia conorii appears an endemic disease for some regions in Bulgaria. Frequently the disease has a severe course with multiple organ lesions. The early and adequate treatment is of extreme importance for the outcome of the disease. Searching an alternative antibiotic treatment of this disease we considered macrolides for their good cell and tissue penetration and dose-dependent bacteriostatic and bactericide effect. We treated 27 MSF patients with doxycycline 2 x 100 mg/day, 25 patients with clarithromycin 2 x 250 mg/day, as well as 25 patients with midecamycin 2 x 400 mg/day and midecamycin acetate 30 mg/kg/day. As a surrogate marker for treatment evaluation the effect on the febrile syndrome was used. Our findings showed that by the 5th day of treatment the fever normalized in 89.47, 88.24 and 76.47% of the patients treated with doxycycline, clarithromycin and midecamycin, respectively. For the same period the patient fever decreased below 38 °C in 100, 100 and 94.12%, respectively. The intoxication symptoms were influenced within the same period equally in all treated patients. Conclusions: We suggest that the new macrolides appear a good alternative of tetracycline on patients with MSF.


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In the recent 2 years we tested Erythromycin sensitivity of 474 species of Gram +/– cocci isolated from throat and nose secretions, ear and eye effusions, sputa, cerebrospinal fluid and blood cultures, vaginal and urethral secretions, urine and fecal samples from patients with inflammatory diseases of the listed organs and systems. Staphylococcus aureus, Staphylococcus coagulase 1–1, Streptococcus a-haemolyticus, Enterococcus were isolated. Of these microorganisms S. aureus was the most abundant. Our resistograms revealed sensitivity of the Gram +/– cocci in 76.97 and 68.60% for 2000 and 2001, respectively, and resistance of 23.03 and 31.40%, respectively. In the tests with Midecamycin and Midecamycin aceta the same microorganisms showed sensitivity of 85.38% and resistance of 14.62%. The clinical findings showed excellent effect of the new macrolides including Clarithromycin and azalides—Azithromycin. We conclude the resistance of Gram +/– cocci and especially of S. aureus to Erythromycin increases very quickly and has reached dramatical extent. By now, the new 14, 15, and 16-membered ring macrolides and azalides show high antibacterial activity and good clinical effect.

Quinupristin/Dalfopristin: how insensitive . . . PS144

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Quinupristin/dalfopristin (Q/D) is a novel injectable streptogramin antibiotic which initiation in therapeutics was hailed as an important step towards treatment of vancomycin-resistant Enterococcus faecium (VREF) species. Initial reports concluded in an excellent response of VREF to Q/D. Reports of Q/D-resistant strains of E. faecium have emerged, both in USA and Europe. We report two cases of E. faecium bacteremia in which the responsible isolate was not sensitive to Q/D. The first patient was a woman with acute leukemia and septicemia. E. faecium was cultured from blood samples: the species was resistant to almost all antibiotics, exhibiting sensitivity only to tetracycline (T), while its sensitivity to Q/D was intermediate. The second patient was a man with endocarditis, in whom blood cultures isolated E. faecium sensitive to a number of antibiotics, including ciprofloxacin and vancomycin; still the sensitivity to Q/D was intermediate. Q/D has not been officially introduced to the antibiotic arsenal of Greek
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Vegetable tannins possess a wide range of biological activities. The aim of the present study was to evaluate the cytotoxicity of five purified vegetable tannins against MDBK cells. The maximal non-toxic concentrations (MNC) and the concentrations required to inhibit cell growth by 50% (CC50) were evaluated after 24, 48 and 72 h periods of action. MNC values after 48 h indicated that compounds stimulated cell surveillance when applied in concentrations lower than 0.01 M. CC50 values indicated: (i) a decrease in cytotoxicity after 48 h as CC50 were up to 70 times lower than those observed after the 24 h period, and (ii) a re-increase in cytotoxicity when the period of action was prolonged up to 72 h as CC50 were 2500 times lower than those observed after the 48 h period. These data thus appear to reveal the capability of the investigated natural polyphenolic products to stimulate cell surveillance in a time-dependent manner.

Antibacterial effect survey of enoxolone on periodontopathogenic and capnophilic bacteria isolated from specimens of patients with periodontitis PS146

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Objectives: Most of the microorganisms associated with periodontitis are capnophilic and anaerobic bacteria. Purpose of this study was to detection of antibacterial effect of enoxolone on periodontopathogenic and capnophilic bacteria.

Methods: In this study 136 periodontopathogenic and capnophilic bacteria were isolated from 400 specimens of patients with periodontitis by culture method. An anti-bacterial activity of enoxolone against these microorganisms was investigated by minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) methods.

Results: Based on our findings the MIC, MBC and Lethal does (LD50) of Enoxolone for Actinobacillus actinomycetemcomitans, Eikenella corrodens and Capnocytophaga were ‘8, 16, 64’, ‘16, 16, 32’, and ‘8, 16, 32’ µg/ml, respectively.

Conclusion: Our results show enoxolone has antibacterial effect on A. actinomycetemcomitans, E. corrodens and Capnocytophaga spp.

Synthesis of new derivatives of 5-aminothiazole and antibacterial activity PS147

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We have synthesized diamides of dicarboxylic acids, with components such as 5-nitrothiazole benzolsulphamides and triazol. All the above compounds exhibited bacteriostatic activity towards some microorganisms. For further studies of bacteriostatic activity of amides and diamides of dicarboxylic acids, as well as for determination of ‘structure—activity’ relationship, we have synthesized a range of monoamides. Antibacterial activity of the synthesized compounds was studied in vitro by agar dilution methods. For this purpose, approximately 50 various Gram-positive and -negative microorganisms including clinical strains of Staphylococcus aureus, Bacillus subtilis, Serratia marcescens, Escherichia coli, Proteus morgani, Micrococcus luteus, Staphylococcus epidermidis, Shigella sonnel, Salmonella typhimurium, Yersinia enterocolitica. Minimum inhibitory concentration was expressed in µg/ml. Nitazoxane was used as a comparison substance. Analysis that new derivatives of 5-nitrothiazole have high antibacterial activity relative towards certain microorganisms included strains obtained from infection department’s patients. Results will be shown.

Microbial susceptibility to the essential oil of Ziziphus clinopodiodes Lam. PS148

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Purpose of the study: Antimicrobial activities of essential oils vary from oil to oil and from one micro organism to another. The antimicrobial and chemical properties of essential oil from Ziziphus clinopodiodes Lam. has not been studied and hence the present study was planned to evaluate those properties against a series of micro organisms viz. Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumonia, Bacillus subtilis, Bacillus licheniformis, Streptococcus faecalis, Candida albicans and Saccharomyces cerevisiae.

Results: Z. clinopodiodes Lam. essential oil was found to have remarkable antimicrobial property against all the microorganisms but P. aeruginosa. The oil exhibited its best antimicrobial activity within a maximum of 45 min. Seventeen components were identified by Gas Chromatography and Mass Spectrometry (GC and GC/MS) analysis of the oil, out of which Pulegone (24.5%), Neomenthol (12.8%), Cyclohexene,5-methyl-3-(1-methenyl)trans (12.2%), 2,4-cycloheptadien-1-one,3,6,6-trimethyl (9.2%), Piperitone (4.2%), and Limonene+1,8-cineole (4.1%) constitute major parts of the oil.

Conclusion: Monoterpenes seem to have antimicrobial role. It seems necessary to explore antimicrobial properties of new harmless antimicrobial agents from natural sources as substitutes for common chemical drugs.

Methanol extract of Carpobrotus edulis enhances killing of methicillin resistant Staphylococcus aureus phagocytosed by THP-1 human monocyte derived macrophages and promotes the release of modulators of cellular immunity PS149

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Although alkaloids from the family Mesembryanthemaceae have anti-cancer activity, species of this family have received little attention. Because these alkaloids also exhibit properties normally associated with compounds that have activity at the level of the plasma membrane, we have studied a crude methanol extract of Carpobrotus edulis, a common plant found along the Portuguese coast, for properties normally associated with plasma membrane active compounds. The results of this preliminary study show that the extract is non-toxic at concentrations that prime THP-1 human monocyte-derived macrophages to kill ingested methicillin resistant Staphylococcus aureus and promote the release of lymphokines associated with
cellular immune functions. The extract also induces the proliferation of THP-1 cells within 1 day of exposure and 2 days earlier than that induced by phytohemagglutinin. Similar results were obtained with monocyte-derived macrophages isolated from human peripheral blood. The active component or components of the plant extract may be exploited as intracellular active anti-bacterials as well as modulators of cellular immunity.

Enhancing of Erythromycin production by Saccharopolyspora erythraea NUR001 with common and uncommon oils PS150

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Enhancing effect of various oils on the erythromycin production by Saccharopolyspora erythraea NUR001 were evaluated in a complex medium consisting soybean flour and dextrin as the main substrates. The biomass, erythromycin, dextrin and oil concentrations, and pH value were measured on a daily basis. Also, the kinds and frequencies of fatty acids of the oils used were determined. Saturated fatty acids in the shark oil were higher than that of vegetable oils used. Erythromycin concentration in the melon (Cucumis melo var. inderus cultivar mashhad) seed oil containing medium was 4.56 times higher than that of the control medium (without oil) and 1.18 times higher than that of rapeseed oil containing medium. Erythromycin concentration in the other oil containing media, including rapeseed, soybean, shark (Carcarhinus dussumieri), and safflower oils was 3.88, 3.03, 2.59, 2.44 time higher than that of control medium, respectively. The melon seed oil had the least enhancing effect on the biomass production, and thus decreasing the cost of the biomass separation.

Can varicella be eliminated by universal childhood vaccination ?— Epidemiological and economic data from Germany PS151

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Purpose: Universal varicella vaccination in childhood is expected to reduce substantially the number of uncomplicated cases of chickenpox and to decrease the number of complicated cases requiring hospitalization. To generate fundamental data for decisions of the health authorities epidemiological and health-economic data were collected in two large studies. Using an age-structured decision analytic model the benefits, costs and cost-effectiveness of a varicella immunization program over a period of 30 years were assessed.

Results: It could be shown, that the vast majority of varicella cases occur in children aged less than 8 years. In 16.3% of the cases a severe course was assessed. Overall incidence of complications was estimated to be 5.7%. A routine varicella vaccination program targeting healthy children could prevent 82.6% of varicella cases and over 4700 major complications per year provided the coverage rate would be 85%. Under these conditions the elimination of varicella is predicted to be achievable within 15–20 years. A combined measles, mumps, rubella and varicella vaccine is expected to provide the required coverage.

Conclusions: Routine childhood varicella vaccination appears to be a highly efficient strategy to significantly reduce the sizeable burden of varicella and leads to significant savings from both societal and payer’s perspective.

Immunisation against influenza of children with allergic diseases PS152

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Objective: To estimate efficacy of vaccine Influvac at children with allergic diseases.

Methods: Twenty children aged 3–18 years with allergic diseases received vaccine Influvac (Solvay Pharma). For the control group of children, with allergic pathology did not receive this vaccine because of an intolerance of chicken protein (10 children).

Results: All vaccinated children for the observable season of 6 months did not get influenza. General and aboriginal reactions to a vaccine did not occur. In control group for the observable season two children were ill with influenza and four children with acute respiratory virus infection (60%). Among vaccinated children there was an increase in titre to a protective level (1:40 and above) to all to three strains of influenza 30 days after injection. Vaccine Influvac can be recommended for an immunisation against influenza of children with an allergic pathology because of efficacy and absence of side effects.

Pharmacoeconomic impact in immunizing adults against influenza PS153

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Objectives: Our study examines the possible economic impact of the influenza on health working adults in Argentina, and the intervention cost saving with immunization.

Methods: This is a theoretical study based on a mathematical model. Population data was published in 2001s national statistics. The global incidence of influenza infection was estimated at 5%. We have estimated the direct cost on influenza infection (outpatient visits, drugs and hospitalization) and indirect cost (work absenteeism and productivity loss) and projected net saving for the 20–64 year-old vaccinated group. The vaccine effectiveness was estimated at 70 and 90%. The price of vaccine was $8 each.

Results: The total population in Argentina was 36.027.041 in 2001, while 19.337.487 of the people were 20–64 year-old (53.67%). Considering an incidence of 5%, 996.874 people had influenza infection during the year. The direct cost was of $23.962.647 and the indirect cost was of $250.453.421. The saving cost avoiding influenza was of $192.091.178 and $246.974.371 and the net saving amount (avoided cases—vaccine cost) was of $8.383.051 and $63.288.245 for 70 and 90% of effectiveness, respectively.

Conclusion: Influenza vaccination is effective in diminishing cases of flu and reducing working-day loss. Its a safe and cost-effective vaccine.

Impact of vaccination against flu in a health institution PS154

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Flu infection is a major cause of illness and one of the most common cause of work absenteeism, increasing institution costs, healthcare provider visits, use of drugs, and decreasing work productivity. Vaccine against flu has an effectiveness between 70 and 90%, in health adults.
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Objective: Evaluate the impact of flu-like respiratory tract infections in a health institution staff during 1 year, comparing vaccinated with not-vaccinated groups.

Methods: We evaluated all causes of absenteeism along 1 year (2001), based on the written note made by the professional who has evaluated ill people, selecting flu-like respiratory infection causes. We evaluated age, working days lost related to illness, and cost on vaccinated and not-vaccinated groups.

Results: One hundred and sixty eight of the total staff (479 people) were vaccinated. 21 of them had flu-like infection, resulting in 40 working days lost. For not-vaccinated group, 33 people had flu and 56 lost days. Lost cost for vaccinated group was of $1267, and for not-vaccinated group, $1874.

Conclusion: We observed a decrease in working days lost and money waste related to flu-like infections on the vaccinated group. Because of safety and effectiveness of vaccine against flu, the implementation of vaccination will be cost-effective for all institution staff.

Using recombinant α2β interferon in complex therapy of bronchial asthma at children PS155

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We studied functioning of the interferon system in 108 children with atopic bronchial asthma (BA) at the age of 2–14 years. The control group included 10 healthy children. We investigated the interferon status (method of Grigoryan S.) and serum concentrations of IFN-gamma (IFNγ) (ELISA). There was a decrease in the IFN-producing ability of leukocytes to the synthesis of IFNγ at 50% and IFNγ at 84% of children with BA. Serum level of IFN of children with BA during all period of illness is compared to the children without predisposition to atopy (94.9 ± 10.3 and 192.3 ± 7.8 pg/ml accordingly) was significantly decreased. Production of IFNγ increased after using viferon (recombinant α2β IFN and antioxidants). Decreased ability of gamma-interferonogenesis in the most children was not affected by the action of immunomodulators. There was shown interferon system’s dysfunction in the development of atopy and increasing predisposition to respiratory infections and to persistent of atypical infections in children with BA.

One case with Congo-Crimean haemorrhagic fever PS156

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Congo-Crimean haemorrhagic fever is viral disease with a high rate of mortality that is caused by a Nairoivirus, Bunyaviridae species. This is a zoonotic disease, which affects sporadically humans and is geographically distributed even in Eastern Europe and Balkan. During the months of May and June 2001, in northeast of Albania were reported eight cases of haemorrhagic fever. Serologic tests performed in the laboratory of reference in Thesaloniki, Greece confirmed the diagnosis of Congo-Crimean haemorrhagic fever. In the mean time, WHO reported the outbreak in southwest Kosovo of 69 cases suspected for haemorrhagic fever from which 18 were confirmed laboratory as Congo-Crimean haemorrhagic fever. We are describing here the clinical history of one of eight cases with CCHF in Albania. From the epidemiological point of view this case was considered peculiar, as it was the only one hospitaly acquired, and due to the gravity of the haemorrhagic syndrome was admitted at the intensive care unit at infectious diseases service, University Hospital Center of Tirana.

Prevalence of active chronic hepatitis B among the HBsAg-carriers in Smolensk, Russia PS157

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Purpose: To estimate the frequency of active chronic hepatitis B among the HBsAg-carriers in Smolensk.

Results: In the study were included 150 patients ≥18 years of age with documented HBsAg-carrier ≥6 months (average age—39.4 years, male—58%, female—42%). HBV DNA in serum was tested by qualitative and quantitative PCR (commercial test-system Ampli-Sens HBV). HBeAg, HBeAb, HBsAg were detected by ELISA (Hoffmann La Roche). HBV DNA by qualitative PCR was detected in 41% patients, by qualitative PCR was detected in 13% patients in the concentration ≥10^5 copies/ml, in 4.3% ≥10^7 copies/ml, in 4.3% ≥10^7 copies/ml, in 2.1% ≥10^9 copies/ml (Fig. 1).

Inducible nitric oxide synthase expression in chronic viral hepatitis and its relation with histological severity of disease PS158

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The exact potential of nitric oxide in the pathogenesis of chronic viral hepatitis is not known. The elevated nitric oxide production is assumed to be responsible for the pathological changes in many inflammatory conditions, mainly via peroxynitrile, a potential oxidant that is produced by the reduction of superoxide anion with nitric oxide. The intensity and the distribution of the immunohistochemical...
staining of intrahepatic inducible nitric oxide synthase were studied in the biopsy specimens obtained from 63 patients with viral hepatitis and 13 patients with elevated transaminase levels from other etiology. Hepatic inducible nitric oxide synthase staining was significantly more intense in the viral hepatitis group \((P = 0.000)\). Inducible nitric oxide synthase staining levels correlated well with the severity of the viral hepatitis using the Knodell’s liver histological activity index \((r = 0.393, P = 0.002)\). Among the viral hepatitis group, the pathological distribution of the inducible nitric oxide synthase staining favored the periporal regions whereas less staining was observed in the bile duct and parenchyma regions. As nitric oxide mediated nitration of hepatocellular proteins is found to be elevated in the inflamed hepatic tissues and it well correlated with the severity of the disease, we suggest that inducible nitric oxide synthase can possibly have a critical role in the pathogenesis of chronic viral hepatitis.

**Treatment with ursofalk of patients ill with chronic hepatitis of viral and other aetiologies \(PS159\)**

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There were 36 patients under observation who were divided into two groups, the first of 18 patients (eight chronic virus hepatitis; three chronic virus hepatitis + steatosis; four steatohepatitis; three chronic cryptogenic hepatitis; there were 14 men and four women aged from 35 to 74. The second group consisted of 18 patients, eight with chronic virus hepatitis; four with steatohepatitis; six with chronic cryptogenic hepatitis. There were 15 men and three women aged from 40 to 80. Diagnosis was confirmed with the help of clinical data, biochemical tests, serological markers, PSR-diagnostics and ultrasound examination and computer tomography of the abdomen. In the first group of patients the treatment with ursofalk was administered at the dosage of 1.75 mg/l. In the second group of patients the treatment was carried out with various hepatoprotectors during the courses from 1 to 6 months. Before the average index of ALT activity was being carried out — 105.88 U/l, after — 62.06 U/l and AST — 156.44 and 95.05 U/l; ALP — 196.39 and 171.87 U/l; GGT — 163.2 and 82.86 U/l; CHOL — 5.38 and 4.88 mmol/l; TG — 2.15 and 1.75 mmol/l. In the second group of patients the treatment was carried out with various hepatoprotectors during the courses from 1 to 6 months. Before the average index of ALT activity was being carried out — 181.3 U/l, after — 165.5 U/l; AST — 126.9 and 129.0 U/l; ALP — 229.8 and 213.5 U/l; GGT — 204.2 and 238.0 U/l; CHOL — 5.85 and 5.67 mmol/l; TG — 1.72 and 1.8 mmol/l. Treatment of patients suffering from hepatitis of viral and other aetiologies with ursofalk produces a positive effect on both clinical symptomatic and biochemical indices. Remission was more stable during a long period of taking the preparation. The hepatoprotective effect of ursofalk during the 3 years was sustained for the whole of the period of the treatment. After stopping, an acute attack of cytolitic syndrome was observed. With other hepatoprotectors we did not get any improvement in clinical scene of the disease or in biochemical indices.

**Herpes-virus hepatitis \(PS160\)**

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HSV-1 and -11 have possibility to damage different organs and systems. Sometimes they cause damage of the liver, which resemble viral hepatitis. The etiology of such hepatitis may be confirmed only by results of liver biopsy.

We have diagnosed 12 cases of herpetic hepatitis: eight children and four adults. Clinical course was different. In five cases the acute beginning took place: high temperature, the jaundice at the 2–3 day (the level of bilirubin was 200–350 mmol, especially direct), cholestasis, the pain in upper right part of abdomen. The ascites was found in three patients with acute hepatitis during 1st week from the beginning of disease. In seven cases the beginning was gradual. The temperature was subfebrile, prolonged; malaise and moderate pain in upper part of abdomen were constant complaint. The jaundice was moderate; bilirubin increased until 120 mmol. The level of ALT was moderately increased \((5–7\text{ }\text{t}imes)\). The blood analysis showed moderate leukocytosis with neutrophilia, and increased SRE.

The serological markers of hepatitis A, B, C, D were negative in all cases. HSV-1 and -2 were found in the blood. The diagnosis was defined by the results of histochemical investigations, when the viruses were found in liver biopat, and confirmed with the results of specific treatment. Specific damage of liver cells was found: protein dystrophy and specific inclusions in cell nucleus.

In all cases the treatment with acyclovir were given. The results we have observed during 1st week: the temperature became normal, the jaundice decreased and bilirubin was normal during 5–10 days.

In one case the recidive took place 2 weeks later after treatment. The second course of acyclovir with Intron A gave good results.

**Hepatitis G virus infection in individuals at high risk of transmission of viral hepatitis \(PS161\)**

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The large number of unsolved cases of acute and chronic hepatitis has most probably the viral etiology. In mid 1990s, two independent groups of authors reported a new human hepatotropic virus, with flavivirus like genomes, hepatitis G virus (HGV). The aim of this pilot study was to determine the prevalence of hepatitis G viral infection among patients at high risk of exposure to blood and blood products, as well as to evaluate if the risk of HGV infection was higher among them than in the general population. Immunoenzyme test on microtiter plate for detection antibodies against HGV E2 antigen in plasma or sera (R & D Systems, Minneapolis, USA) was used for evidencing anti-HGV IgG antibodies in sera. Anti-HGV antibodies were detected in the control group (blood donors) in 8.3% (2/24) patients. Prevalence of anti-HGV antibodies among i.v. drug users was evidenced in 42.8% (9/21), in hemophiliacs 41.2% (7/17), in patients acquiring multiple blood transfusion 42.8% (3/7), in hemodialyzed patients 33.3% (4/12) and in patients with transplanted organs 57.14% (4/7). Our results suggest that patients exposed to blood or blood products have a higher risk of HGV infection than general population.

**Evaluation of Ortho Total HCV Core antigen assay in assessment and follow-up of patients treated for chronic HCV \(PS162\)**

Lunel F, Veillon P, Payan C. *CHU Angers, Laboratoire de Bactériologie-Virologie, Angers, France*

An assay to quantitate ‘Total’ HCV Core antigen (HCV Ag) in serum or plasma, may reflect viral load, has been developed by Ortho-Clinical Diagnostics.

**Methods:** We evaluated HCV Ag with two quantitative assays for
Hepatitis C virus RNA and HCV Core antigen kinetics predict the efficiency of interferon-alpha and ribavirin therapy in naive patients infected by HCV genotype 2 or 3 PS163

Lunel E1, Veillon P2, Payan C3, Loustaud-Ratti V4, Rifflet H5, Foucard-Hubert I6, Causse X7, Abergel L8, CHU Angers, Laboratory of Bacteriology-Virology, Angers, France, 2CHU Dupuytren, Service de Médecine Interne A. Limoges, France, 3CHG Ajaccio, Service de Médecine B. Ajaccio, France, 4CHU Angers, Service de Médecine A. Angers, France, 5CHU la Source, Service d’Hépatogastroentérologie, Orleans, France, 6Hôpital Hotel-Dieu, Service d’Hépatogastroentérologie, Clermont-Ferrand, France

Fifty-five patients infected by genotype 2 or 3 were treated with a primary dose of 3 (if hepatitis C virus (HCV) RNA < 3 Meq/ml) or 6 million units of interferon alpha-2b (IFN) thrice weekly for 12 months. Ribavirin was added at month 3 (M), until M12 if HCV RNA was found positive after M2 of IFN. The viral kinetic was assessed during the follow up by serial measurements of HCV RNA (bDNA 3.0 and Monitor 2.0) and using a new assay from Ortho-Clinical Diagnostics which is able to quantify total HCV core antigen. Sustained virologic response was observed in 65% of the patients (36/55). After 1 month of IFN treatment, sustained responders had a fall of HCV RNA and HCV Core antigen higher than non-responders (4.3±1.84 log IU/ml versus 0.15±0.31 log IU/ml, P < 0.001, for HCV RNA) and (1.68±0.89 log (pg/ml × 10000) versus 0.17±0.18 log (pg/ml × 10000) P < 0.001, for HCV Core antigen). After 1 month of IFN, the Positive and Negative Predictive Values of sustained response were, respectively, 100 and 17.4% for HCV RNA negativiation and 97.5 and 37.5% for HCV antigenemia negativiation. These results suggest that both kinetics of viral load and antigenemia are highly predictive of sustained response.

Prevalence of hepatitis B, hepatitis C and genotypic analysis on economic immigrants in Greece PS164

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Greece has accepted a big number of economic immigrants lately. We investigate the prevalence of hepatitis B/C as well as the epidemiological features that might influence the public health. 1,235 economic immigrants from: Albania 630, Eastern Europe 411 and from Asiatic-African countries 194, visited our hospital to be checked in order to get a health certificate to obtain the green card. They where tested for hepatitis B/C. The serological markers were determined by immunoenzymatic method. All HbsAg (+) and anti-HCV were further tested for HBV DNA and HCV RNA by competitive RT PCR. HCV RNA (+) were genotyped by strip hybridization immunomassay.

In 630 Albanians 17.5% were HbsAg (+), 14.6% HBV DNA(+), 1.1% anti-HCV(+) and 0.8% HCV RNA(+). In 411 East Europeans 5.1% were HbsAg(+), 4.4% HBV DNA(+), 2.43% anti-HCV(+) and 1.9% HCV RNA. In 194 Asians-Africans, 2.6% were HbsAg(+) and 2% HBV DNA(+). In 101 Pakistanis, 26.7% were anti-HCV(+) and 22.0% HCV RNA(+). Of the rest of Asians-Africans, 11.82% were anti-HCV(+) and 9.3% HCV RNA(+). Albanians: higher prevalence of HBV infection (14.6%). Greek blood donors: 1% Pakistanis: HCV infection is 22% (predominance of 3a type), General Greek population: 2%. Public health services in Greece and Europe must take appropriate measures.

Hepatitis-B vaccine and murine schistosomiasis PS165

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The purpose of the study was to investigate the influence of schistosomal suppression on the antibody response to hepatitis-B vaccine (HBV) and to study if the vaccine has any protective effect on experimental infection. The results obtained revealed that infection reduced the serum antibody level against HBV. Parasitological and histopathological findings showed significant protection against infection. The conclusion reached was; in order to reduce the incidence of virus-B infection especially in schistosomiasis endemic areas, public health officials should evaluate a policy for regulation of HBV booster vaccination to enhance the population immunity against hepatitis B infection.

Family adherence to anti-retroviral therapy for African immigrant children in London PS166

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Sustained anti-retroviral combination chemotherapy requires excellent adherence to the regimen so as to suppress viral replication sufficiently to delay the emergence of resistance. If chemotherapy were taken to scale, e.g. in Africa, erratic adherence might soon lead to multi-resistant circulating virus. We reviewed our experience in a well established London family clinic with a team including community nurses. We reviewed the records of the 23 African immigrant children, aged 2–14, treated with anti-retrovirals exclusively at our centre throughout 2001. Whereas 14 had undetectable HIV RNA within the year, only four had undetectable RNA throughout the year. Four failed therapy through proven resistance mutations, but nine were considered through circumstantial evidence to have rising viral loads primarily because of poor adherence. Three were known to have stopped taking drugs for extended periods. The three boys over 11 years were unreliable in adherence, but the one girl in this age-group was fully adherent. Our preliminary assessment is that for the children in our families, despite a team approach and home visits, non-adherence to HAART may be twice as common as selection of a dominant viral mutant as a primary cause of failure to sustain viral suppression.
Ghaderi B, Alaghebandan R, Rastegar lari A. Department of Microbiology, Iran University, Tehran, Islamic Republic of Iran

Prevalence of lipodystrophy in a cohort of black African patients PS167

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The prevalence of HIV related lipodystrophy-syndrome depending on the definition and severity of lipodystrophy ranges from 5 to 80%. We have retrospectively reviewed the medical records of 58 African patients followed. The characteristics are shown in table.

| Months on therapy (x ± SD) | 16.57 ± 16.26 |
| Months on the last regimen | 12.76 ± 11.72 |
| Patients taking d4T (%) | 17 (29.3%) |
| Months on d4T (x ± SD) | 15.7 ± 14.4 |
| Patients taking IP (%) | 31 (53.4%) |
| Months on IP (x ± SD) | 13.7 ± 12.2 |
| CD4 cell count before initiating ART (x ± SD) | 265.4 ± 185.56/mm³ |
| Last CD4 cell count (x ± SD) | 367.4 ± 252/mm³ |
| Viral load decreased | −2.4 log10 |

The 3.4% of Africans had triglycerides > 200 mg/ml and 1.7% had cholesterol > 250 mg/ml, none had both metabolic alterations. Glycemia > 120 mg/ml was observed in 8.6% patients. It is interesting highlight that in any the Africans morphological changes were noted and all of them showed weight stable. Although the low prevalence of metabolic alterations may be attributed to the different ethnic alimentary behavior if self-body perception by African is not as accurate as by caucasian on the estimation of the body changes have to be investigated.

Maternal anti-HAV prevalence and vaccination age PS168

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Hepatitis A virus (HAV) infection is usually asymptomatic in children. However, it may occasionally cause a severe disease with high morbidity and mortality, and loss of school or business days. In a previous study, we have shown that every one of two to three school children from upper social classes living in Adana carries high risk of HAV infection. It is well known that maternally transmitted anti-HAV antibodies interfere with HAV vaccination. In an effort to determine the optimal age for HAV vaccination, 122 babies (52% girls and 48.5% boys) born in our hospital were prospectively followed up at least 24 months for the presence of maternal antibodies to hepatitis A (anti-HAV IgG). Anti-HAV IgG titers were measured from the blood specimens obtained at birth from the mothers and from the offsprings at months, 0, 3, 6, 9, 12, 15, 18, 21 and 24. The prevalence of positive anti-HAV at birth (95%) was similar to those of HAV seroprevalence studies carried out in adults in our area. The disappearance of antibodies occurred between the 1st and 21st month of life. The prevalence of anti-HAV IgG among children aged 0, 9, 12, 15, 18 and 21 months were 95, 60, 32, 9, 4 and 0%, respectively. In light of these findings, we suggest that hepatitis A vaccination be given after 21 months of age. Earlier vaccination may be ineffective due to interference with maternally transmitted anti-HAV antibodies.

Epidemiology of entestinal amoebiasis in an Iranian hospital PS169

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Diarrhoea is a major public health problem in developing countries. Amoebiasis is one of the most common causes of diarrhoea in Iran as an endemic area for amoebiasis. Little, however, is known about the extent of the condition in our society. The aim of this study is to determine socio-demographic and clinical characteristics of patients with intestinal amoebiasis. During July and August 2001, we collected 90 patients with diarrhoea among 5000 patients who visited at a referral hospital in Shahrriar area (in countryside of Tehran), Iran. Thirty out of 90 patients (33%) had intestinal amoebiasis and were followed up prospectively until the resolution of the illness. Nineteen of 30 (63.3%) patients were male and the remaining of 36.7% was female. The patients were aged 1–76 with mean of 28.4 years. Most of the patients (70%) were below 30 years of age and the peak of occurrence was between the age of 17 and 26 years. Watery diarrhoea with abdominal cramps was the main clinical feature. Seventy percent of patients were resident in urban area and the remaining (30%) in rural area. Average family income was low and all patients were in low socioeconomic level. Water supplying system for all patients was pipeline water. Low socioeconomic level associated with poor personal hygiene was the most important factor for highly prevalence of this problem in our society. Also it seems that food plays important role in transmission of protozoa then water.

The new strategy for allele identification of the genes coding for pertactin and pertussis toxin subunit S1 in Bordetella pertussis PS170

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Bordetella pertussis strains demonstrate a significant polymorphism in toxin S1 subunit and pertactin, which are major protective antigens of the organism. Monitoring the changes in prevalence of particular alleles of genes coding for these proteins in local B. pertussis populations is an essential issue in cases of the observed decrease of vaccination effectiveness. We have developed a new method for allele identification of these genes, which eliminates the necessity of DNA sequencing. The approach is based on the identification of the number of repeats or the presence of specific nucleotides in the polymorphic regions or residues, respectively, of the genes and utilises products of their full or partial PCR amplification. The nucleotide heterogeneity in each polymorphic site is analysed either by the differential digestion of the amplicons or by the ARMS (amplification-refractory mutation system) methodology. Numbers of repeats in particular regions of the genes are revealed by the size analysis of the adequate PCR products or their restriction fragments. In all cases the presence, size or pattern of DNA molecules obtained is visualised by the agarose gel electrophoresis. The preliminary analysis of the recent and archival B. pertussis strains identified in Poland was performed using the described approach. The presented strategy provides a much easier, faster and more cost-effective than DNA sequencing mean to study the polymorphism of the major B. pertussis antigens.

Vaccination coverage and history of vaccine preventable infectious diseases among students in second year of medicine and pharmacy of tours university PS171

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The purpose of this study was to determine the level of infectious risk in students who will be exposed to patients. Information was
obtained by a questionnaire for each student, and by checking medical records for immunization coverage and vaccine preventable infectious diseases. Answers could be specified for 138 students, of whom 97 females (F) and 41 males (M). The number of non-immunized students was against diphtheria: two; tetanus: three; pertussis: four; poliomyelitis: two; hepatitis B: six; and hepatitis A: 127, respectively. Among the 52 students non-vaccinated against measles, 14 (nine F and five M) had no history of that disease. Among 56 (31 F and 25 M) non-vaccinated against rubella, 17 (10 F and seven M) had no history of that disease, uncertain in seven others (six F and one M). The date of vaccination was often late regarding recommendations. Fifteen students had no history of varicella. One student had not received BCG vaccination. Fifty-eight students had received two, and 14 three BCG vaccines. Post-BCG tuberculin skin testing was missing after 28 first BCG, 14 second and 3 third BCG. The date of the first tuberculin test was often late regarding recommendations. Fifteen students had no history of varicella. One student had not received BCG vaccination. Fifty-eight students had received two, and 14 three BCG vaccines. Post-BCG tuberculin skin testing was missing after 28 first BCG, 14 second and 3 third BCG. The date of the first tuberculin test was often one or several years after BCG vaccination. Adverse effects of vaccination were rarely reported: two cases of fever (DT polio, measles); three cases of local reaction (DT polio, DTP polio). One case of contraindication for influenza vaccine: egg allergy. The survey shows failure in immunization coverage actually recommended in health care students.

Rabies—the morbidity in Lasi county between 1971 and 2000 PS172

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Objectives: To present the morbidity of rabies and evaluate the efficiency of our prophylaxis scheme in Lasi county.

Material and method: We made a retrospective study of the rabies cases in the patients admitted in our unit in a 13th-year period. We have analysed all the clinical, epidemiological and biological aspects.

Results: In a 30-year period, 22 cases of rabies were admitted in the Clinical Infectious Diseases Hospital Lasi. The highest incidence was for 1986–1990—eight cases (36%); the highest yearly cases were three cases in 1974 and 1986. Most of the patients were male (59%), came from suburban areas (21 patients). Eight cases occurred in May–June, wild animals were involved in half the cases (fox, wolf). For 18 patients, no prophylaxis was performed and an incomplete course in four cases. The period of time to the appearance of the first symptom was 18–120 days. The prophylaxis scheme led to a good protection.

Conclusions: In Lasi county, rabies is a problem with a prevalence of 0.73%/year.

Trends in antimicrobial drug use in the community—Riyadh 2000 PS173

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Trends in the use of antimicrobials in Riyadh in 2000 were analyzed. Data was obtained from a survey of 652 randomly selected families of school children aged 6–8 years in a 3-month period in 2000. One hundred and ninety-nine (33.8%) students were on antibiotics in the month preceding the study; 108 (56%) received antibiotics for the diagnosis of pharyngitis; 177 (90%) students antibiotics were prescribed by a physician; and in 161 (83%) the duration of antibiotics was less than 1 week.

This study shows a major problem in antibiotics prescription in our community and also the need to establish effective antibiotics policy in general practice to limit the potential emergence of drug resistance bacteria in the community.

Decision making in the selection of antibiotics for urinary tract infections and prophylaxis PS174

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Antibiotic susceptibility spectrum of childhood urinary tract infection agents are geographical variation. The current antibiotic regimens and the selection of antibiotics for prophylaxis should be re-evaluated periodically. The objective of our study was to determine the local resistance rates to antibiotics and to give a direction for the selection of antibiotics in UTI treatment. We evaluated 4124 urinary culture assays retrospectively, sent from Pediatrics and Pediatric Surgery inpatient and outpatient clinics of our hospital during the last 6 months, and investigated the isolated pathogens and the resistance rates to antibiotics. In addition, the data obtained were compared with of 5 years ago. Table shows the flora of Aegean region. There is no significant difference between the results we obtained and of 1996. However, the frequency rate of the most common UTI pathogen, that is Escherichia coli, decreased from 62 to 41.5%.

<table>
<thead>
<tr>
<th>Isolate</th>
<th>1996 (%)</th>
<th>2001 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>62</td>
<td>41.5</td>
</tr>
<tr>
<td>Klebsiella sp.</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>P. aeroginosa</td>
<td>8</td>
<td>7.2</td>
</tr>
<tr>
<td>Proteus sp.</td>
<td>5</td>
<td>7.3</td>
</tr>
<tr>
<td>Others</td>
<td>13</td>
<td>28</td>
</tr>
</tbody>
</table>

With respect to the resistance rates to antibiotics of UTI pathogens, the resistance rates of E. coli for carbapenems, aminoglycosides and third generation cephalosporins were 1, 10 and 10%, respectively as before, but the rates for ampicillin increased from 67 to 75% and for TMP-SMX it increased from 49 to 61%. We concluded that the resistance profiles to antibiotics should be reviewed every 5 years at least and thus the selection of proper antibiotics would lessen the morbidity as well as the medical expenses.

Economic aspects of infectious disease control in Georgia PS175

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Purpose: Since 1991 infectious diseases (ID) are increasing in Georgia. This study is aimed to reveal economic barriers of effective ID control by assessing financial contribution to ID from Public and Private sources, household’s total spending on health and their capacity to pay.

Sources:
1) National Household Expenditure and Revenue survey.
2) WHO Fair Financial Contribution Methodology.
3) Meta-Analysis.

Results: 51.8% of population leaves under the poverty level; 70% out of total household expenditure (average 270 GeL; US$ 130) 30% is spent on food—non-subistence income covers expenditures on goods and services including health; 15% of population refuses health services
because of inability to pay; Public Spending on Health comprises 33% of total health expenditures; Public Spending on ID control is below 1 Gl. per capita; Almost all private spending goes to ID treatment and equals to 28.6 Gl. per patient.

Conclusions: Insufficient public spending on ID control transfers the burden to the population with extremely low capacity to cover health expenses. Refusal to utilize health services, and incomplete treatment and increases the threat of ID spread and drug resistance. Government should increase the allocations to ID from public sources for effective ID control in Georgia.

Antimicrobial consumption trends in children’s university hospital PS177

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Local surveillance of antimicrobial (AM) consumption is essential to promote the rational use of this group of drugs. The purpose of this study was to analyze the trends of AM use in the Children University Hospital in 1998 and 2000. Data on AM usage were obtained from the hospital drugstore requests in the 250-beds multi-ward Children University Hospital. Consumption was expressed as the number of DDD per 100 bed-days (b-d). The total AM consumption figures were similar in 1998 and 2000 (7.7 and 8.2 DDDs/100 b-d, respectively) with notable differences in AM prescribing patterns. Penicillin consumption increased from 1.8 to 3.8 DDDs/100 b-d mostly due to amoxicillin. The overall aminoglycoside usage remained comparable (0.95 vs. 0.82 DDDs/100 b-d) though amikacin has considerably replaced gentamicin. There was a sevenfold increase of ciprofloxacin (0.03 vs. 0.2 DDDs/100 b-d) along with the evident decrease of tetracycline and co-trimoxazole consumption found (1.5 vs. 0.9 DDDs/100 b-d and 0.8 vs. 0.1 DDDs/100 b-d, respectively). The tendency to prescribe more effective in respect of the local resistance data and/or more safe AM was detected in 2000 comparing with 1998 that can be explained by the introduction of the local guidelines for infectious diseases management in 1999.

Community-acquired infections

Clarithromycin in the treatment of chronic prostatitis caused by Chlamydia trachomatis—a pilot study PS178

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The aim of this study was to determine the efficacy and tolerability of clarithromycin in the treatment of chronic prostatitis caused by Chlamydia trachomatis (CT). Fifty-two patients older than 18 years of age with diagnosed chronic Chlamydial prostatitis were enrolled. The presence of CT in expressed prostatic secretion or urine specimen voided immediately after prostatic massage was confirmed by isolation on McCoy cells and Lugol staining. The majority of patients suffered from suprapubic pain and pain in the groin. Twelve patients had no clinical symptoms. According to rectal palpation, prostate gland was normal in 35 patients, tender and soft in 12 and firm in five patients. Clarithromycin was administered orally 500 mg twice daily for 14 days. Simultaneously the patients’ partners received 500 mg orally twice daily for 7 days. Clinical efficacy and tolerability of administered clarithromycin were evaluated 1–7 days and 4–6 weeks after the end of treatment. Bactericidal efficacy of administered drug was evaluated 4–6 weeks after the end of treatment. The eradication of CT was achieved in 30 out of 40 patients, while 28 patients were clinically cured. Two patients had nausea and elevated serum transaminases. In asymptomatic patients, the eradication of CT was achieved in 10 of 12 patients who reported no side effects. This pilot study has shown an excellent efficacy and tolerability of clarithromycin in the treatment of patients with chronic Chlamydial prostatitis.

Association of selected virulence factors with alpha-haemolytic Escherichia coli strains isolated from various clinical material PS179

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Women with diagnosis of urinary tract infections (UTI) often demonstrate vaginal colonisation with alpha-haemolytic Escherichia coli strains. In the present study we decided to evaluate a distribution of virulence genes encoding for cytotoxic necrotizing factor type 1 (cnf1), P-fimbriae, SF1C-fimbriae aerobactin (aer), and ala genes in alpha-haemolytic E. coli strains isolated from gynaecological material in our region and to compare the detected sequences in clinical isolates of other diagnostic groups. Of 127 alpha-haemolytic E. coli strains, 41 were isolated from urine, 44 from gynaecological specimen, and 42 were faecal strains. E. coli strains were tested for the production of haemolytic phenotype on blood agar plates. The amplification of virulence factors was performed by PCR according to previously described protocols (Le Bouguenec et al., 1992; Blanco et al., 1996; and Yamamoto et al., 1995). We found that all gynaecological alpha-haemolytic strains were positive for cnf1, (P < 0.001 compared to 78% of urine strains, and P < 0.0001 compared to 61% of faecal strains). Similarly, safaoc specific DNA sequences were found in 100% of gynaecological isolates (P = 0.01 compared to 85% of urine strains and P = 0.005 compared to 83% of faecal strains). From this point of view, the female genital tract seems to be a potential reservoir of these uropathogenic E. coli strains.

Azithromycin in the treatment of pelvic inflammatory disease caused by Chlamydia trachomatis PS180

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The aim of this study was to examine the efficacy and tolerability of parenteral administration of azithromycin in the treatment of pelvic inflammatory disease (PID) caused by Chlamydia trachomatis. In the period from November 1, 2000 to October 31, 2001, azithromycin was
administered in 35 hospitalized patients with chlamydial PID. The diagnosis was made prior to hospitalization. Microbiological analysis of urine, blood and swab specimens collected from endocervix, vagina and urethra confirmed C. trachomatis to be the single suspected causative pathogen of PID. The presence of C. trachomatis in swab specimens from endocervix was examined by DNK/RNK hybridization. Azithromycin was administered 5–7 days after samples for microbiological analysis were collected in dose of 1 x 500 mg iv for 5 days. Clinical efficacy and tolerability of therapy were assessed 1–7 days after the end of therapy and clinical and microbiological analysis 3–4 weeks after completion of therapy. The eradication of C. trachomatis and normalization of gynecological findings were achieved in 33 and disappearance of subjective symptoms in 30 patients. No side effects and deviations from normal values in hematologic and biochemical blood parameters were recorded. This study showed high bactericidal efficacy, rapid clinical effect and good tolerability of once-daily administration of 500 mg azithromycin for 5 days in the treatment of patients with PID caused by C. trachomatis.

A novel method for diagnosing vaginitis: AFFIRM VPHI PS181

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Diagnosis of the causative organism of the vaginitis is usually based on clinical criteria. A standardized, laboratory based and rapid diagnostic test for the identification of these organisms is desirable. To determine the laboratory method that best predicted the causative organism, we calculated the sensitivity, specificity and predictive value of positive and negative test for clinical criteria, an oligonucleotide probe test (AFFIRM VPHI-BD USA) and compared them with the combination of positive vaginal culture and Gram-stained vaginal smear. We evaluated 40 consecutive women aged 21–48 years, attending for vaginal discharge. Vaginal swab specimens were used for culture of Gardnerella vaginallis, Trichomonas vaginalis and Candida sp, preparation of a vaginal smear for Gram-stain interpretation and wet mount evaluation and AFFIRM test. AFFIRM detected G. vaginallis in 10 (25%), Candida sp in three (7.5%) women and no trichomoniasis case found by any methods. The sensitivity and negative predictive values of AFFIRM test and clinical signs were same (100%) in identifying of bacterial vaginosis. However, AFFIRM test was more specific (94 vs 72%) and also has higher positive predictive value (80 vs 53%) than clinical signs. We did not evaluate the results for patients with candidiasis because of less number.

According to these results AFFIRM-microbial identification tests are objective and specific for the rapid diagnosis of the bacterial vaginosis.

Comparison of efficacy of single dose of tinidazole with standard dose of metronidazole in Giardia lamblia infection (Preliminary report) PS182

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Objectives: Giardia lamblia is the most common intestinal protozoa in developing countries. Treatment of the infection with metronidazole, the drug of choice, requires a long course of therapy and produced some side effects. The object of this study is to determine efficacy and side effects of tinidazole in G. lamblia infection. This is a preliminary report of an ongoing trial.

Methods: A randomized controlled clinical trial was carried out and 47 subjects with G. lamblia infection were treated with tinidazole or metronidazole. Tinidazole 50 mg/kg single dose and metronidazole 25 mg/kg three times a day for 7 days were given orally to 24 and 23 children, respectively. Parasitological cure was documented when there were consecutive negative stool examinations at 1–2 weeks after therapy.

Results: Twenty-one of 23 individuals treated with tinidazole and 20 of 24 children treated with metronidazole had parasitological cure. Cure rates between two groups were not significant statistically. No major side effects were observed except one case in metronidazole group who had mild headache and abdominal pain for 2 days.

Conclusions: We concluded, tinidazole at the dose has efficacy equal of metronidazole in the treatment of G. lamblia infection. Because of single dose prescription, short course of therapy and good compliance of patients, this preparation is preferred to metronidazole in giardial infection.

Prophylactic effect of β-carotene against S. mansoni PS183

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β-Carotene was given in different doses starting from 2.5 to 10 mg/kg body weight (b.w.) for different groups of albino mice 4 days before infection with S. mansoni. Infection of animals was done by body immersion using 80 Egyptian strain of S. mansoni cercariae/mouse. Forty-nine days after infection the animals were sacrificed and hepatic and mesenteric worms were extracted and determined. Ova count in liver and intestinal tissue and the total number of worms/animals were also determined in experimental groups comparing with infected control animals. The results indicated marked decrease in number of worms and ova count in both liver and intestine comparing with control ones. This reduction increased significantly with increasing dose. It was concluded that β-carotene could be used as a prophylactic agent against S. mansoni infection.

Optimal choice of antimicrobial therapy for Pseudomonas aeruginosa urinary tract infections in outpatients PS184

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The aim of this study is to determine frequency of Pseudomonas aeruginosa urinary tract infection (UTI) in outpatient’s population in South Croatia and to suggest optimal antimicrobial treatment for these patients. During 3 months long observation period, from total number of 13158 examined urine specimens, significant bacteriuria was found in 2341 specimens. P. aeruginosa was the sixth most common isolate, it was isolated from 94 specimens (4.02%). These 94 specimens were taken from 57 different patients. Susceptibility testing was performed by disk diffusion method, and the following results were obtained: resistance to cefetobrun occurred in 94.74% patients, to norfloxacin in 49.12%, to ciprofloxacin in 47.37%, to gentamicin in 40.99%, to amikacin in 24.56%, to ceftazidine in 3.51% and to imipenem in 1.75% patients. P. aeruginosa strains showed better susceptibility to tested parenteral antibiotics than to antibiotics for oral use which complicated treatment in outpatients. The best susceptibility was shown to imipenem, but this drug is inappropriate for use in outpatients setting, so the best choice for treatment P. aeruginosa UTI in our outpatients is treatment with ceftazidine,
and the second choices are aminoglycoside drugs amikacin and netilmicin.

**Biofilm in patients with complicated urinary tract infection**  PS185

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We studied the clinical efficacy of oral treatment with ciprofloxacin/CPF/ alone and combined with clarithromycin in patients with complicated urinary tract infection/CUTI/ with or without an indwelling catheter. Patients were randomly allocated to 600 mg CPF/CPF group/ or to 600 mg CPF plus 600 mg CAM/combo group/ for 14 days. Evaluation was done on day 14 according to the criteria advocated by the Japanese Urinary Tract Infection Committee. In patients with a urinary catheter, the combination achieved a higher complete bacterial elimination rate /50/\(^{a}\) and clinical efficacy / 84/\(^{a}\) than CPF alone /30 and 61.5/\(^{a}\), respectively/. While no significant difference was found in the bacterial elimination rate between the two groups, the clinical effect of the combination /40/\(^{a}\) was superior to that of CPF alone /23/\(^{a}\) in patients with an indwelling catheter. The better clinical efficacy of the combination may partly be attributed to the antimicrobial effect of CAM in the clinical setting. The results also indicated that difficulties still remain in the treatment of CUTI in patients with an indwelling catheter. In conclusion, clinical study suggested that CAM might have an inhibitory action on biofilm formation in the clinical setting. Combination of CAM with other appropriate antimicrobial agents may have a favorable effect on the treatment of CUTI.

**Vesicoureteral reflux and urinary tract infections— the management of primary vesico-ureteral reflux in children**  PS186

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The children studied presented with primary vesicoureteral reflux at Derer's University Hospital in Bratislava between 1974 and 1994. Seven hundred and sixty patients, 179 boys and 581 girls, suffering from primary vesicoureteral reflux in age from 6 months to 18 years were tested and systematically analyzed outcomes data for seven treatment alternatives. Key outcomes identified were probability of reflux resolution, likelihood of developing pyelonephritis and scarring, and possibility of complications of medical and surgical treatment. Available outcomes data on the various treatment alternatives were summarized and the relative probabilities of possible outcomes were compared for each alternative.

**Conclusions:**

1) Increased of urinary tract infection, vesicoureteral reflux nephropathy includes early diagnosis, appropriate evaluation, effective ATB therapy, and surgery indicated.

2) The main determinants of renal damage are bstruction, age, sex, predisposition on renal scarring, reflux grade and laterality, therapeutic delay, individual susceptibility, bacterial virulence and immunogenetic status.

3) The one and only absolute indication for surgical management is failure of medical therapy to prevent chronic recurrent pyelonephritis, renal injury or other reflux complications and eliminations of the reflux condition will minimize their likelihood.

4) Genetically conditioned immunopathogenic mechanisms are involved in the pathogenesis of the chronic recurrent pyelonephritis in patient suffering from VUR.

5) For most children we recommended continuous antibiotic prophylaxis as initial treatment-medical therapy is based on the principle that reflux often resolves with time, and antibiotics maintain urine sterility and prevent infections while the patients awaits spontaneous resolution.

6) VUR predispose an individual to renal infection, the immunological and inflammatory reaction caused by a pyelonephritic infection may result in renal injury or scarring.

**Urinary tract infections in the elderly**  PS187

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Elderly patients with UTI are believed less likely to be cured by antimicrobial therapy than younger patients. The reasons for this poorer outcome have not yet been clarified. We have investigated the efficacy of antimicrobial therapy in elderly patients with complicated UTI. Five hundred patients, 260 men and 240 women, who had complicated UTI/268 symptomatic and 240 symptomatic and were 21–80 years of age, were treated with one of three different drugs, one was a never quinolone and two were oral cephems. Multivariate logistic regression analysis of treatment outcome revealed that the clinical response was significantly related to general underlying diseases and diseases of the urinary tract, but not to age, symptomatic or asymptomatic UTI, or infection site such as the kidney or bladder. We concluded that the clinical effectiveness of an antimicrobial agent was not directly related to age, and that urological examination for underlying disease and control of them is quite important for effective treatment and control of complicated UTIs, especially in elderly patients.

**The study on the frequency and antimicrobial resistance of Escherichia (E) coli in urine isolates of patients admitted to Maribor Teaching Hospital in 1998 and 2000**  PS188

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**Purpose:** The aim of the study was to determine the frequency and antimicrobial resistance of *Escherichia coli* isolated from urine samples of patients admitted to Maribor Teaching Hospital in 1998 and 2000. The frequency and the antimicrobial resistance were compared between years 1998 and 2000.

**Methods:** In the prospective study going on between 1998 and 2000, all urine isolates from patients at Maribor Teaching Hospital were collected and analysed. Urine cultures were done using the modified Sanford method. The susceptibility testing was performed by disk diffusion method according to NCCLS.

**Results:** In the year 1998, 2563 urine isolates and in the year 2000, 2325 urine isolates were analysed. *E. coli* represented 39.1% of urine isolates in 1998 and 39.4% of urine isolates in 2000.
E. coli resistance rates (%) to amoxycillin was 39.5 in the year 1998 and 38.4 in the year 2000; to amoxycillin/clavulenate was 15.4 and 10.5; to cefotaxin was 7.8 and 5.7; to cefaclor 2.8 and 2.18; to trimethoprim sulfamethoxazole was 15.0 and 18.4; to ciprofloxacin was 4.9 and 6.9; to gentamicin was 2.3 and 2.2. The frequency of E. coli isolated from urine samples is similar to that in the year 2000. The resistance to amoxycillin, cefaclor and gentamicin is stable. The resistance to trimethoprim sulfamethoxazole and ciprofloxacin is increased and the resistance to amoxycillin/clavulenate and cefotaxin is decreased.

Prevalence of the resistance to metronidazole, furazolidone and nitrofurantoin in Helicobacter pylori clinical strains PS189

de la Obra Sanz P, Roman JL, Lomas E, Villar H, Lopez-Brea M.

The objective of this study was to determine the prevalence of metronidazole, furazolidone and nitrofurantoin resistance in Helicobacter pylori clinical isolates. Methods: A total of 286 strains of H. pylori were included in this study. All these were tested against metronidazole, and 164 against furazolidone and nitrofurantoin by an agar dilution method. Resistance was defined as: metronidazole, MIC > 8 mg/l, and MIC > 4 mg/l for furazolidone and nitrofurantoin. Results: Sixty-eight strains were resistant to metronidazole (23.8%). The MIC50 and MIC90 values were 1 and 32 mg/l, respectively. Three of 164 strains (1.8%) were furazolidone resistant (MIC = 4 mg/l), two of these strains were metronidazole resistant (MIC = 16 mg/l) and they had MIC of 2 mg/l for nitrofurantoin. The MIC50 and the MIC90 were 0.125 and 0.5 mg/l, respectively for furazolidone. Only one of the 164 strains (0.6%) was nitrofurantoin resistant (MIC 4 mg/l), this strain was metronidazole resistant (MIC 128 mg/l) and it had MIC = 1 mg/l for furazolidone. The MIC50 and the MIC90 were 0.5 and 1 mg/l, respectively for nitrofurantoin. Conclusion: The low frequency of furazolidone and nitrofurantoin resistance, compared to metronidazole suggests that the furazolidone and the nitrofurantoin may be good alternatives to metronidazole for treatment of H. pylori infections.

Antimicrobial resistance of Campylobacter isolated from human origins PS190

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The purpose of the study was to determine the antimicrobial resistance of 50 thermophilic enteropathogenic Campylobacter spp. (TEC) isolated from human under acute diarrhoea in 2001 in Moscow. Among 50 TEC strains 45 C. jejuni and five C. coli were identified. The antibiotic tested by disk diffusion test on Mueller-Hinton agar with sheep blood were ampicillin (A), amoxycillin/clavulanate (AC), imipenem (I), meropenem (M), erythromycin (E), clarithromycin (Cl), tetracycline (T), doxycycline (D), gentamicin (G), azithromycin (Az), chloramphenicol (Ch), lincomeyin (L), ciprofloxacin (C), nalidixic acid (NA). The resistant rate of the TEC isolates was highest for NA (42%) followed by A (38%), T (36%), D (20%), N (20%) and Cl (16%). A moderate resistance rate was obtained for A (8%), Ch (6%), Az (6%), AC (2%). None of the isolates demonstrated resistance to M and G and four of 50 isolates (8%) were sensitive for all the antibiotics tested. MIC90 to NA was estimated as 64 mg/l. Among 21 NA resistant TEC strains 20 (95%) were identified as C. jejuni and one (2%) as C. coli. Among C. jejuni and C. coli NA resistant rate was 44 and 20%, respectively. One NA resistant C. coli and nine NA resistant C. jejuni were resistant to ciprofloxacin.

Resistance of Salmonella isolates from poultry meat to various antibiotics PS191

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Aim of the study: Poultry meat is known to be often contaminated with Salmonella and other foodborne pathogens and thus has to be considered as a possible source for human infections. The aim of the study was to monitor the resistance of Salmonella isolates from poultry meat of different European countries to various antibiotics. Material and methods: From September 2001 to December 2001 a total of 422 samples of frozen poultry meat from France, Germany, Italy, Spain, The Netherlands and Portugal were examined for the prevalence of Salmonella using classical cultural detection as well as RFLP-PCR. All isolates were tested for their sensitivity towards ampicillin, kanamycin, ciprofloxacin, tetracycline, trimethoprim, sulfamethoxazole, nalidixic acid and erythromycin using standard procedures. Results: From 18.01% of all examined samples Salmonella spp. were isolated. Of these isolates 32.9% were characterized as Salmonella, 42.1% as S. hadar and 17.1% as S. typhimurium. Nearly 100% of all isolates were resistant to erythromycin. Resistance towards four or more isolates was observed in several cases. Discussion: The consumption of poultry meat, if insufficiently prepared, has still to be considered as a major source for human infection with Salmonella spp. The question arises whether the resistance of the isolates to various antibiotics is of clinical importance in the treatment of the patients.

Epidemiological aspects of Salmonella carriers and Salmonella resistance to the antibiotics PS192

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Objective: To provide insight into the epidemiologic situation of Salmonellosis for the Nis area (the largest area in Serbia, with inhabitants—648,000).

Methods: The material was processed at the Institute for Public Health (Epidemiology and Microbiology divisions). Isolation of microorganisms was performed on apparatus for rapid identification (Vitek-Biomerieux) and by applying ELISA tests and classical microbiological methods.

Results: In the period 1992–2000, 2857 Salmonella laboratory confirmed cases were reported. The greatest number of disease in the 0–4 years group. The most frequent isolated salmonellae were: S. enteritidis (83.7%) and S. typhimurium (11.25%), S. hadar, S. agona, S. virchow, S. infantis, S. derby, S. enteritidis showed the greatest sensitivity to antibiotics with the infrequent resistance to ampicillin and trimethoprim-sulfamethoxazole. S. typhimurium showed the greater resistance to the wide spectrum of antibiotics and some isolates were resistant to all antibiotics tested. The less common types of Salmonella were sensitive to all antibiotics except trimethoprim-sulfamethoxazole and ampicillin.

Conclusion: Specific resistance to some antibiotics was related to serotypes.

Typhoid fever—retrospective study of 52 cases in Lebanon PS193

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Objectives: To present epidemiological and clinical features of typhoid fever in Lebanon.

Methods: Fifty-two patients were seen at Hotel-Dieu Hospital of
Beirut between 1995 and 1999. Diagnostic criteria were positive blood culture for *S. typhi* or paratyphi and/or a somatic O agglutinin titer ≥ 1/160 as determined by the Widal test with symptoms suggestive of typhoid fever. We also present an epidemiological study of 3864 cases registered by the Ministry of Health during the same period.

**Results:** Among the 3864 cases, 40% of the patients’ ages were between 15 and 40 years and 33% were less than 14 years. The overall male to female ratio was 0.98 and 24% of cases were seen on January, February and November. Among the 52 patients, young adults were the most affected. Average duration of symptoms before the diagnosis was 10 ± 8 days. The main presenting symptoms were fever (96%), diarrhea (37%), abdominal pain (31%) and headache (29%). Complications were noted in 33% of cases and digestive complications were the most prevalent. Leucopenia was not a helpful diagnostic marker. *S. typhi* was the most frequent (84%) serotype identified. Resistance to ampicillin was 13%, to cotrimoxazole and chloramphenicol 10% for each. The mortality rate was 2%.

**Conclusion:** Typhoid fever is still an endemic disease in our country and the occurrence of resistant strains of *S. typhi* will favor ceftriaxone or fluoroquinolones in the treatment.

**Psoas abscess (about 25 cases) PS194**

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Although it is not very frequent, the psoas abscess is not an exceptional entity. In order to specify its clinical, biological, radiological and evolutionary features, a retrospective study has been led in our service, on a period of 14 years (January 1988 – December 2001). On the whole, 25 cases have been listed. They were 16 men and 9 women. The age average was 40 years (extreme 14–74 years). The study did not find any underlying diseases, except diabetes mellitus for three patients. The clinical symptoms were dominated by fever with abdomino-lumbar aches (20 cases), and poitios (eight cases). Biology showed an inflammatory syndrome in all cases and a hyperleucocytosis in 17 cases.

The diagnosis of psoas abscess, evoked on clinical data, has been confirmed by the imagery data: Ultra-Songraphy (16 cases), CT scanning (six cases), Magnetic Resonance Imaging (three cases).

The tubercular etiology has been confirmed in six cases, among which two were associated to *Escherichia coli* (one case) and to *Brucella melitensis* (one case). The other etiologic agents were dominated by *Staphylococcus aureus* (eight cases), *B. melitensis* (two cases), *E. coli* (one case), *Bacteroides fragilis* (one case), *Streptococcus anginosus* (one case), *Fusobacterium nucleatum* (one case) and *Candida glabrata* (one case).

All patients received an anti-infectious treatment adapted to the micro organism in question. A drainage of the abscess has been realized for 15 patients (percutaneous: nine cases, surgical: six cases). The evolution was favourable for 23 patients. However, two patients had a relapse after stopping the treatment.

**Conclusion:** The diagnosis of the psoas abscess, difficult on the clinical data, is based on the imagery techniques (US, CT, RMI). The percutaneous drainage guided by the imagery is recommended (in an etiologic and therapeutic aim). Associated to an adapted antibiotherapy, it allows to defer a surgical drainage.

**Abdominal changes in patients with human brucellosis PS195**

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Purpose: To make a list of the most frequent abdominal changes in patients with human brucellosis.

**Materials and methods:** There were 769 new patients with human brucellosis, between 01 1991 and 12 2001. Diagnosis was made based on standard clinical, biochemical and serological investigations (BAB, Wright, COOMBS, RVK, 2-mercaptoethanol, ELISA IgM and IgG), and specially ultrasound examination of the abdomen and retro peritoneum.

**Results:** Weight loss is the most frequent change, presented in 665 (86.5%) patients. Follow atypical abdominal pain in 89 (5.3%), vomiting in 59 (7.7%), diarrhea in 44 (5.3%), enlarged liver in 594 (77.2%), enlarged spleen in 573 (74.5%) and hepatic lesion with increased AST and ALT in 174 (22.6%).

**Conclusion:** Although frequent, abdominal changes seldom could be missed in patients with human brucellosis. We recommend routine ultrasound examination with standard biochemical test for liver function, due to avoid unnecessary complications.

**Importance of C-reactive protein in Brucella sacroilutis PS196**

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Osteoarticular complications are common in Brucellosis. The most common site of involvement is the sacroiliac joint. The osteoarticular complications such as, sacroilitis and spondylitis are diagnosed with radiologically. In the present study, we aimed to determine the severity (grade) of sacroilitis by using some laboratory parameters such as ESR, CRP and tube agg test. Seventy-two (34 male, 38 female) patients with Brucellosis were included in the study. Osteoarticular involvement was present in 44 patients. The most common osteoarticular finding was sacroilitis in the patients (86%). Twenty (20) healthy subjects were formed the control group. There was statistically significant difference between patients and controls regarding ESR, CRP, and tube agg test (P = 0.000, 0.0017, 0.000, respectively). In addition, sacroilitis has an effect on ESR and CRP. There was a positive correlation between the grade of sacroilitis and the value of CRP (P = 0.006, r = 0.414). In conclusion, it has been suggested that, CRP may be used as an auxiliary or a secondary parameter in grading sacroiliac joint involvement in Brucellosis.

**Epididymoorchitis and spondylitis due to Brucella melitensis PS197**

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A 65-year-old Greek farmer was admitted to the hospital because of painful scrotal swelling, hepatosplenomegaly, lumbar pain and low-grade fever accompanied by profuse sweating. His life style included occupational animal exposure ingestion of raw milk and dairy products. The laboratory data were within the normal ranges. Focal hypoechoic right testicular lesions, swelling of the concurrent epididymis along with an increase in the vascularity of the right testis were seen on an Echo examination. These findings were consisting in unilateral epididimo-orchitis. A CT scan of the lumbar spine area showed a decrease of the signal intensity localized in the anterior
Complications and focal forms of Brucellosis  PS198

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Aims and scope: To determine the incidence and forms of complications associated with Brucella infection.

Patients and methods: We studied the 100 most recent patients, in all larger series approaching 1000, diagnosed as suffering from Brucellosis, and assessed the presence of signs and symptoms of arthritis and spondylitis, or other forms of bone involvement. The diagnosis of Brucellosis was based on serology or isolation of Brucella species from blood cultures or cultures from other media.

Results: Osteoarticular complications were noted in 23 patients, 13 presenting with arthritis, and 10 presenting with spondylitis. Eight patients presented with genitourinary complications, either orchepoepididymitis (four patients), or hematuria resolving with treatment (four patients). Meningitis was present in two patients. Gastrointestinal complications (vomit and diarrhea) were present in three patients, while one patient presented with ascites. Respiratory tract complications, in the form of pneumonia (four patients) or bronchitis (three patients) were noted in seven patients, while one patient with pneumonia exhibited pleural fluid. Skin rashes, of macular type, were present in three patients. No patient presented with complications from the heart. Hematologic complications were frequent, in the form of severe (one patient) or moderate (two patients) pancytopenia, isolated thrombocytopenia (three patients), or lymphocytosis (eight patients).

Osteoarticular complications of Brucellosis  PS199

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Aims and scope: To determine the incidence and modes of bone and joint involvement in the course of Brucellosis.

Patients and methods: We studied the 100 most recent patients, in all larger series approaching 1000, diagnosed with Brucellosis, and assessed the presence of arthritis and spondylitis. The diagnosis of brucellosis was based on serology or isolation of Brucella species from blood cultures.

Results: Twenty-three patients exhibited a form of osteoarticular involvement. Arthritis was present in 13 patients, most often involving the knees, but also the hips, elbows, even smaller joints as interphalangeal joints of the hand. Synovial fluid, when aspirated, was often characterised by an intense mononuclear infiltrate. Spondylitis was present in 10 patients, most often involving the lumbar spine, but also the thoracic spine. The characteristic erosion on the upper anterior crest of the vertebral body was visible in plain X-rays in three patients, while MRI and bone scan were helpful in other cases.

Discussion: Osteoarticular involvement in the course of brucellosis is the most common focal presentation of the disease. Acute brucellosis is often accompanied by bone and joint ache, especially of the lumbar spine, still frank involvement in the form of arthritis and spondylitis is not rare. Arthritis usually presents in the acute form of the disease, while spondylitis tends to be characteristic of a chronic form of the disease, often necessitating prolonged use of antibiotics.
doxycycline seems to be promising, because chloroquine may increase the lysosomal pH, enhancing the doxycycline bactericidal activity.

**Abstracts**

**Neurological manifestations in murine typhus: a study of 84 cases**  
Bompolaki I, Doukakis S, Triantafillidou D, Polimili G, Kastanakis M, Nikiforakis K, Vittorakis E, Kastanakis S. *First Medical Department, ‘Saint George’ General Hospital, Chania, Greece*

A severe frontal and/or retroorbital headache represents the most common neurologic manifestation of murine typhus. Other neurologic manifestations as confusion, stupor, nuchal rigidity and in severe cases delirium, extreme agitation or coma appear less commonly. Eighty-four patients with compatible clinical status of murine typhus and high serological titers of antibodies against *Rickettsia typhi*, were studied from our team. Seventy-four patients (88%) presented headache and nine patients (11%) presented confusion. One patient (1.1%) presented nuchal rigidity in combination with severe headache and confusion giving us the suspicion of meningitis. In this case a lumbar puncture was performed emergently and the cerebrospinal fluid (CSF) was examined. The findings of CSF were proteins: 9 mg/dl, WBC: 16/ml and glucose: 73 mg/dl and its culture was negative. All patients were treated with a specific anti-rickettsial treatment. The outcome of murine typhus was favorable for all 84 patients (100%). No one patient presented neurologic sequelae.

**Conjunctivitis in murine typhus: a study of 83 cases**  
Doukakis S, Bambili K, Triantafillidou D, Vittorakis E, Bompolaki I, Kastanakis M, Evagelopoulos A, Kastanakis S. *First Medical Department, ‘Saint George’ General Hospital, Chania, Greece*

Conjunctivitis usually accompany rickettsial diseases such as Rocky Mountain spotted fever, epidemic typhus and murine typhus. Eighty-three patients with compatible clinical status of murine typhus and high serological titers of antibodies against *Rickettsia typhi*, were studied from our team, during a period of time between January 1993 and the first semester of 1998. The clinical examination of these patients revealed the presence of conjunctivitis in 21/83 patients (25.6%). In the same time these patients referred retroocular pain and mild photophobia. This study showed that in murine typhus the injection of conjunctivae is rather common. Almost a quarter of the patients presented conjunctivitis despite the fact, that this ocular manifestation is less severe than in other typhus and spotted fevers.

**Blood picture in murine typhus: a study of 83 cases**  
Doukakis S, Bambili K, Polimili G, Girousis N, Kastanakis M, Vittorakis E, Bompolaki I, Tomazinakis I, Kastanakis S. *First Medical Department, ‘Saint George’ General Hospital, Chania, Greece*

Eighty-three patients with compatible clinical status of murine typhus and high serological titers of antibodies against *Rickettsia typhi*, were studied from our team, during a period of time between January 1993 and the first semester of 1998. Three blood samples were obtained from each patient for the study of their hematological abnormalities. The first sample was obtained on admission, the second sample 2 weeks after the first, the third sample, 1 month after the second. On admission 26/83 patients (31%) presented anemia, 6/83 patients (7%) presented leukopenia and 42/83 patients (51%) presented thrombocytopenia. The mean value of hematocrit, white blood cells and platelets was 12.4 g/dl, 6.1 x 10^3 and 147 x 10^3/ml, respectively. Two weeks later anemia was presented in 45/83 patients (54%), 3/83 patients (4%) presented thrombocytopenia, 3/83 patients (4%) presented
leucocytosis and 15/83 patients (18%) presented thrombocytopenia. The mean value of hematocrit, white blood cells and platelets was 11.3 g/dl, 7.0 x 10^3 and 248 x 10^3/μl, respectively. One month later 11/82 patients (26%) had anemia and 2/82 patients (5%) presented thrombocytopenia. The mean value of hematocrit, white blood cells and platelets was 12.4 g/dl, 6.4 x 10^3 and 242 x 10^3/μl, respectively. Our study showed that early thrombocytopenia and anemia are frequent in murine typhus and that white blood cells count is usually normal.

Renal function in murine typhus: a study of 83 cases  PS207

Doukakis S, Polimili G, Triantafillidou D, Kastanakis M, Vittorakis E, Pall A, Kastanakis S. First Medical Department, 'Saint George' General Hospital, Chania, Greece

The clinical course of murine typhus is usually uncomplicated and the mortality rate is low (< 1%). Advanced age and prolonged interval before administration of a specific anti-rickettsial treatment are correlated with severity of the disease. Renal function in murine typhus is usually unaltered except in elderly patients with prolonged hypotension. Eighty-three patients with compatible clinical status of murine typhus and high serological titres of antibodies against Rickettsia typhi, were studied from our team, during a period of time between January 1993 and the first semester of 1998. Three blood samples were obtained from each patient for the study of their renal function. The first sample was obtained on admission, the second sample approximately 2 weeks after the first, the third sample, taken from the half of the patients, was obtained one month after the second. On admission 4/83 patients (5.0%) presented acute renal failure. The outcome of murine typhus was favourable for all 83 patients (100%). The four patients who presented acute renal failure reversed after the administration of anti-rickettsial treatment and careful administration of fluids. In murine typhus the induction of hypovolaemia insufficiently corrected by normal homeostatic mechanisms may lead to pre-renal azotaemia. In these cases the immediate onset of an anti-rickettsial treatment and the correction of hypovolaemia are essential for the rapid clinical improvement of the patient.

Experimental ocular toxoplasmosic clinical, histopathological, immunological and therapeutic studies  PS208

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The purpose of the study was to investigate clinical, histopathological, immunological and therapeutic features of an experimental model of ocular toxoplasmosis in sensitized and non sensitized rabbits and to assess the influence of treatment by interleukin2 (IL-2) on ocular lesions. The results obtained was that 'Toxoplasma' retinchoroiditis developed in both groups of rabbits with more pronounced effect in non sensitized animals. Administration of IL-2 improved ocular lesions in both groups with more evident effect in sensitized rabbits. Immunological findings were consistent with clinical and histopathological observations. The conclusion reached was that; ocular lesions were manifested in non sensitized rabbits more than in sensitized ones. IL-2 revealed a significant impact on improving the host defense against toxoplasmosis in eye. Immunotherapy with IL-2 would open the way for a new range of treatment based on immunomodulation.

Express-diagnostic of Streptococcus antigen for the adequate antibiotic therapy in patients with pharyngitis  PS209

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The purpose of the study: Evaluation of effectiveness of Streptococcus express-diagnostic for the adequate antibiotic therapy in patients with pharyngitis.

Results: We deal with clinical and microbiological comparison in 53 patients with pharyngitis. Using of Streptococcus antigen express diagnostic in swabs from the backside of pharynx allowed to get positive results in the last cases (13.2%). Following cultural study has confirmed these results. Positive test was more probable in patients with pronounced fever (more than 38 °C), headache, weakness and in cases associated with chronic tonsillitis. Isolated Streptococcus pyogenes was susceptible to ampicillin, claritromicin, erytromycin, azitromycin, clindamycin, ceftriaxon, levafloxacín, oxacillin, cefuroxim, roxytromicin.

Conclusion: Using of the express diagnostic of Streptococcus antigen allows to restrict groundless prescription of antibiotic therapy in patients with other types pharyngitis (i.e. viral, candidal etc.).

Necrotising soft tissue infections as a complication of chickenpox: three case reports  PS210

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Chickenpox is a common viral infection that usually follows a benign, self limited course in healthy children. The most common complication in children with varicella is superimposed cutaneous infections with pyogenic bacteria (Streptococcus pyogenes and Staphylococcus aureus). Varicella gangrenosum, a necrotising soft tissue infection complicating the vesicular eruption of chickenpox, is rare. Here we present three cases with necrotising soft tissue infections following chicken pox.

These children were admitted because of common crusted lesions and necrotising soft tissue infection over the neck, the back, and the inguinal area. They all had the contact history and ensuing vesiculo-papular rash. These infections were caused by group A streptococci in two cases, and S. aureus in one case. After instituting of appropriate antibiotic therapy, each patient underwent a surgical exploration with fasciotomies and debridement.

Widespread use of varicella vaccine may decrease invasive infections in children, adolescents, and adults, thus decreasing the burden the disease with its complications impose up on the family and the society.

Cefprozil in the treatment of Streptococcal tonsillopharyngitis in 58 children and adolescents  PS211

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Cefprozil is a second generation cephalosporin. The aim of this open, multicentre, non-comparative study was to investigate the efficacy and safety of cefprozil in the treatment of streptococcal tonsillopharyngitis. Fifty-eight patients were clinically assessed for signs and symptoms of streptococcal infection. Laboratory confirm-
Successful treatment of craniocervical necrotizing fasciitis (CCNF) with antibiotics+rHuGM-CSF at our hospital from January 1997 to December 2001 was performed. Five patients were identified with the diagnosis of CCNF. Ages ranged from 33 to 71 years; there were three women and two men. Dental infection was the most common source of CCNF in 90%.

Objectives: To describe the features of the cases with acute meningitis in adults who were admitted at a general hospital of Athens, Greece.

Methods: We studied the cases of patients > 15 years of age who presented with acute meningitis during the period of January 1997 to December 2001.
community acquired meningitis was diagnosed at Red Cross Hospital of Athens, Greece, during 2000–2001.

Results: Forty-eight patients were included in this study. The etiological agents were: viral (n = 26, 54.2%, mean (x) age = 28 years), Streptococcus pneumoniae (n = 8, 16.6%, x age = 53), Neisseria meningitidis (n = 7, 14.6%, x age = 28), S. viridans (n = 6, 12%, x age = 34), P. multocida (n = 1, age 75). The peak incidence of bacterial meningitis was in winter (pneumococcal 73%, meningococcal 86%, s. viridans 83%). The cerebrospinal fluid (CSF) findings in viral meningitis were: x white cells 340/mm3, x PMN = 27%, x glucose CSF/ serum 0.55, x protein 39 mg/dl and in bacterial meningitis were: x white cells = 5800/mm3, x PMN = 80%, x glucose CSF/ serum = 0.2, x protein = 350 mg/dl, Gram stain was positive in 55%, culture was positive in 45%. All pneumococcal and meningococcal strains were susceptible to penicillin. The case fatality rates for pneumococcal and meningococcal meningitis were 25 and 14.3%, respectively. Conclusions: The cases of bacterial meningitis were according to typical epidemiological features of age and season. The case fatality rate of pneumococcal meningitis appear to be high regardless of susceptibility to penicillin. None had received pneumococcal vaccine prior to becoming ill.

Diagnosis and therapy of meningococcal meningitis—trend and particularities of a ‘Romanian model’  PS216

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Background: Newer diagnosis methods and antimicrobials are expected to change the management of meningococcal meningitis (MM) and to improve its prognosis. Objectives: To determine the changes in the diagnosis methods and therapy of MM patients in a Infectious Diseases Hospital. To compare MM management in Bucharest with literature data.

Methods: Retrospective review of MM in adult patients hospitalized over a 6-year period. Our results were compared with other studies made in the 90s, taken from MEDLINE.

Results: There were 97 episodes of MM during the study period (52 episodes in 1995–1997 and 43 episodes in 1998–2000). We noticed a defined diagnosis increase and increased blood culture specificity. The antimicrobial monotherapy was maintained but penicillin was replaced by ceftriaxone. HHC was replaced by dexamethasone in pathogenic therapy. We noticed a shorter length of treatment and a reduced lethality. The most important differences between our results and other studies are: monotherapy regimens are less frequent and therapy lengths are longer; however, prognosis is similar.

Conclusions: The MM management has been modified in the last 3–4 years: prognosis is improved, but the changes do not bring clear cost/ effective benefits.

Tunisia: infective endocarditis of 108 cases  PS217

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Objectives: In order to study epidemiological, clinical and therapeutical characteristics of the infective endocarditis (IE).

Methods: We reviewed all the cases of IE fulfilling the Duke criteria. Data were collected during a 19-year period (1980–1998) in the unit of infectious diseases.

Results: One hundred and eight episodes were identified. The mean age was 45 years. Sex ratio was 0.8. Eighty-five IE (76.8%) occurred in patients with native valve, and 23 IE (21.4%) with prosthetic valve. Fever was the most common sign, 12% had a congestive heart failure, 26.9% had cutaneous signs. The most common primary focus of IE was orthodontic. Blood cultures were positive in 63% of cases. In one case, serological test identified Rickettsia conorii. Streptococci and staphylococci were isolated in 27.8 and 25.9%, respectively. Echocardiography detected abnormalities in 63.4% of cases. Rheumatic heart disease was the most predisposing condition. Empirical therapy was based on combination of b lactam with aminoglycoside. Recovery was obtained for 60 patients. Cardiac surgery was performed in 26 cases. Overall mortality rate was 19.4%.

Conclusion: IE affects young persons. Prevention needs eradication of acute rheumatic arthritis.

A major outbreak of Legionnaires’ disease in Spain: diagnostics aspects  PS218

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Objective: To evaluate the value of different methods (serological tests, culture of respiratory secretions, blood cultures and urinary antigen testing) for the diagnosis of Legionella pneumophila pneumonia during an outbreak in Spain.

Results: We have studied 542 patients from a recent outbreak of legionellosis in Murcia (Spain). The diagnosis was achieved in 305 patients. Urinary antigens were positive in 187 patients. In the 355 patients with urinary antigen negative the serological response was demonstrated by indirect immunofluorescence (IFA) in 118 patients. All Blood cultures processed were negative. Sputum samples were obtained from 154 patients, of these L. pneumophila was isolated only in six patients. In all of them direct immunofluorescence test (DFA) was positive.

Conclusions: Although the serological diagnosis was the most sensitive method the urinary antigen testing was of great value in the rapid diagnosis of the legionella’s outbreak in Murcia. The isolation of L. pneumophila by culture showed a poor sensitivity probably because of the low severity of the illness.

Chloramphenicol as a first choice antibiotic in treatment of purulent meningitis  PS219

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Purpose: To evaluate chloramphenicol for an initial empiric antibiotic treatment of purulent meningitis in adults. Study group: One hundred and twenty patients hospitalized for the diagnosis purulent meningitis in the department in years 1997–2000, 67 males and 53 females, age range 15–81 years, mean age 52.6 years. Children up to 15 years were not included.

Method: A retrospective analysis of the study group focused on antibiotic treatment both initial and changes during treatment.

Results: Chloramphenicol was used as an initial antibiotic in 59 (49%), 3rd generation cephalosporin in 30 (25%), penicillin in 21 (17%), ampicillin in five (4%) and other antibiotic in five (4%), respectively. During treatment chloramphenicol was switched for 3rd gen cephalosporin in seven of 23 patients with Streptococcus pneumoniae meningitis and in five of 28 patients with meningitis of unknown etiology. The reason for the change was non-improving CSF formula in three, persisting CSF culture positivity in two and persisting coma in seven patients.
Conclusion: Because of repeated necessity to switch chloramphenicol for 3rd gen cephalosporin during treatment of purulent meningitis of pneumococcal and unknown etiology the initial treatment strategy was changed in 2001. Third gen cephalosporin is now used as a first choice antibiotic, what is in consent with international recommendations of treatment. To evaluate and compare groups treated initially with chloramphenicol and with 3rd gen cephalosporin will need several more years.

Low prevalence of multi-drug resistant Mycobacterium tuberculosis in Jerez de la Frontera-Cadiz (SPAIN) PS220

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Introduction and aim: Previous reports indicate that multi-drug resistance Mycobacterium tuberculosis (MTB) is an worldwide problem. The aim of this study was to review the resistance of MTB to the first-line antimycobacterial agents in our area.

Material and methods: Over a period of 4 years (1998–2001), 151 strains of MTB isolated from non-treated patients with tuberculosis (38 strain in 1998, 48 in 1999, 37 in 2000 and 28 in 2001) were studied. These isolates were tested for in vitro drugs susceptibility to Isoniacid-1, Rifampicin-R, Streptomycin-S and Ethambutol-E using the Bact/Alert method (Organon Teknika) as described by the manufacturer.

Results: Our results showed that 10.6% (16/151) strains were resistant to one or more drugs. Single drug resistances were detected on nine strains to I (6.3%), one to R (0.66%), two to S (1.3%), one to E (0.66%). Three MTB strains were resistant to more than one drug but only one was multi-drug resistant (I-R). The incidence of I-resistant strains over the period fell from 13% in 1998 to 3.6% in 2001.

Conclusions: (1) Multi-drug resistance is not an important problem in our area. (2) Isoniacid resistance was declined to an admissible level.

Resistence of Mycobacterium tuberculosis to anti-tuberculosis drugs in Greece PS221

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Purpose: To study the problem of resistant tuberculosis in Greece. Materials and Methods: One hundred and seven cases of non-HIV TBC infections hospitalized since 1997 in our service. Sputum and other biological materials were cultured. We studied the sensitivity to pyrazinamide (PZ), streptomycin (SM), isoniazid (INH), rifambicin (RIF) and ethambutol (EMB) using the radiometric method BACTEC.

Results: (a) Overall resistance PZ: 11.21% (12 patients), SM: 17.75% (19 patients), INH: 17.75% (19 patients), RIF: 12.15% (13 patients), EMB: 8.41% (nine patients). (b) Resistance to one drug: 6.54% (seven patients) PZ: 0.0%, SM: 2.8% (three patients), INH: 2.8% (three patients), RIF: 0.9% (one patient), EMB: 0.0%. (c) Resistance to two drugs: 4.67% (five patients) SM-INH: 2.8% (three patients), PZ-SM: 0.93% (one patient), INH-RIF: 0.93% (one patient). (d) Multi-resistance—two drugs: 4.67% (five patients) SM-INH-RIF: 1.87% (two patients), PZ-SM-INH: 0.93% (one patient), PZ-INH-EMB: 0.93% (one patient), PZ-SM-EMB: 0.93% (one patient)—to four drugs: 0.93% (one patient) PZ-SM-INH-EMB—to all (five) drugs: 5.61% (six patients) PZ-SM-INH-RIF-EMB.

Conclusion: The observed high resistance, probably due to the large number of immigrants during the last years, imposes continuous surveillance.

The decline of high drug resistance rate of pulmonary Mycobacterium tuberculosis isolates from a Southern Taiwan medical centre, 1996–2000 PS222

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To investigate the anti-tuberculosis drug resistance pattern of pulmonary tuberculosis isolates in southern Taiwan, an area with higher tuberculosis incidence and mortality than other regions of the island, we performed a hospital-based surveillance at a southern Taiwan medical center from 1996 to 2000. The combined drug resistance rates to at least one of five first-line agents was 84.8%, and to both isoniazid and rifampin (multi-drug resistance, MDR) was 11.4%, indicating high resistance rates compared with those reported in the WHO/UITLDL global project and in northern Taiwan. The resistance rates to second-line drugs, cycloserine, and kanamycin, were 75.7 and 23.7%, respectively. A significant decreasing trend in resistance rates to all drugs except streptomycin was observed during the 5-year period. Though combined drug resistance rate may not be the most accurate tool as it includes previously treated cases which inflates the resistance rate, the observation of trends in the susceptibility of pulmonary tuberculosis in accompanying with the increasing percentages of tuberculosis patients receiving complete treatment course and the decreasing percentages of cases lost of follow-up in Kaohsiung after the institution of new governmental regulations for case management in 1997 suggest the usefulness of intervention programs.

Lipid profile in patients with multidrug resistant pulmonary tuberculosis PS223

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As shown experimentally, tuberculosis (TB) infection may contribute to development of atherosclerosis. Also antituberculosis drugs may effect atherosclerosis. The aim of our study was to evaluate serum level of total cholesterol (TCH), triglycerides (TG), low density lipoprotein (LDL), very low density lipoprotein (VLDL), high density lipoprotein (HDL), Apoprotein A (APO A), Apoprotein B (APO B) and lipoprotein A (lp(a)) in multidrug resistant tuberculosis (MDR-TB) patients. The study group consisted of 20 MDR-TB and age–sex match 20 healthy controls. The mean age of the MDR-TB patients was 37.95 ± 11.50 and control’s 53.75 ± 11.81 years and smoking habits was 17.70 ± 11.96 package/year (p/y) and 19.1 ± 17.335. From measuring parameters, TCH concentration was found in patients/controls, 144.70 ± 36.48/185.3 ± 42.83 mg/dl, HDL concentration 44.40 ± 16.47/
36.65 ± 5.33 mg/dl, LDL 78.55 ± 26.4/122.2 ± 40.14 mg/dl, VLDL concentration 19.75 ± 22.80/31.7 ± 16.06 mg/dl, TG concentration 19.75 ± 22.80/31.7 ± 16.06 mg/dl, APO A concentration 102.15 ± 32.33/128.15 ± 23.66 mg/dl, APO B concentration 102.15 ± 32.33/128.15 ± 23.66 mg/dl. Lp(a) concentration 27.90 ± 26.28/17.59 ± 15.23 mg/dl, respectively. In MDR-TB patients TCH, TG, LDL, VLDL, APO B concentrations were statistical significant lower than controls (P < 0.000, 0.000, 0.000, 0.000, 0.000).

**Conclusion:** In our study group, MDR-TB patients do not have a risk of atherosclerosis.

A case of tuberculosis presenting with an abscess extending from suprasternal region to anterior mediastinum PS224

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Extrapulmonary tuberculosis may sometimes present with confusing clinical manifestations. A 77-year-old female patient was admitted with a history of recurrent supra-sternal abscess for 1 year. MRI confirmed the presence of sternal osteomyelitis and an anterior mediastinal mass. The diagnosis of tuberculosis was proved by histologic examination and acid-fast stain. The patient was treated with first-line agents, which isoniazid, rifampin, pyrazinamide, and ethambutol.

**Tobacco smoking as a factor of the decrease of chemotherapy effectiveness and of the development of the drug resistance in patients with pulmonary tuberculosis** PS225

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Studies of the effect of smoking on the results of chemotherapy of 798 patients with tuberculosis of lungs. Intensive tobacco smoking slowed down clearance of positive sputum and of lung tissue destruction (in smokers 92.1% and 70.1 vs. 98.0% and 90.6% in non-smokers, P < 0.01). Drug-resistant MTB strains have been found to be isolated more often in smokers—43.4 vs. 19.4% in non-smokers, P < 0.01. Resistance to streptomycin and isoniazid prevailed, reaching in heavy smokers 50.0 and 30.5%, respectively. Resistance to rifampicin increased 1.5 times. The concentration of rifampicin in the blood serum of heavy smokers decreased in 1.8 times. Clinical data are in complete correlation with the findings of our experiments: 67% of experimental cultures developed resistance to streptomycin, isoniazid and less to rifampicin in the study of drug sensitivity under the effect of tobacco smoke condensate. Thus, our findings show the development of drug resistance in MTB under the effect of components of tobacco smoke and also showed less effectiveness in therapy.

Thoracic actinomycosis: still a problem PS226

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Actinomycosis is a chronic disease characterized by abscess formation, tissue fibrosis and draining sinuses. It is caused by anaerobic bacteria belonging to the genus actinomyces. Thoracic actinomycosis may involve the lungs, pleura, mediastinum or chest wall. The authors present a case of pulmonary actinomycosis complicating a cervico-facial site. A 32-year-old man with a history of cervicofacial actinomycosis treated by penicillin G 2 years ago was admitted because of right-sided chest pain for 2 months before presentation, cough and fever. Physical examination shows a painless indurated mass in the neck with multiple fistula of the sternum. Chest radiograph and CT scan revealed a mass in the upper lobe of the right lung with an infiltrate of the upper lobe of the left one. Magnetic resonance imaging confirms the previous lesions, with extending process to the sternum and right collar bone. Bronchoscopy was performed while patient was on antimicrobial therapy. Culture of bronchoalveolar lavage fluid was negative. Transbronchial biopsy was not conclusive. Fungal serologies were negative for aspergillosis, histoplasmosis, blastomycosis. Bacterial examination of purulent drainage from sternal wound shows inclusion bodies identified as actinomyces. He was treated then with penicillin IV for 2 months, than switched to doxycycline. After 8 months of treatment, he is asymptomatic with radiological improvement.

**Resistance of Achromobacter xylosoxidans isolated from CF patients** PS227

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**Introduction:** Achromobacter xylosoxidans is a rare human pathogen. It is an important cause of bacteremia in patients with cardiac diseases, malignancies and immunosuppression. It has been recently recognized as an emerging microorganism in Cystic Fibrosis (CF), whose its pathogenic role is unknown.

**Aim:** To investigate the sensitivity to eleven different antibiotics of 27 A. xylosoxidans strains isolated from adults with CF, during 2001.

**Methods:** The susceptibility was tested by Kirby Bauer and microdilution methods (Wider I, Francisco Soria Melguizo, S.A.), according to NCCLS recommendations.

**Results:** The resistance to antibiotics was as follows : Gentamicin, Tobramycin, Aztreonam 100%, Amikacin 96%, Cefazidime 85%, Ticarcillin 66%, Carbapenem, Cotrimoxazole 59%, Colistin 51% and Piperacillin 22%.

**Conclusions:** (1) A. xylosoxidans isolated from CF patients appeared resistant to the most usually tested antibacterial agents. (2) Colistin which used as aerolized antibiotic for CF patients seems to be effective in the half of the isolated strains. (3) Piperacillin was the most active antibiotic against A. xylosoxidans.

**Comparative in vitro activities of alafosfalin in combination with various antibiotics against Burkholderia cepacia and Pseudomonas aeruginosa strains from patients with cystic fibrosis** PS228

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Alafosfalin, 1-alanyl-L-1-aminoethylphosphonic acid, is an antibiotic peptide mimetic which inhibits peptidoglycan biosynthesis. We report the in-vitro activity of this compound in combination with ceftazidime, cefsludin, fosfomycin, piperacillin/tazobactam, aztreonam, ciprofloxacin and timentin. Drug combinations were evaluated against 20 Burkholderia cepacia strains, and 20 Pseudomonas aeruginosa strains isolated from patients with cystic fibrosis. For this purpose a chequerboard technique was adopted using doubling dilutions of each antibiotic incorporated into a highly defined agar medium free of antagonists. The minimum inhibitory concentrations (MICs) and fractional inhibitory concentrations (FICs) of all the
antibiotic combinations were determined which revealed the antibiotic interaction occurring. Alafosfalin in combination with ceftazidime, meropenem, piperacillin/tazobactam and timentin demonstrated the highest percentages of synergy in both *B. cepacia* and *P. aeruginosa*. Synergy was shown to occur in 15, 15, 10 and 10% of *B. cepacia* strains respectively, and in 10, 5, 5 and 5% of *P. aeruginosa* strains. These four combinations were re-tested with all 40 isolates and the results were shown to be reproducible. Alafosfalin shows potential as a treatment for cystic fibrosis patients colonised with *P. aeruginosa* and/or *B. cepacia*, when applied in combination with these agents.

Community-acquired pneumonia—does its aetiology matter? PS229

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The aetiology of pneumonia is not one of the criteria used to determine pneumonia’s severity. However, it is accepted that identified base-identified therapy is less expensive (and possibly more effective). **Objectives**: Our study aims were to: (1) to evaluate the role of aetiology identification in pneumonia; (2) to evaluate the first-line therapy in pneumonia. **Methods**: We conducted a retrospective study in an Infectious Diseases Hospital on 1126 patients with pneumonia. We excluded all the cases with nosocomial pneumonia. Primary end-point was the 28-day clinical failure (deaths, ICU admission), secondary end-points were the average time of fever and length of stay and the antimicrobial regimen changes. **Results**: Causative agent identification rate was 24.6%. The evolution was different for patients with identified aetiology compared with other patients in terms of: 28-day failures, length-of-stay and changes of the antimicrobial regimen. The 61 patients with inadequate first-line therapy had a more severe course of illness with a greater rate of 28-day clinical failure, longer fever and length-of-stay. **Conclusions**: Pneumonia’s treatment was better for the patients with identified causative agent. That is why we should include aetiology among the pneumonia severity criteria, especially at an ‘after 3-day therapy’ re-evaluation.

Pneumococcal acute otitis media in Greek paediatric population: increasing evidence for antimicrobial resistance PS230

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**Purpose**: To determine the incidence of *Streptococcus pneumoniae* (S.pn) in acute otitis media (AOM) in 229 children attending as outpatients in Pediatric Departments of three Children’s Hospitals located in the area of Athens during a 15-month period (September 2000–November 2001). Also, the drug-resistance and serogrouping of S.pn isolates were evaluated. **Results**: Pneumococcal AOM was detected in 94 children (41.0%) and S.pn. was the only pathogen in 89.9%. The resistance rates of the organism to antibiotics were as follows: penicillin 48.9% (MIC < 1 μg/ml; intermediately resistant 31.9%, MIC 1.5 μg/ml 8.5%), clindamycin 11.7%, cotrimoxazole 41.5% and chloramphenicol 6.4%. All isolates were uniformly susceptible to rifamycin and vancomycin.

The large majority of pneumococcal isolates (80.8%) had the M-phenotype and the remaining strains (19.2%) the constitutive MLS phenotype. A various of serogroups were detected; the serogroup 19 was the most predominant one (50.0%), followed by serogroups 14 (14.9%), 23 (10.6%) and 6 (6.4%). The non-typable S.pn. strains compromised the 8.5% of the strains. **Conclusions**: High prevalence of resistance to penicillin, macrolides and cotrimoxazole in pneumococcal AOM of childhood was recognized. A strategy for preventing AOM caused by drug-resistant pneumococci is mandatory to start.

Antibiotic resistance of *Streptococcus pneumoniae* isolated from adults in a General District Hospital (1998–2001) PS231

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**Aim**: To investigate the ‘in vitro’ activity of antibiotics against *Streptococcus pneumoniae* strains isolated from adults sputum–bronchial secretions during a 4-year period (1998–2001). **Material and methods**: A total number of 82 strains were examined. The sensitivity test was performed by Kirby Bauer, microdilution method (Pusco, Difco) according to NCCLS guidelines and by E-test. **Results**: A percentage of 5.5% of *S. pneumoniae* strains revealed high level resistance to Penicillin (MIC ≥ 2 μg/ml), while the 28% showed intermediate resistance (MIC 0.12–1 μg/ml). The resistance to Erythromycin and Cotrimoxazole was 8.3% (MIC ≥ 1 μg/ml) and 5.5% (MIC ≥ 4/76 μg/ml) respectively. All strains were sensitive to Cefotaxime (MIC 0.05 μg/ml), Vancomycin (MIC ≤ 0.5 μg/ml), Meropenem (MIC ≤ 0.25 μg/ml) and Levofloxacin (MIC ≤ 2 μg/ml). **Conclusions**: (1) The prevalence of high resistance *S. pneumoniae* to Penicillin seems to be low in examined strains (5.5%). (2) Intermediate resistance to Penicillin of *S. pneumoniae* isolates was high as expected (28%). (3) Most of the strains were sensitive to Erythromycin (91.7%) and Cotrimoxazole (94.5%). (4) *S. pneumoniae* isolates were completely (100%) sensitive to Levofloxacin, Vancomycin and Meropenem.

Five years survey of Antibiotic Therapy in Acute Exacerbations of COPD (AE-COPD) PS232

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**Aim**: of this study was a retrospective (1997–2001) evaluation of the more effective and practical antibiotic treatment in 1058 AE-COPD patients (pts) admitted to our Unit. **Methods**: before introducing any antimocrobial drug, sputum specimens were collected for microbiological purposes, while blood analysis, to monitor adverse systemic effects, were performed at the beginning and the end of treatment. Antibiotic treatment ranged from 8 to 15 days according to four regimens: Regimen A (832 pts) = oral therapy only: 30.9% with AMC 1 g b.i.d.; 24.4% with CIP 500 mg b.i.d.; 17.4% with DOX 100 mg u.i.d.; 10.2% with LEX 750 mg u.i.d.; 8.5% with CLA 500 mg b.i.d.; 7.8% miscellaneous. Regimen B (94 pts) = sequential therapy (c.v. for 3 days → oral); 56.4% with AMC 1 g b.i.d.; 37.2% with CLA 500 mg b.i.d. Regimen C (68 pts) = c.v. therapy only: same drugs. Regimen D (64 pts) = an association of two antibiotics. **Results**: of 1058 evaluated pts, only 199 (19.6%) required a second regimen of treatment because of failure of the previous one: 19.7% of Regimen A; 12.7% of Regimen B; 23.5% of Regimen C, and 14% of
Regimen D. Mild adverse effects were detected only in four pts. Our results confirm that oral antibiotic treatment is practical, safe, and effective, and can be considered as the first line regimen also in hospitalized patients with AE-COPD.

**Oral cefixime therapy reduces bacterial load and inflammatory indices in patients with infection-induced exacerbations of severe chronic obstructive pulmonary disease** PS233

Becher G*, Gillissen A*, Rothe M*. *St. George Medical Center, Robert-Koch-Hospital, Leipzig, Germany, bFILT, Lung and Chest Diagnostics Ltd., Berlin, Germany

Patients with severe form of chronic obstructive pulmonary disease (COPD) are prone by frequent exacerbations. Bacterial infections are judged to cause at least half of exacerbations. *Haemophilus influenzae* and *Streptococcus pneumoniae* are the most frequent isolates, Gram-negative bacilli account for the severe cases, aggravating the inflammatory process in the airways eventually leading to respiratory insufficiency. The aim of this ongoing placebo controlled, parallel group, mono center study trial is to evaluate beneficial effect of cefixim to reduce bacterial load and pulmonary inflammation in patients (n = 30) with acute bacterial exacerbation of severe COPD. Thus, 30 patients received in randomized fashion either Cefixim (400 mg/day) or placebo (5 days). On days 1, 2, 5 and 8 breath condensate is collected using ‘Ecoccreen’ (Jaeger Germany) for LTBI, IL-8, Nitrite- and PH-analysis. In parallel sputum gathered for detection of bacterial strains, and for LTBI- and IL-8 quantification purposes. These data are compared to clinical outcome parameters such as lung function tests, radiographic findings, serum inflammatory markers and length of hospital stay. The preliminary data obtained confirm successful antibiotic therapy with oral Cefixim in bacterial related acute exacerbations of COPD is a useful approach to reduce bacterial load, and concomitantly lower inflammatory indices of the central and peripheral airways leading to clinical improvement of the patients.

**Streptococcus pneumoniae** serotypes and in vitro activity of cefixime and 10 other antimicrobials in Southern European countries (ARISE Project) PS234


**Purpose:** To describe the susceptibility of *Streptococcus pneumoniae* against cefixime and 10 other antimicrobials by serotype at a multicenter study in South Europe was carried out. A total of 877 strains were collected between September 2000 and March 2001 from adult patients (more than 16 y.o.) with respiratory tract infection (respiratory tract samples and blood cultures). All the isolates were sent to a central Laboratory (Fundacion Jimenez Diaz, Madrid, Spain) where susceptibility test was performed by broth microdilution (Sensititre) following NCCLS recommendations. Serotype was determined by Quelling reaction and Dot Assay in Carlos III Institute in 806 strains.

**Results:** A total of 25 strains (3.1%) were not typable. The most prevalent serotypes were 23 (15.4%), 6 (11.4%), 19 (10.8%), 3 (9.6%), 14 (8.9%) and 9 (8.1%). Two hundred and sixty-four strains were grouped in 27 different serotypes. The proportion of susceptible strains by serotype to penicillin, erythromycin and levofloxacin were: serotype 3 (90.9, 93.5, 100%); 6 (50.0, 34.8, 96.7%); 9 (36.9, 86.2, 93.8%); 14 (38.9, 48.6, 94.4%); 19 (60.9, 44.8, 97.7%); 23 (58.9, 49.2, 99.2%). The MIC 90 to cefditoren was ≤ 0.03 (serotype 3); 0.5 (serotype 6, 9 and 19) and 1 mg/l (serotype 14 and 23).

**Conclusions:** The most prevalent serotype was 23. The susceptibility was higher in serotype 3 than in serotypes 14 and 23.

**Community acquired pneumonia—a study among closed military community of young people** PS235

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**Purpose:** The etiology of pneumonia is still partly unknown. We should like to clear up an etiological role of respiratory pathogens in community-acquired pneumonia among youth. And we had chosen for it a model of a closed community both investigation of etiology of disease and for further investigation of mechanisms of transmission drug-resistant mechanisms.

**Methods:** We studied 300 adults in age of 17–25 from closed military collectives who presented to two public hospitals (one urban and one rural) with acute radiologically confirmed pneumonia during winter 2000–2001. We did blood and lung-aspirate cultures, myco-bacterial cultures, serotype-specific pneumococcal antigen detection, and serology for viral and atypical agents.

**Results:** *Streptococcus pneumoniae* is recognized as an important cause of community-acquired pneumonia, it probably accounts for 65% of cases of community-acquired pneumonia among youth. *Chlamydia pneumoniae* and *Mycoplasm pneumoniae* responsible for approximately 20% of cases. *Haemophilus influenzae* caused 7.5% severe cases of disease, 3% of all cases were due to *Moraxella catharralis*.

**Conclusion:** Pneumococcal infection accounted for 65% of the cases diagnosed. *S. pneumoniae* was the most common bacterial infective agent, with a low incidence of both *M. pneumoniae* and *S. pneumoniae*. Other causative pathogens occurred only within groups of individuals with deficiency of immunological status.

**Nasopharyngeal colonization by Streptococcus pneumoniae (SP) in children with acute bacterial infections** PS236

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To determine antimicrobial susceptibility of SP isolated from the upper respiratory tract, we collected NP swab specimens from 80 children, between 3 months and 5 years old. Those children attended the outpatient clinic in S. Paulo City, with diagnosis of bacterial infection requiring antibiotic therapy between March 15, 2000 to May 20, 2001. Penicillin susceptibility of isolates was determined by screening with oxacillin 1 mcg disk and performing the minimal inhibitory concentration by the E-test. We performed also susceptibility test for amoxicillin and cefaclor.

**Results:** SP was recovered from NP of 42 children (52.5%). The carriage of SP was more prevalent in children attending day care centers, children with young siblings at home, and children with tobacco users at home. The prevalence of penicillin non-susceptible strains was 40.4% all of them with intermediate resistance. All the strains were susceptible to amoxicillin and 19.2% were resistant to cefaclor. Serotypes 14, 6B, 19F, 9N, 4, 6A and 5 were the most common. These findings suggest that nasopharyngeal isolates of *Streptococcus pneumoniae* from children with upper respiratory infections can be used to conduct surveillance for antimicrobial resistance in a defined geographic area. We were able to conclude
also that penicillin intermediate resistant strains can be susceptible to amoxicillin.

**Streptococcus pneumoniae: 2 years of epidemiological surveillance in Monterrey, Mexico** PS237

Hinojosa RM*, Saenz A*, Collazo M*, Echamiz G*. *Universidad Autonoma de Nuevo Leon, Infectologia, Monterrey, Mexico, Instituto Nacional de Salud Publica, Epidemiologia, Cuernavaca, Mexico*

The emergence of penicillin- and multidrug-resistant pneumococcal strains has become a global concern, necessitating the identification of the epidemiological spread of such strains.

**Material:** Ninety Streptococcus pneumoniae clinical isolates were collected from March 1997 through March 1999. Typing was done by the capsular reaction with pooled, type, or group antisera. Susceptibility testing to 11 antimicrobials was done by the E-Test and the disk diffusion method.

**Results:** Only 46 (51%) S. pneumoniae strains were classified by serotyping: the most frequent types were 6A/B, 23F, 9V, 19F and 4. The Oxacillin screening test detected 37.2% penicillin-resistant S. pneumoniae strains isolated from children and 44.6% from adults. The susceptibility percentage of S. pneumoniae to Ceftriaxone was 93% in both children and adults. S. pneumoniae isolates from children exhibit a susceptibility of 88% to Azithromycin, while in adults 91% of the isolates were susceptible. For the rest of the antimicrobial agents, the susceptibility ranged from 69 to 89%. S. pneumoniae had a lower susceptibility to cefazidime and ciprofloxacin.

**Conclusions:** Ceftriaxone and Azithromycin had a good in-vitro activity against S. pneumoniae strains. But the percentage of penicillin-resistant S. pneumoniae detected in this study is alarming, therefore we conclude that a continuous surveillance system is necessary in Mexico.

**Prognostically unfavourable factors in patients with ambulant pneumonia** PS238

Vertkine AL, Prokhorovitch EA, Alexanyan LA. *Department of Clinical Pharmacology and Internal Medicine, Moscow State Medico-Stomatological University, Moscow, Russian Federation*

A retrospective analyses of 221 cases of ambulant pneumonia with fatal outcome was made. Among the patients who died from ambulant pneumonia the prevailing age was over 60 (63.8%) and the prevailing sex was male (68.8%). 95.9% had pneumonia accompanied with some pathology: chronic lung disease (43.9%), alcoholism (26.2%), diabetes mellitus (10.4%). 62.5% of the patients had a big volume of lungs lesion—55.7% of the patients suffered from bilobular pneumonia and 6.8%—from trilobate pneumonia. In 57.0% of the cases pneumonia was complicated with abscess formation and/or exudative pleurisy. We studied the antibiotics therapy used for the patients treatment. The change of antibiotics was made only in 53 cases (24.0%) whereas in the other cases no change of preparations was made though the signs of the therapy non-effectiveness were obvious. Thus, the rational antibiotics therapy with the timely change of non-effective antibiotic drug is significantly important. While choosing the antibiotics, the patient’s age, the accompanying diseases, the volume of the lungs lesion and complications which define pneumonia seriousness are to be taken into consideration.

**Survey on the perception, attitudes and knowledge of general practitioners concerning lower respiratory tract infections in adults** PS239


**Objectives:** To describe the management of lower respiratory tract infections (LRTI) in healthy adults, by general practitioners (GP).

**Methods:** A questionnaire was sent to a representative national sample of 4092 GPs. This questionnaire assessed their perception and management of LRTI, the indication for antibiotics (AB) in a case of LRTI in a healthy adult with no focal signs and no signs of severity, knowledge of the micro-organisms responsible for acute bronchitis and knowledge of the AFSSAPS (French Agency for the Safety of Health Products) recommendations.

**Results:** Three thousand seven hundred and thirty-eight GPs, who reported seeing an average of 131 patients per week, including 10.3 ± 9.6 patients with LRTI, returned the questionnaire. The main results are presented in the following table.

<table>
<thead>
<tr>
<th>GP declarations</th>
<th>% of GPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>The main objective of the visit to determine the indication for antibiotics</td>
<td>58</td>
</tr>
<tr>
<td>Rarely see acute lobar pneumonia (ALP)</td>
<td>64</td>
</tr>
<tr>
<td>Often see atypical pneumonia</td>
<td>27</td>
</tr>
<tr>
<td>Diagnosis of ALP easily suggested at the first visit</td>
<td>49</td>
</tr>
<tr>
<td>Diagnosis of atypical pneumonia easily suggested at the first visit</td>
<td>23</td>
</tr>
<tr>
<td>The diagnosis of whooping cough is rare</td>
<td>77</td>
</tr>
<tr>
<td>Chest X-ray: rarely requested/never requested</td>
<td>50/19</td>
</tr>
<tr>
<td>Laboratory assessment (CBC, CRP): rarely requested/never requested</td>
<td>59/24</td>
</tr>
<tr>
<td>Declare to know and apply AFSSAPS recommendations</td>
<td>57</td>
</tr>
</tbody>
</table>

**Approach to LRTI in a healthy adult, with no focal signs and no signs of severity (%)**

<table>
<thead>
<tr>
<th>Micro-organisms responsible for acute bronchitis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate antibiotics</td>
</tr>
<tr>
<td>Antibiotics if symptoms persist</td>
</tr>
<tr>
<td>If antibiotic, macrolide</td>
</tr>
<tr>
<td>If antibiotic, beta-lactum antibiotic</td>
</tr>
<tr>
<td>Virus</td>
</tr>
<tr>
<td>*Haemophilus influenzae</td>
</tr>
<tr>
<td>Atypical bacteria</td>
</tr>
<tr>
<td>*Pneumococcus Bordetella pertussis</td>
</tr>
<tr>
<td>Bordetella pertussis</td>
</tr>
</tbody>
</table>

*Several possible replies.

**Conclusions:** For the majority of GPs, the main objective of the visit is to determine the indication for antibiotics. According to GPs, ALP and whooping cough are rare, while atypical pneumonia is frequent. GPs also declare that the diagnosis of ALP is often easy right from the first visit, in contrast with that of atypical pneumonia. Complementary investigations are not often requested. GPs consider that they often delay prescription of antibiotics (41%) and declare that they tend to prescribe a macrolide as first-line treatment. Finally, GPs have poor knowledge concerning the micro-organisms responsible for acute bronchitis and the majority of GPs declare to be familiar with AFSSAPS recommendations.
Epidemiological survey on the general practice management of lower respiratory tract infections in healthy adults  PS240

Perronne C	extsuperscript{a}, Rouveix B	extsuperscript{b}, Guillenet D	extsuperscript{c}, Zuck P	extsuperscript{d}, Reitz C	extsuperscript{e}, Tsatsaris N	extsuperscript{f}.	extsuperscript{a}Hôpital Raymond Poincaré, Service de Maladies Infectieuses, Garches, France, 	extsuperscript{b}Hôpital Cochin, Paris, France, 	extsuperscript{c}Institut Pasteur, Paris, France, 	extsuperscript{d}Hôpital de Metz, Metz, France, 	extsuperscript{e}Laboratoires Abbott, Rungis, France

Objectives: To study the management of one case of lower respiratory tract infection (LRTI) in adults by general practitioners (GPs).

Methods: Prospective study conducted on a representative national sample of 4092 GPs. Each GP had to include the first healthy adult patient seen during the 3-week data collection period, either on a home visit or in the office for recent cough and acute fever > 37.8 °C. Clinical data, the diagnostic perception and the therapeutic approach to the patient were collected by means of a standardised questionnaire, distributed by Abbott laboratories.

Results: Three thousand seven hundred and thirty-eight general practitioners included 3738 patients.

| Patients |
|---------------------|------------------|
| Age | Ex-smoking |
| 42.8 years ± 13.9 | 13% |
| Sex ratio | Allergy |
| 2.47 | 12% |
| Current smoker | Chronic sinusitis |
| 57% | 6% |

Duration of signs before visit

<table>
<thead>
<tr>
<th>Sign</th>
<th>Frequency of signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (&gt; 37.8 °C)</td>
<td>Sputum: 86%</td>
</tr>
<tr>
<td>2.8 days ± 1.5</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>Parulent sputum: 71% of the 86%</td>
</tr>
<tr>
<td>4.5 days ± 3.8</td>
<td></td>
</tr>
<tr>
<td>Sputum</td>
<td>Normal auscultation: 15%</td>
</tr>
<tr>
<td>3 days ± 2.8</td>
<td></td>
</tr>
<tr>
<td>Focal signs: 4%</td>
<td>Crepitations: &lt; 1%</td>
</tr>
</tbody>
</table>

Diagnosis

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute bronchitis</td>
</tr>
<tr>
<td>Bacterial superinfection of acute bronchitis</td>
</tr>
<tr>
<td>Atypical pneumonia</td>
</tr>
<tr>
<td>Acute lobar pneumonia</td>
</tr>
</tbody>
</table>

Micro-organism presumed to be responsible

<table>
<thead>
<tr>
<th>Organism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus</td>
</tr>
<tr>
<td>Atypical bacteria</td>
</tr>
<tr>
<td>Pneumococcus</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
</tr>
<tr>
<td>Bordetella pertussis</td>
</tr>
</tbody>
</table>

Antibiotic treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Immediate</th>
<th>Deferred if symptoms persist</th>
</tr>
</thead>
<tbody>
<tr>
<td>87%</td>
<td>10%</td>
<td></td>
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</tbody>
</table>

Conclusions: During LRTI in adults, GPs observe few focal signs, confirming the marked predominance of bronchitis compared to pneumonia. In view of the frequency of the signs, the diagnosis of pneumonia appears to be overestimated. One-third of clinical situations were diagnosed as 'bacterial superinfection of acute bronchitis', despite it is not a recognised diagnostic entity. Antibiotic prescription was immediate in 87% of cases and delayed in 10% of cases. This last point shows that clinical practice differs from the GP's perception of their described prescribing practice shown in a simultaneous survey (36% of GPs declared that they prescribed antibiotics immediately, while 41% delayed this prescription).

Characteristics of severe community acquired pneumonia in a Greek intensive care unit  PS241

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Purpose: To determine the characteristics of severe CAP in a Greek ICU.

Results: Thirty-three patients (20 men, mean age 49 b 19 years, mean APACHE II score 15.3 &bdquo; ± 7.3) during the years 1998–2001 were prospectively studied. Thirteen patients (39%) had no identifiable risk factor for severe CAP. An etiologic factor was revealed in 15 patients (45%). In 14 of them this was achieved with noninvasive methods. PSB cultures were taken from eight patients and were positive in only 1. The offending organisms included: Streptococcus pneumoniae in six cases, GNB as the sole pathogen in six cases, Haemophilus influenzae (with S. pneumoniae or Klebsiella pneumoniae) in two cases, S. aureus in two and Legionella pneumophila in one patient. Initial antibiotic regimen a combination of marodile ± 3rd gen cephalexin + aminoglycoside was successful in 12 patients who all survived and had to be changed empirically or according to culture results in 17 patients who had a mortality of 65%. The overall mortality rate was 42%. The identification of the causative factor did not seem to have any impact on survival.

Conclusion: Severe CAP in our ICU was most often caused by S. pneumoniae and GBN. The high mortality of this entity seems to be influenced by the immediate use of the appropriate antibiotic combination and not by the identification of the causative organism. This underscores the need for knowledge of topical microbiology which helps in designing an effective empirical initial antibiotic regimen.

Patterns and predictors of antibiotic usage during hospital pneumonia management in a region of Belarus  PS242

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Purpose: The study aims were to assess the spectrum and predictors of the antibiotic use during pneumonia management in a regional emergency hospital in Belarus. Patients, treatment and physicians characteristics of 195 cases (2000–2001) were collected and possible associations were examined with using defined daily doses methodol-ogy (DDD) and American Thoracic Society (ATS) guidelines.

Results: The mean treatment duration was 13.9 ± 7.4 days, the total antibiotic DDD/100 bed-days was 130.4. The DDD/100 bed-days of the most used antibiotics were: penicillins 54.0; aminoglycosides 29.5; macrolides 21.9; cephalosporins 9.8; tetracyclines 8.2. In MANOVA associations were examined with using defined daily doses methodol-ogy (DDD) and American Thoracic Society (ATS) guidelines.
Acute exacerbation of COPD: most frequent infecting agents and their susceptibility to the different types of penicillins. Analysis of medical documentation  PS243

Pertseva TO, Bogatska KE, Gashynova KY. DSMA, Internal Medicine, Dniepropetrovsk, Ukraine

Number of COPD cases has been increased in Ukraine. Treatment of acute exacerbation (AE) of COPD is not always successful because of inadequate antibiotic therapy. The aim of study was to reveal most frequent infecting agents and their susceptibility to the different types of penicillins in patients with AE of COPD. Medical documentation of 48 patients with AE of COPD (type 1) was studied. Data of sputum analysis and susceptibility of isolated agents to penicillin, ampicillin, oxacillin and amoxicillin/clavulone acid were evaluated. There were patients with *Haemophilus influenzae/parainfluenzae* (43.8%), *Klebsiella pneumoniae* (25%), *Staphylococcus aureus* (12.5%), *Pseudomonas fluorescens*, *Pseudomonas putida*, *Serratia marcescens*, *Serratia liquefaciens* (6.6%) each, *Streptococcus agalactiae*, *Acinetobacter baumannii* (4.1% each) in samples of sputum. In 31.3% cases there was mixed infection, 6.8% had no any bacterial agents. Only 10% of agents were susceptible to penicillin, 35%—to ampicillin, 15%—to oxacillin. However, 70% of microorganisms were susceptible to amoxicillin combined with clavulone acid. This study has shown that most frequent infecting agents caused AE of COPD were Gram-negative microorganisms and *S. aureus*. According to antibiogram the prescription of amoxicillin/clavulone acid is most expedient in this case.

Efficacy and safety of azithromycin (sumamed) in treatment of acute exacerbation of chronic obstructive bronchitis  PS244

Pertseva TO, Bogatska KE, Konopkina LI, Kireeva TV, Gashynova KY. DSMA, Internal Medicine Department, Dniepropetrovsk, Ukraine

We examined 32 patients (22 men, mean age 52.3 ± 4.7 years) with acute exacerbation of COB (type 1). The most frequently isolated agents were *Haemophilus influenzae* and *parainfluenzae*—eight patients, Gram-negative rods in 8, *Staphylococcus aureus* in two and mixed in six and one patient had no bacterial agents isolated in their sputum. High susceptibility to azithromycin was found in all cases of Gram-positive agents and in *H. influenzae* and *parainfluenzae*. Other Gram-negative agents were resistant to this drug in vitro. However, treatment with 500 mg/day during 3 days was clinically effective in 93.7% of cases. Only 25.0% of patients had a further acute exacerbation of COB. There were peculiarities of the infecting agents causing acute exacerbation of COB in this study: *Klebsiella pneumoniae* and *S. aureus* were found more frequently than in other studies. High efficacy of sumamed in the treatment of acute exacerbation of COB was established in 68.7%. 25.0% had partial positive clinical effect after this therapy. There were no patients with adverse events.

Efficacy and tolerance of amoxicillin 30 mg/kg bid versus amoxicillin 15 mg/kg tid in the treatment of acute otitis media (AOM) in children ≤ 2 years  PS245

Borek M*, Guggenbichler JP*, aBiochemie GmbH, International Medical Department, Kundl, Austria, bDepartment of Pediatrics, University of Erlangen, Erlangen, Germany

Five hundred and sixteen patients (mean age 4 ± 2.6 years) with clinical and otoscopic diagnosis of AOM were included in a randomized, double blind, multicentre study, and were treated 10 days either with AMOX 30 mg/kg bid or AMOX 15 mg/kg tid. Assessments were made during therapy (day 3–5), after End of Therapy (EOT, day 12–14) and Follow Up (FU, day 38–46). The primary efficacy endpoint was the clinical response at EOT defined as success (cure/improvement) or failure.

Results in the subgroup aged ≤ 2 years

<table>
<thead>
<tr>
<th></th>
<th>30 mg/kg bid</th>
<th>15 mg/kg tid</th>
<th>95% C.I.</th>
</tr>
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<tbody>
<tr>
<td><strong>Clinical success at EOT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITT</td>
<td>Success 59/64 (89.1)</td>
<td>51/60 (85.0)</td>
<td>−7.8, 15.9</td>
</tr>
<tr>
<td></td>
<td>Cure 42/64 (65.6)</td>
<td>29/60 (48.3)</td>
<td>0.1, 34.5</td>
</tr>
<tr>
<td>PP</td>
<td>Success 50/53 (94.3)</td>
<td>39/42 (92.9)</td>
<td>−8.5, 11.4</td>
</tr>
<tr>
<td></td>
<td>Cure 37/53 (69.8)</td>
<td>25/42 (59.5)</td>
<td>−9.0, 29.6</td>
</tr>
<tr>
<td><strong>Clinical recurrence at FU</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITT</td>
<td>Success 65/67 (98.5)</td>
<td>9/51 (17.6)</td>
<td>−20.3, 6.0</td>
</tr>
<tr>
<td></td>
<td>Cure 45/67 (67.2)</td>
<td>4/39 (10.3)</td>
<td>−14.4, 9.9</td>
</tr>
<tr>
<td>PP</td>
<td>Success 46/53 (88.8)</td>
<td>35/42 (83.3)</td>
<td>−11.0, 17.9</td>
</tr>
<tr>
<td></td>
<td>Cure 42/53 (79.2)</td>
<td>29/42 (69.0)</td>
<td>−7.5, 27.9</td>
</tr>
</tbody>
</table>

Both regimens were well tolerated; one or more drug-related adverse events (AEs) were reported in 17.2% (11/64) of bid patients and in 21.7% (13/60) of tid patients. The most frequently reported drug-related AEs in each group were gastrointestinal symptoms (bid 11.5% vs. tid 13.5%), which were mainly of mild or moderate severity. Both regimens were clinically equivalent. The higher cure rates in the bid group suggest a possible higher benefit from bid therapy in children ≤ 2 years.

Influence of child care on Nasopharyngeal (NP) carriage of *Streptococcus pneumoniae* (SP) and *Haemophilus influenzae* (HI) and antibiotic use  PS246

Dunais B, Carsenti H, Pradier C, Fontas E, Martin C, Develey B, Dellamonica P. Infectious Diseases Department, Nice University Hospital, Nice, France

Children attending family day-care (FDC) should be less exposed to upper respiratory tract infections than those in group day-care (GDC) and therefore to antibiotic treatment; fewer should thus carry resistant bacteria. To test this hypothesis, NP carriage of SP and HI with reduced susceptibility to penicillin (PDSP and HI BL), respectively was investigated among children in FDC (maximum three children) and in GDC (25–100 children) in the Alpes Maritimes (France) between November 1999 and March 2000. A two stage cluster sample of children attending GDC or FDC was selected. NP samples were cultured for SP and HI. Penicillin susceptibility was tested by disk diffusion and E-test, and β-lactamase production by API-NH® tests (BioMerieux, Lyon). Two hundred and thirty-five children in FDC and 298 in GDC aged 6–36 months were sampled. Age and sex
distribution were similar in both groups. SP was isolated in 80 children in FDC (54%), and in 163 (54.7%) children in GDC (P < 10^-6 ). Proportions of PDSP were 52.5 and 55.8%, respectively (P = 0.6). HI was present in 37.6% of children in GDC vs. 23.8% in FDC (P < 0.001). Proportions of HI BL+ were 40.2% vs. 46.4%, respectively (P = 0.4). Antibiotic exposure during the previous 3 months concerned 46.2% of children in GDC vs. 48.7% in FDC (P = 0.6). There was no correlation between antibiotic use and carriage of PDSP or HI B+ strains. SP and HI carriage rates are significantly lower among children in FDC than in GDC. Advising alternative types of day-care for children attending GDC should reduce exposure and thus limit the spread of resistant bacteria. However, the proportion of PDSP and HI BL+ is similar in both groups and comparable patterns of antibiotic use are observed. Continued efforts must concentrate on parental education and enforcement of recommendations for management of pediatric upper respiratory tract infections.

Invasive Haemophilus influenzae isolates in Tunis: antibiotic susceptibility, serotype and biotype  PS247

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During a period between January 1999 and August 2001, 43 invasive Haemophilus influenzae (Hi) isolates had been collected at the Children’s Hospital of Tunis, We used Haemophilus Test Medium to test antibiotic susceptibility. The MIC of beta-lactams was measured by E-test. Beta-lactamase production was determined by using the cefinase test and biotyping by ApiNH. Presence of capsular antigen was determined by using Hi typing anti sera. Hi strains were isolated from meningitis (35), bacteremia (5) and arthritis (3). All strains were serotype b and 62.2% of them belonged to biotypes I and II. Amoxicillin resistance with beta-lactamase producing mechanism occurred in 34.8%. MIC90 of beta-lactamase producing strains was 32 vs 0.5 mg/l in non-producing one. There is no beta-lactamase-negative amoxicillin resistant among those invasive isolates. Antibiotic resistance concerned chloramphenicol: 9.3%, trimethoprim-sulfa methoxazole: 11.6%, tetracycline: 4.6% and kanamycin: 11.6%. Invasive Hi infections in tunisian children’s were always associated with type b strains. Introduction of a Hib vaccine programme in Tunisia is recommended.

Analysis of the clinical course and effects of treatment of neuroborreliosis in children  PS248

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The aim of this study was to analyse the clinical picture and treatment of neurological manifestations of neuroborreliosis in children. The study included 22 children (2–16 years) with neuroborreliosis diagnosed on the basis of the clinical and serologic criteria. Symptoms of facial palsy occurred in six children symptoms of III – VI cranial nerves palsy in three children, meningitis in four and paresthesias in three. Symptoms of V or VIII nerve palsy, mental disturbances, radiculoneuritis or cerebellitis were found in singular cases. All children received ceftriaxone intravenously 3 – 4 weeks. Total recovery was obtained in 18 children following the first course of therapy. Recovery following the second course of therapy (amoxicillin) occurred in one child with mental disorders and one with VI nerve palsy. Improvement was achieved after the second course in the patient with radiculitis, however, muscular atrophy persisted. Irreversible, unilateral deafness was found in a child with VIII nerve palsy in spite of three courses of therapy applied. Infection with Borrelia burgdorferi in children causes a wide spectrum of neurological manifestations. Facial palsy was the most common sign in our study. Applying ceftriaxone in the treatment of neuroborreliosis is characterised by a good effectiveness.

Double infection by C. pneumoniae and M. pneumoniae as a cause of cystic changes in the lungs  PS249

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Chlamydia pneumoniae and Mycoplasma pneumoniae are human respiratory pathogens manifested in early childhood. Immunological disbalance could trigger autoaggressive diseases. The authors describe the case of a 15-year-old girl with development of multiorgan failure and septic state, which followed multiple cystic changes in the lungs. The girl did not have a diagnosis of cystic fibrosis. The authors consider that cystic changes are a consequence of double infection by C. and M. pneumoniae.

‘Baby-friendly’ hospital initiative and decreasing of neonatal infections  PS250


UNICEF Skopje has supported a nationwide Safe Motherhood Needs Assessment in representative samples of hospitals. Eighteen of 28 maternity wards and facilities renovated and certified as ‘baby-friendly’. All mature newborns with successful adaptation to extra uterine life and satisfactory vital parameters are 24 h during the day with their mothers at rooming-in system.

Aim: With rooming-in system we reached decreasing of incidence of neonatal infections.

Material and methods: History records of newborns from our department. For the period of 9 months, 907 neonates have been born. With suspicion of infection there—49 babies (5.4%). Newborns born through meconium stained liquid—40 (4.4%).

Results: Microbiological findings: from blood culture—Staphylococcus coagulaza negative from swabs—Staphylococcus aureus, Escherichia coli, Staphylococcus epidermis.

Conclusion: In 1999, from all babies who had risk factors for infection in 56 newborns (5%) we had positive findings and in year 2000 (before rooming-in sistem), in 44 (3.9%). After that period (with rooming-in) 15 newborns (1.5%). With rooming-in system we reached decreasing in incidence of neonatal infections by breaking the chain of infection—only mothers take care of their babies with help of the staff. Newborns are in their micro environment, the same they will have at their home. With this practice we have also reduction of nosocomial infections.

A study on antibiotic susceptibility and resistance factor transmissibility among antibiotic resistant salmonellae isolated from children affected to diarrhea  PS251

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In spite of happened drug resistance, antibacterial therapy still is the best route of treatment of Salmonellosis in man and animals. In order to detection of dominants serotypes of salmonelae in children and detection of antibiotic susceptibility and R-factor transmissibility among those isolated salmonelae. This study was conducted on 400 diarrheic stool samples were collected from children affected by diarrhea in Ayatollah Kashany hospital of Shahrekord, during Spring of 1999 to Autumn of 2000. After isolation and identification of salmonelae, seven serotypes were detected. One of those was S. typhi and another six serotypes were S. paratyphi B. In order to detection of antibiotic different antibiotic disks were used in disk diffusion method. Best results were taken from Cefizoxim, Cephtriaxon, Cephazolin and Chloramphenichol. The R-factor were transferred from isolated salmonelae to Escherichia coli K12 in all of cases of resistance to Penicillin and Ampicillin.

Macrolides in infancy—comparative characteristic of their clinical efficacy

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Serologic studies performed in 1999 – 2000 showed that Mycoplasma pneumoniae, Chlamydia pneumoniae and C. trachonnis were causes of bronchitis and pneumonia at least in 37.9% of cases in children under 4 years old with acute low respiratory tract infection. A comparative study of clarithromycin, spiramycin, midecamycin and azithromycin clinical efficacy was performed during the therapy of 98 children 2 months–4 years old. Groups of patients were comparable in age, gender and clinical characteristics of disease. Rate of excellent and good results was 82.1% in group treated by clarithromycin, 94.5% in group treated by spiramycin, 61.4% in group treated by midecamycin and 96.0% in group treated by azithromycin. The rate of side effects in most groups was similar—about 4%. But the group treated by midecamycin showed allergic reactions (15.4%), diarrhoea (15.4%), and rate of liver enlargement in 7.6% of cases.

Colonization by Streptococcus pneumoniae and group A Beta haemolytic streptococci in school-children in Riyadh, Saudi Arabia

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Pharyngeal colonization by Streptococcus pneumoniae and group A BHS were evaluated in 652 randomly selected school children aged 6 – 8 years in Riyadh, Saudi Arabia. Fifty-six children (8.6%) had positive culture for either organisms of the 56 isolates from school children, 17 (30%) were S. pneumoniae, of them 14 (82%) were penicillin-sensitive, three (18%) were penicillin-resistant, and two (11.7%) were resistant to two antimicrobials. Forty isolates of BHS (71%) were group A BHS. All isolates were penicillin and erythromycin sensitive. The carrier rate among school children for penicillin-resistance S. pneumoniae and resistance to two antimicrobials were (4.6%) and (3%), respectively. The carrier rate of group A BHS was (6.1%). Riyadh has a low rate of antibiotic-resistant S. pneumoniae and a similar rate of group A BHS carriers among school children as that seen in temperate areas.

The acute pharyngitis is a very frequent pathology in which Group A Streptococcus is the most incriminated bacteria. However, other non A β-haemolytic Streptococcus (SBNA) could be responsible. The aim of this work is to determine the part of each non A β hemolytic streptococci (SBNA) in acute pharyngitis and the related antibiotics susceptibility pattern. The study was realized in Sousse-Tunisia (north Africa) during 5 months from May 2001. The origin materials of isolates are throat swab (Transystem Venturi, Copan, Bovezzo). The mean age of patients is 23 years with extremes 3 – 72 years. The samples are cultured on blood agar plates in a delay of 3 h maximum. Identification was done to samples that have over than 20 β-hemolytic colonies, groupage with pastorex STREP. Sanofi Pasteur France. Susceptibility pattern according to NCCLS norms, MIC is determined by E-test. The control strain is S. pneumoniae ATCC 49619. Twenty-one clinical isolates of SBNA are distinguished from 80 clinical isolates of β-hemolytic streptococci recovered from 143 patients with acute pharyngitis without symptoms of viruses’ infections (tearing, corysa, sneeze). All β-hemolytic Streptococcus represents 55.94% of all collected samples. SBNA were 26.25% of the isolates. SBNA were 11 strains Group G streptococci, seven strains Group C streptococci and three strains Group F streptococci. Susceptibility pattern of each SBNA to antimicrobial agents is as follow: Group G streptococci: Peni G = 100%, Amoxicillin = 100%, Clindamycin = 100% and Erythromycin = 45.46%, Tetracyclin = 9.1%, Telithromycin = 63.6% and Levofloxacin = 45.45%, Group C streptococci: Peni G = 100%, Amoxicillin = 100%, Clindamycin = 100% and Erythromycin = 57.15%, Tetracyclin = 42.86%, Telithromycin = 71.42%, Levofloxacin = 100%, Group F streptococci: Peni G = 100%, Amoxicillin = 100%, Clindamycin = 100% and Erythromycin = 33.34%, Tetracyclin = 66.66%, Telithromycin = 100%, Levofloxacin = 66.66%. All SBNA have MIC to Penicillin G under 0.1 mg/l. According to available data, Penicillin G and Amoxicillin still the reference treatment of acute bacterial pharyngitis in spite of the new antibiotics introduction.

Comparison of cefaclor and amoxicillin in the treatment of pediatric Streptococcal tonsillopharyngitis in S. Paulo (Brasil)

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A multicenter, open label, prospective, randomized trial in which patients 2 – 16 years of age with proven GABHS pharyngitis were randomized to receive either 10-day course of the broad spectrum oral cephalosporin, cefaclor or a 10-day course of amoxicillin. Patients were included if they have signs and symptoms of Streptococcal tonsillopharyngitis and a rapid streptococcal rapid test positive. Patients were evaluated at days 3 – 5, 13 – 16 and 24 – 35 posttherapy. Pharyngeal cultures were conducted at baseline and at follow-up visit (13 – 16 days). We considered for bacteriologic eradication analysis only patients with positive culture to GABHS. There were 148 patients with a rapid streptococcal rapid test. Clinical success were achieved in
around 95% of the patients. For evaluate eradication of the initial pathogen we considered 42 patients of the amoxil arm and 40 patients of the cefaclor arm. Thirty-four of 42 patients of the amoxil arm (80.9%) and 36 of 40 (90%) patients of the cefaclor arm were considered bacteriological cured at the second culture performed at day 13–16. Ten days of a penicillin or amoxicillin therapy may not be the best therapeutic choice for all pediatric patients. In developing countries where rheumatic fever is still an important problem to evaluate the bacterial eradication achieved with the different antibiotics may be important.

**Prophylactic affect of Saccharomyces boulardii for antibiotic-associated diarrhea in a paediatric age group**  PS256

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The process resulting in antibiotic associated diarrhea is the alteration of enteric flora due to bacteria. *Saccharomyces boulardii* is a yeast, isolated from cover of a kind of hazelnut and its usage became widespread recently. There is no enough study about *S. boulardii* activity at pediatric ages. We aimed to define *S. boulardii* activity on azithromycin and sulbactam-ampicilene, and associated diarrhea at pediatric age group. The 18.9% of cases only with antibiotic usage developed diarrhea, whereas rate was 5.7% for probiotic using group (*P* < 0.05). All of the Clostridium difficile toxin A defined cases were from sulbactam-ampicilene using group. The rate of diarrhea for sulbactam-ampicilene using group was 25.6%, while it was 5.9% for group used *S. boulardii* as probiotic beside sulbactam-ampicilene (*P* < 0.05). It was observed that probiotic usage decreases diarrhea rate four times (*P* < 0.05). When age groups considered, the rate of sulbactam-ampicilene associated diarrhea increased at 1–5 ages and *S. boulardii* effect on preventing diarrhea was significant at 1–12 ages (*P* < 0.05). Antibiotic associated diarrhea is a common clinical problem at pediatric age group. *S. boulardii* is a hope giving probiotic especially for sulbactam-ampicilene associated diarrhea.

**Infections in neonates of mothers with a past history of abortion**  PS257

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*The purpose of the study:* The aim of the study was to find out, whether artificial abortion of a mother has impact on neonatal infection of her future baby.

*The results obtained:* Therefore, we compared 39 neonates with infection, who were born to mothers with past history of abortion (1–7 artificial abortions within 10 years), with the babies of mothers, who have not experienced abortion before. Control group consisted of 207 neonates hospitalized at the same clinic, at the same time period. According to the analysis of risk factors for neonatal infections, it was found, that prematurity (28–32 weeks of gestation) (30.77 vs. 14.01%, *P* 0.019) and low birth weight (500–2500 g) (58.97 vs. 39.13%, *P* 0.03) were significantly more frequently observed in babies of mothers with past history of abortion. Drug abuse (heroin) (12.82 vs. 1.45%, *P* 0.003) and nicotine use (15.38 vs. 2.42%, *P* 0.0027), were more significantly related to neonatal infections in babies of mothers with past history of abortion. Etiological analysis showed that only *Candida albicans* (5.13 vs. 0%, *P* 0.024) was significantly related to neonatal infections in mothers with past history of abortion.

*The conclusion reached:* In conclusion, artificial abortion has not only direct impact to the health of the mother, but also on her next pregnancy.

**Bacteraemia and patient mortality in a paediatric intensive care unit**  PS258

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*Purpose:* This study will identify the factors that significantly contribute to mortality in patients with bloodstream infections (BSI) at a pediatric intensive care unit (PICU). *Results:* Medical records of 63 patients who were admitted to the PICU and had a documented BSI were reviewed. There were 74 separate episodes of BSI’s, with nine patients having multiple BSI’s during their hospital stay. A case-control model was used. Cases were BSI’s with eventual mortality (*N* = 27; 36.5%) and controls were those who survived BSI (*N* = 47; 63.5%). Patients who died were older (5.7 vs. 2.4 years; *P* < 0.01), more likely to have a nosocomial BSI (42.9 vs. 16.7%; *P* < 0.05), longer hospitalization prior to BSI (30.5 vs. 9.8 days; *P* < 0.05), and have a polymicrobial BSI (66.7 vs. 30.6%; *P* < 0.05). Infection related mortality (IRM)-defined as death within 7 days of BSI—was significantly higher in those receiving inadequate antibiotic treatment at the time of diagnosis of BSI (54.5 vs. 12.7%; *P* < 0.01), as well as in those with gram negative bacteremia and/or fungemia (35 vs. 13%; *P* < 0.05). Logistic regression was used to adjust for potential confounding variables.

*Conclusions:* We found that being older, multiple organisms, and a longer hospitalization prior to the BSI were significantly associated with overall patient mortality. IRM was significantly higher for those with inadequate initial antibiotic coverage and in those with gram negative bacteremia and/or fungemia.

**Teicoplanin treatment for serious Gram-positive infections in children**  PS259

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Teicoplanin is a glycopeptide antibiotic active against a broad range of Gram-positive pathogens including methicillin-resistant staphylococci and offers the advantages of once daily administration, choice of administration route, lack of requirement for routine therapeutic drug monitoring and lower propensity to cause nephrotoxicity and anaphylactoid-like reactions. In this study the efficacy and safety of teicoplanin were evaluated retrospectively in children with serious bacterial infection.

Sixty-three children (18 girls, 45 boys) aged between 1 month and 15 years were treated with teicoplanin (three loading dosages of 10 mg/kg at 12 h intervals, followed by a maintenance dosage of 10 mg/kg/day). The infections treated were pleural empyema (*n* = 25), joint and bone infections (*n* = 22), septicemia (*n* = 9), skin and soft tissue infections (*n* = 4), and lung abscesses (*n* = 3). The pathogens isolated were *Staphylococcus aureus* (*n* = 30, 16 of which were methicillin resistant), coagulase-negative staphylococci (*n* = 4), *S. pneumoniae* (*n* = 4), and Group A hemolytic streptococci (*n* = 2). The duration of therapy ranged from 14 to 81 days (median 28 days). Clinical success (cure plus
The treatment of febrile neutropenia (FN) in children with Acute Lymphoblastic Leukaemia (ALL) and Acute Myeloblastic Leukaemia (AML) PS260

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The risk of infection is present in all children with acute leukemia. Two hundred and sixty episodes of febrile neutropenia were analyzed in 149 children (aged 1.5–16 years) with AML—43 cases and ALL—106 cases over 10 years during cytostatic therapy (protocols: mBFM—87 AML and mBFM—90 ALL). A degree of FN occurred in 90% of cases in AML, in 53%—in ALL. The sites of infection were: blood+ central venous catheter (32%) and respiratory tract (49%). Pathogens isolated from blood were: Gram-positive—CNS—70%, Streptococcus spp.—18.7%, Gram-negative—Enterobacteria—41%, Pseudomonas aeruginosa—23%, Candida spp.—23.5%, Aspergillus spp.—5.9%, other—5.9%. For the treatment of FN we used empirical antibiotic regimens. Clinical response was noticed: in 1st line of therapy—cephalosporins 3–4 generation used—45%, carbapenems used—60% as 2nd–3rd lines—vancomycin—70%, amphotericin B—80%. Thirty-two percent of children with AML and 5.2% children with ALL died because of sepsis.

Conclusion: Carbapenems are more active in the 1st line of antibiotics therapy both for patients with AML and ALL. Vancomycin is useful in the 2nd line for patients with ALL. Amphotericin B and vancomycin are useful in combination in the 2nd line for patients with AML.

Our drug of choice in cases of complicated neonatal sepsis PS261

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Our drug of choice in cases of complicated neonatal sepsis I. Pavlenishvili, G, Iobashvili Tbilisi, Medical Academy Georgian Society of pediatrics Chemotherapy (GSPC) with collaborations of Drug and Therapeutic Committee (DTC) of Childrens hospital ‘Republic’ finished the observation study about nosocomial infections of Neonatal ICU in above mentioned hospital. Study begins from November 2000. During this period we observe 45 cases of neonatal sepsis, most of them were due gram-negative bacteria. Thirty-four cases of neonatal sepsis were cause different stains of Escherichia coli, Proteus spp. and Acinetobacter. We notice that during last 2 years the role of Acinetobacter in etiology of neonatal sepsis and nosocomial complications of neonatal sepsis in our hospital is gradually increased. As our observation reveals most optimal in the case of complicated neonatal sepsis was (according criteria of DTS) use of Ceftasidime. Almost in all cases we used Ceftasidime with success. We have only one case of mortality.

Macrolide resistance in pediatric pharyngeal isolates of Streptococcus pyogenes PS262

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Since the macrolide resistance (MR) in Streptococcus pyogenes has been increasing in Europe, we studied the incidence and genetic basis of MR in S. pyogenes in Russia. S. pyogenes isolated at baseline and during follow-up visits from children with acute pharyngitis receiving penicillin or midecamycin (16-membered macrolide) were studied. MR was evaluated by agar dilution (NCCLS), resistance mechanisms—by PCR. A total of 149 S. pyogenes were obtained at the baseline, 21 (14%) of which were erythromycin-resistant: 19 strains (90%) were erm(A)-positive, one—mef(A)-positive, and one was negative for all primers used. All erm(A)-strains were inductively resistant to clindamycin and represented seven PFGE profiles with one profile found in 11/19 strains. In three midecamycin treated patients MR was selected during the therapy (one strain had erm(A), one—mef(A), one—unknown resistance determinant). mef(A)-strain obtained during follow-up visit had different PFGE pattern with mef(A) strain isolated at baseline, while both the baseline and follow-up strains with unknown mechanism of resistance had unique PFGE pattern. These data showed moderate incidence of erythromycin-resistant S. pyogenes in Smolensk. Ribosomal methylation (erm(A)) was the most common mechanism and though the polyclonal nature of MR was established, most erm(A)-strains belonged to only a few clones.

Bacillus cereus infections in traumatology-orthopaedy department: retrospective study and re-evaluation of healthcare practices PS263


Bacillus cereus was cultured for 30 patients from traumatology department who had developed postoperative wound infections between August 1997 and March 2000. All patients presented inferior members open fractures, frequently contaminated with telluric material and requiring external fixators. Genomic study of clinical isolates by pulsed field gel electrophoresis and Random analysis polymorphic DNA, allowed us to eliminate an outbreak. Furthermore, the reduced delay in which patients developed the infection (6 days +/- 2) led us to re-evaluate the protocols used in our institution. Indeed, all patients had received amoxycillin + clavulante IV 2g for antibioticprophylaxis during anesthetical induction then relayed per os for 48 hours. Because of the production of a potent beta-lactamase by the bacteria, this association could not be efficient. Furthermore, according to the AFNOR EN 1040 norm, we have tested clinical isolates' sensitivity to the principal antiseptics used for antisepsis and disinfection (iodophors, chloride derivated and biguanidines) and observed a major resistance of all strains tested. Even if these postoperative wound infections are considered as nosocomial because of the delay in appearance, we actually think that Bacillus cereus were initially present in telluric material. This fact led us to propose a systematic screening for Bacillus at admission for this type of wound and to administrate quinolones such as ciprofloxacin for prophylaxis.

Internal thios and reactive oxygen species in the candidacidal activity exerted by a N-terminal peptide of human lactoferrin PS 264

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The purpose of the study: The emergence of Candida albicans strains resistant to current antifungals points to the need for new antifungal agents, e.g. antimicrobial peptides.

The results obtained: We report that hLF(1-11), a synthetic N-terminal peptide of human lactoferrin, displays excellent killing effect against fluconazole-resistant C. albicans and that sub-optimal concentrations of this peptide combined with fluconazole act synergistically. Previous investigations revealed that hLF(1-11) required an energized mitochondrion, ATP release by Candida, and ligation of ATP receptors for its killing effect. We now report that reactive oxygen species (ROS) are involved in the killing effect of hLF(1-11). Since internal thiols protect cells from oxidative damage, our observation that hLF(1-11) caused a 20% reduction of internal thiols in Candida is of interest. As expected, N-acetyl-L-cysteine (NAC), which is a precursor of glutathione and a ROS scavenger, inhibited the killing effect of hLF(1-11). Diamide, which oxidizes internal thiols, was candidacidal and hLF(1-11) and diamide acted synergistically in killing C. albicans and ROS production. Moreover, the hLF(1-11)-induced activation of mitochondria was inhibited by NAC, indicating that internal thiols/ROS affect mitochondrial activity.

The conclusion reached: The candidacidal activity of hLF(1-11) involves ROS production and reduction of internal thiols.

Sharp rising trend in ciprofloxacin resistance in the haematology unit of a tertiary care hospital: a remedial approach to the problem PS 265

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Introduction: Ciprofloxacin is given as prophylaxis to reduce the occurrence of gram-negative bacteraemia in neutropenic patients and bone marrow transplant [autograft] recipients at hematology ward of Gartnaval General Hospital, Glasgow.

Objective: An audit was conducted to explore the observation of increasing resistance to Ciprofloxacin in enterobacteriaceae isolated from specimens from such patients in the hematologic unit.

Results: Enterobacteriaceae isolates from specimens from such patients processed over the years 1997 to 2001 were examined. Number of specimens per year was—109, 152, 132, 160 and 170 respectively and the annual percent ciprofloxacin resistant enterobacteria from these was 2%, 9%, 12%, 14% and 21%.

Conclusion: Conclusion drawn from the audit was that rapid rise in Ciprofloxacin resistance may possibly be attributed to the use of this fluoroquinolone as a single agent in dose of 250/500 mg [cut off patient weight 40 Kg] twice a day in neutropenic patients till neutrophils exceed 500/c.mm. Subsequent to the audit, prophylaxis protocol was modified to use of oral Colistin 3-mega units/twice a day.

Stopping antiretroviral therapy after intensification, GM-CSF and initiation of therapeutic vaccination (Remune) in chronic HIV disease: results at 104 weeks PS 268

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Purpose: To assess whether antiretroviral therapy (ART) intensification, GM-CSF use and Remune initiation before stopping ART lead to viremia containment, and long periods off ART.

Rhinocerebral zygomycosis: diagnostic dilemma for emergency physician: can the associated morbidity and mortality in this rare but deadly disease be reduced? PS 266

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Rhinocerebral zygomycosis [RCZ] is a rare, invasive, rapidly progressive opportunistic infection caused by ubiquitous fungi of the order mucorales. It usually occurs in diabetics or immunocompromised patients. The emergency physician will typically see patients with RCZ in its earliest stages masquerading as a variety of other less serious diseases. The key markers like necrotic patch on hard palate, nasal septum or turbinate, marked facial pain, and cellulites with marked eye and neurological signs may present late in disease. We report a case of RCZ caused by Rhizopus arrhizus [oryzae] in an 84 year old woman with poorly controlled diabetes. She presented with a right-sided facial droop of short origin and being generally unwell. CT scan was non-conclusive and delayed presentation of key markers of RCZ permitted disease to rapidly progress. Despite an intensive antifungal therapy with AmBisome and Insulin sliding scale, patient rapidly succumbed within 4 days. Fine needle aspiration cytology is less invasive, easier and equally effective alternative to pre op biopsy. The key to successful reduction in morbidity and mortality associated with this rapidly fatal disease is - Increasing awareness of the disease, an early diagnosis, correction of underlying metabolic derangement, prompt intensive antifungal therapy with amphotericin B and radical surgical debridement of the necrotic tissue. An 'optimal dosage' of AmBisome requires discussion.

Clinical audit in the haematology ward of a tertiary care hospital: study of degree of correlation between bacteraemia and oro-pharyngeal screens in immunocompromised patients over five years and role of antibiotic prophylaxis PS 267

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Introduction: A clinical audit was carried out over 5-years [1997-2001] in the immunocompromised patients including neutropenic patients and bone marrow [autograft] transplant recipients in hematology ward of Gartnaval General Hospital, Glasgow, a tertiary care center. Objective: It was aimed to establish the degree of correlation between bacterial isolates in oro-pharyngeal screen during bacteraemia episodes and role of antibiotic prophylaxis.

Methods: 2191 specimens from 255 patients with bacteraemia episodes were screened. Results: 29.4% [75/255] incidence of positive correlation, and 38.4% [98/255] of negative correlation was observed. There was 32.1% [82/255] incidence of coagulase negative staphylococcus [CNS] bacteraemia.

Conclusion: CNS bacteraemia is most commonly associated with intravenous catheter infection, which was predominantly seen. Oro-pharyngeal colonization does account for a significant [29.4%] incidence of bacteraemia in the compromised host including neutropenic and bone marrow transplant [autograft] recipients. Hence, prophylaxis with antibiotic is essential. A break up of the percentage of bacterial isolates to be presented.
Methods: Ten adults with chronic HIV disease, HIV-1 RNA levels (VL) < 1.7 log copies/ml and median CD4+ -T cell count of 385/ml were enrolled. After ART intensification with ddI (6 months) + hydroxyurea [HU](3 mo.) + GM-CSF (3 mo.) and a Remune dose, ART was stopped but Remune continued. ART was resumed if rebound VL did not decrease to < 4.7 log in 3 months or if CD4+ counts decreased to < 200.

Results: VL rebounded in all patients after stopping ART, and 7 developed an acute retroviral syndrome (ARS). CD4+ -T cells decreased, and CD8+38 + increased (5-fold). After a median stoppage of 16 weeks, ART was resumed in 9 patients and VL decreased to < 1.7 log, CD4+ counts were regained, IL-2 and IL-15 levels rose. At the 2nd interruption, 9/9 patients had a rebound, and 3/9 had a 2nd ARS, but peak VL and loss of CD4+ were lower (P = 0.003). After 21.3 weeks off ART, 8 patients resumed therapy. The breadth and magnitude of HIV-specific activity increased and thymus size grew. The patients were off ART for a median of 49.5 out of 80 weeks. Two of them are off ART for 80 and 44 weeks respectively (VL < 4 log).

Conclusions: This approach led to a high ARS incidence, long periods off ART, increases in HIV-specific responses, IL-2 and IL-15 levels, and thymus size.

Urinary tract infection in a hospitalized population

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Urinary tract infection in hospitalized population is a significant problem. This is a study of catherized patients urinary infection in Corfu Hospital. In 2000–2001, 3500 urine cultures were sent to our bacteriology laboratory. 650 of them were collected from the catheters. Clinical data of age and type of disease were analysed. The samples were cultured on Mc Conkey agar-Urotube and Vitek cards. The organisms identified with Vitek automatic system. The sensitivity was tested with Vitek and Kirby-bauer method.

Results: No growth of organisms in 46.5%. Positive cultures 35%. 62.2% of the bacteria were Gram (–) rods (55.6% E. Coli, Pseudomonas spp. 9%), 16% were Gram (+) cocci (Enterococcus spp.) and 22% was Candida spp. The resistance of E. Coli was: 37% to Ampicillin, 17% to Co-Trimoxazol and 2% to quinolons. E. faecalis was resistant 10% to Vancomycin.

Conclusions: (1) The percentage of positive cultures and the organisms’ resistance are acceptable. (2) Pseudomonas spp. is absent. (3) There is a high percentage of Candida spp. (4) There are Vancomycin resistant Enterococci in our Hospital.

Monday, 6 May 2002

Beta-lactam antibiotics

Acetaminophen does not interfere in the therapeutic efficacy of amoxycillin/clavulanate acid or erythromycin in the treatment of acute otitis media caused by Streptococcus pneumoniae

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The possible interference of acetaminophen in the amoxicillin/ clavulanic acid (A/C) or erythromycin (ERY) efficacy in the treatment of acute otitis media (AOM), and its possible role in the evolution to otitis media with effusion (OME), were determined in a gerbil model.

A 23F Streptococcus pneumoniae strain exhibiting a MIC of A/C and ERY of 1/0.5 and 0.12 mg/l, respectively, was used. Both antibiotics were tested at 2.5 and 10 mg/kg. Acetaminophen at 50 mg/kg was administered 30 min before each antibiotic dose. Antibiotic concentrations in serum and middle ear exudate were determined. Both antibiotics significantly reduced the number of culture-positive ears and colony counts, with serum concentrations over the MIC of the microorganism for ≥15% of the dosing interval. Antibiotic concentrations in middle ear exudate were almost identical in animals receiving and not receiving acetaminophen. Clinical and microbiological efficacy was correlated with antibiotic concentrations in middle ear exudate ≥1.7 times the MIC of the microorganism, for both antibiotics. Both antibiotics demonstrated efficacy in the treatment of pneumococcal AOM, with the same rate of OME. Acetaminophen, concomitantly administered, did not interfere the efficacy of the two antibiotics tested and did not prevent the evolution of AOM to OME.

Concomitant administration of acetaminophen and high doses of amoxycillin/clavulanate and erythromycin in the treatment of otitis media with effusion caused by Haemophilus influenzae in a gerbil model

Parra A a, Ponte C a, Cenjor C b, García-Olmos M a, Giménez MF a, Aguilar L b, Soriano F a, aFundación Jiménez Díaz, Medical Microbiology, Madrid, Spain; bFundación Jiménez Díaz, Otocrinolaryngology, Madrid, Spain; aGlaxoSmithKline, Medical Department, Madrid, Spain

A gerbil model of otitis media with effusion (OME) induced by Haemophilus influenzae (amoxycillin/clavulanate-A/C- and erythromycin-ERY-MICs of 1/0.5 and 4 mg/l, respectively) was used to evaluate the efficacy of A/C (10/2 and 15/3 mg/kg) and ERY (20 and 50 mg/kg). Antibiotics were administered subcutaneously 2 h post-middle ear inoculation, and continued t.i.d for 24 h, with or without acetamino-phen (AP), at 50 mg/kg, administered 30 min before each antibiotic dose. Antibiotic concentrations in serum and middle ear (ME) were measured by bioassay. ME samples for colony counting were collected on day 2. A/C reduced (P ≤ 0.05) positive ME samples and colony counts versus untreated controls or ERY: ME positive cultures of 90% for controls, 0% for A/C 15, 7% for A/C 10, 17% for A/C 10+AP, 90% for ERY 20, 57% for ERY 50 and 87% for ERY 50 + AP. This was due to A/C (but not ERY) concentrations in ME exceeding 1.8 times the MIC despite the higher percentage of antibiotic penetration of ERY versus A/C (43 versus 8/14%). Animals receiving AP showed less polymorphonuclear cells and more bacteria in ME than those receiving only antibiotics, suggesting that the anti-inflammatory drug diminish the phagocytes and therefore, the efficiency in bacterial clearance.

Amoxycillin treatment for acute otitis media caused by penicillin-resistant Streptococcus pneumoniae. A pharmacodynamic analysis

Parra A a, Ponte C a, Cenjor C b, García-Calvo G a, Giménez MF a, Aguilar L b, Soriano F a, aFundación Jiménez Díaz, Medical Microbiology, Madrid, Spain; bFundación Jiménez Díaz, Otocrinolaryngology, Madrid, Spain; aGlaxoSmithKline, Medical, Madrid, Spain

Purpose: To determine the amoxycillin minimal dose obtaining therapeutic and microbiological efficacy in an experimental otitis media model caused by a penicillin-resistant pneumococcus.
**Methods:** A serotype 23F *Streptococcus pneumoniae* strain exhibiting a MIC of amoxycillin of 1 mg/l was used in an experimental model performed in gerbils (*Meriones unguiculatus*) following previously described procedures. Amoxycillin was tested at the following doses: 0.2, 0.4, 0.8, 1.25, 2.5 and 5 mg/kg. Amoxycillin concentrations in serum and middle ear exudate were determined after drug administration.

**Results:** Doses of ≥ 2.5 mg/kg significantly reduced the number of culture-positive ears, colony counts and otorrhea (P ≤ 0.05) as compared with untreated controls or animals treated with doses lower than 1.25 mg/kg. Doses of ≥ 2.5 mg/kg achieved antibiotic concentrations in the middle ear 1.4–2.4 times higher than the MIC of the infecting strain and serum concentrations over the MIC for 14–19% of the dosing interval.

**Conclusions:** Amoxycillin at doses achieving serum concentrations similar to those obtained in children after standard doses, obtained therapeutic and microbiological efficacy regardless the susceptibility of the infecting strain. Better correlation was found between antibiotic efficacy and antibiotic concentrations in middle ear exudate than between efficacy and serum concentrations, which were suboptimal from the pharmacodynamic perspective.

Increasing prevalence of amoxycillin-clavulanate–resistance among *E. coli* strains in a Hungarian university hospital  PM104

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**Background:** Amoxycillin–clavulanate resistance (ACR) is an emerging problem in *Escherichia coli* as reported from different parts of Europe. The aims of the present study were to evaluate statistically the prevalence of ACR among *E. coli* isolates and to investigate the genetic background of the resistance.

**Methods:** All *E. coli* strains isolated between 2000 1 1 and 2001 9 1 were screened for ACR by Kirby–Bauer disc diffusion method. The resistance to other beta-lactam–beta-lactamase inhibitor combinations and to different beta-lactam antibiotics were also tested. Selected strains underwent determination of beta-lactamase activity. Confirmatory tests for suspected extended spectrum beta-lactamase were performed. PCR testing for TEM and SHV genes were carried out on plasmids isolated from selected strains.

**Results:** In 2000 out of 1109 *E. coli* strains 102 (9.2%) were found to be resistant to amoxycillin clavulanate (AMC). Most of the resistant strains (95%) were obtained from the genitourinary tract and no ACR isolate was found in blood cultures. In 2001 out of 2167 isolates 239 (11%) proved to be ACR and 2.5% were isolated from blood cultures and 66.9% from the genitourinary tract. Thirty-five selected strains were further analysed. Thirty-two were also resistant to (SAM) and six were further resistant to TZP. Quantitative beta-lactamase determination showed increased activity in strains which were partially susceptible to AMC. The presence of ESBL could be proved only in three ACR isolates.

Comparative analysis of cefitubuten (CEF) versus cefixime (CFIX) in the treatment of uncomplicated urinary tract infection (UTI)  PM105

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This open parallel-group study compared the efficacy and tolerability of CEF with CFIX 400 mg once daily in the treatment of community acquired uncomplicated UTI. Seventy-eight female patients were randomized to receive either oral CEF or CFIX for 5 or 10 days. The efficacy of treatment was evaluated by clinical response (by symptoms of UTI dysuria frequency urgency suprapubic pain and by clinical signs) by bacteriologic response and health status measures at baseline and posttherapy.

**Results:** The clinical cure (complete resolution of symptoms and signs) rate for patients receiving CEF was 95.12% of the 41 evaluable patients and 89.18% of the 37 patients receiving CFIX. Bacteriologic response (based on the results of urine cultures obtained posttherapy) the pathogen was eradicated in 82.3% for CEF 73.3% for CFIX. No drug related side effects have been reported in CEF and side effects were experienced by 5.40% of the patients receiving CFIX. Improvement in health status comparing visual scale scores baseline and poststudy to have detected a higher change in average score from 17 to 94 in CEF, from 20 to 82 in CFIX. Wilcoxon improvement value was significant on the 3rd day of therapy in case of CEF and on the 5th day of therapy in CFIX group. In conclusion, the results of this study indicate that CEF course is more effective than CFIX in producing a favourable clinical outcome and achieving higher bacteriologic eradication rate, furthermore CEF was better tolerated.

Pharmacokinetics of cefepime in bile and gall bladder tissue  PM106

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Cefepime is a fourth generation cephalosporin that has a broader spectrum of antibacterial activity than the third generation cephalosporines and is more active in vitro against Gram-positive aerobic bacteria. The purpose of this study was to measure cefepime concentrations in plasma, bile fluid and gall bladder tissue in patients undergoing cholecystectomy. Thirty patients 12 male, 18 female, mean age: 48 years had data acceptable for analysis and were included in this study. All patients received 4 g of cefepime. Several hours after administration and at different time intervals, during surgery, samples were obtained from plasma, bile fluid and gall bladder tissue concomitantly. Antibiotic levels were measured by an agar diffusion method. The mean delta time was 284±255 min. The values for plasma, bile fluid and gall bladder tissue were 33.6±28.5, 6.6±4.3 and 16.1±12.9 µg/ml, respectively. The plasma/bile fluid ratio was 2.6±2.4. There was a significant correlation between plasma and gall bladder tissue concentration (r = 0.871, P = 0.0001). A correlation between bile fluid and plasma cefepime concentration was not observed.

The minimum inhibitory concentration (MIC) data from previous in vitro studies indicate that the cefepime concentration observed in plasma bile and tissue samples of this study would be adequate against typical biliary tract pathogens. Furthermore, these cefepime concentrations correlated well with the favorable clinical outcome reported in previous clinical studies in biliary tract infections. There was also good correlation between delta time and plasma and tissue concentrations and if the dose were given closer to the time of surgery, cefepime concentration would be higher reducing the possibility of an infection.

In vitro activity of Cefepime against *E. coli* and *Klebsiella* strains  PM107

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Cefepime (FEP) is a fourth generation cephalosporin, recently introduced clinical usage in a wide range spectrum. The in vitro
A novel therapy in prevention of antibiotic-induced changes in faecal microflora PM108

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Objectives: The use of antibiotics may lead to decreased colonization resistance and increased formation of resistant bacteria. Present concept was developed to overcome these untoward effects.

Methods: β-Lactamase of Bacillus licheniformis was overproduced in Bacillus subtilis. This targeted recombinant β-lactamase enzyme (TRBL) was released in the small bowel from a controlled-release formulation. Beagles (n = 6) were treated BID with either 20 mg/kg ampicillin (i.v.) + placebo (p.o.), 20 mg/kg ampicillin (i.v.) + TRBL (p.o.) or only placebo (i.v. + p.o.). Stool was collected at days 4 and 10. Samples were cultured for total and main groups of aerobic and anaerobic bacteria and yeast. Temperature gradient gel electrophoresis (TGGE) was used to separate the ribosomal RNA genes.

Results: Ampicillin + placebo group had clearly decreased counts of both aerobic and anaerobic bacteria during the treatment, whereas those receiving TRBL had only minor overall changes and some occasional changes by single species. Intravenous ampicillin decreased the fecal similarity percentage to 60%. The similarity percentage during treatment with ampicillin + TRBL did not differ from that of placebo (86 vs. 81%).

Conclusions: According to our results the TRBL can maintain the large intestinal microflora almost unchanged. These results indicate that TRBL is a promising novel approach for overcoming the ecological adverse effects on gut flora caused by β-lactam antibiotic agents.

Pharmacokinetic interactions of aztreonam and amikacin PM109

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Since broad-spectrum β-lactams combined with amikacin are often applied for nosocomial infections, their pharmacokinetic interactions might be interesting. One gram of aztreonam and 0.5 g of amikacin were administered intravenously single and in combination in six healthy volunteers. Blood samples were collected at regular time intervals and concentrations of antimicrobials were determined by a microbiological assay applying a strain developing resistance to single agent after serial passages. Mean concentrations of amikacin in serum when administered alone and in combination with aztreonam were 26.2 and 20.3, 11.8 and 12.3, 8.4 and 12.2, 6.3 and 9.7, 1.8 and 4.3 and 0 and 1.3 μg/ml immediately after and 0.5, 1, 2, 4 and 8 h after infusion of antimicrobials. Respective concentrations of aztreonam were 63.5 and 25.3, 27.5 and 21.6, 24.2 and 10.5, 19.5 and 13.6, 5.8 and 4.4 and 1.8 and 40 μg/ml. AUCs for amikacin when administered alone and in combination with aztreonam were 35.5±10.9 and 50.5±7.8 mg h/l, respectively. Respective AUC for aztreonam were 99.7±35.2 and 76.4±31.5 mg h/l. It is concluded that the co-administration of aztreonam and amikacin results in earlier clearance of aztreonam and in higher levels of amikacin compared to the administration of each single antimicrobial.

Molecular modelling of β-lactams reveals the structural basis for their inhibition of penicillin-binding proteins, susceptibility to β-lactamases and oral bioavailability PM110

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β-Lactam antibiotics are peptide mimetics that act as suicide substrates for transpeptidase enzymes that cross link bacterial cell-wall peptides. For the first time, the structural and electronic features needed for their recognition by transpeptidase have been fully described, using innovative molecular modelling techniques to compare the conformational forms adopted by cell-wall peptides and β-lactams. Comparison of features in the backbone and C-terminal regions of conformers of active β-lactam antibiotics and model cell-wall peptides, has allowed definition of the molecular recognition template required for substrate recognition by transpeptidase. These shared structural features allow both to act as substrates and to acylate the active-site serine. However, a significant difference in a critical backbone torsion between the two substrates, provides an explanation for the inability of the enzyme–antibiotic complex to undergo the deacylation step that causes inhibition of transpeptidase. On the other hand, β-lactamases appear to have evolved molecular mechanisms that facilitate the deacylation reaction through compensating for the altered structural orientations in β-lactams caused by the different backbone torsion. Finally, analysis of the conformer repertoires of β-lactams for structural features required for substrate uptake by peptide transporters, provides insights into how their structures can be tailored for optimal oral absorption.

Antimicrobial susceptibility of Proteus mirabilis clinical isolates producing extended spectrum beta-lactamases (ESBLs) PM111

de Miguel S, De Julián R, Camino N, Martinez VM, Baquero M. Hospital Carlos III, Microbiology, Madrid, Spain

Objectives: The aim of the present study was to determine in vitro susceptibility to antimicrobials of Proteus mirabilis isolated from urinary tract infections.

Methods: We studied the susceptibility profile of ESBL positive P. mirabilis strains in three adopted children from India with age range from 20 months to 2 years. ESBL was identified using the synergic effect of clavulinate with beta-lactams (ceftazidime and cefotaxime). MIC values of each isolate were obtained by automated microdilution MicroScam method.

Results: The results are shown in the next table:
Amoxicillin sub-therapeutic doses combined with specific serotherapy in the treatment of a stereotype 6B penicillin-resistant Streptococcus pneumoniae sepsis: a mouse model

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The in vivo efficacy of amoxicillin (AMX) sub-therapeutic doses (3.12 mg/kg, i.d. for 48 h, achieving serum levels over the MIC of only 3% of the dosing interval) and concomitant specific serotherapy (single intraperitoneal dose of 1/4 diluted hyperimmune serum (HS)) obtained from mice immunized with the heat-inactivated strain (a pneumococcal sepsis BALB/c mouse model. Mice (five mice/treatment group) were intraperitoneally infected with 1.5 x 10^8 cfu/ml of a serotype 6B penicillin-resistant strain (MIC of 2 and 4 mg/l for penicillin and AMX, respectively). Treatments started 1 h after bacterial inoculation. Study groups were: control (K; receiving non-immune serum (NHS)), AMX+HS, HS, and AMX+HS. Survival rates (%) over time were:

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Significant differences (P ≤ 0.01; log rank test) were found between the administration of AMX+HS and other treatments, with a median survival rate of more than 336 h versus 36 h for the other groups. Treatment with concomitant specific antibodies highly increased the efficacy (measured as survival rate over time) of in vivo sub-inhibitory concentrations of AMX.

Imipenem consumption and Gram-negative pathogen resistance to imipenem at Sestre Milosrdnice University Hospital, Croatia

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Purpose of the study: The study was performed to determine the consumption of imipenem and resistance of gram-negative pathogens (Pseudomonas aeruginosa, Acinetobacter sp., Klebsiella sp., Escherichia coli, Proteus mirabilis, Serratia marcescens, Enterobacter sp.) to imipenem. Gram-negative pathogens were isolated at the Sestre Milosrdnice University Hospital from Zagreb, Croatia, in 1999 and 2000. The imipenem sensitivity testing was performed by disk diffusion and E-test methods. The consumption of imipenem was expressed in DDD/100 hospital days in the same periods.

Results obtained: Imipenem resistance of Acinetobacter sp. decreased significantly in the year 2000 (P = 0.0052), especially in the first 6 months (P = 0.021) when the lowest consumption of imipenem was recorded. Imipenem resistance of other gram-negative pathogens did not decrease significantly.

Conclusion reached: Consumption of imipenem might lead to changes in resistance to imipenem among Acinetobacter strains.

Survey of extended-spectrum beta-lactamases production in clinical isolates of Acinetobacter baumannii

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Purpose: Acinetobacter baumannii is becoming increasingly frequent nosocomial pathogen at our hospital, and beta-lactam resistant strains are on the increase, especially among ICU isolates. To study the susceptibility of A. baumannii clinical isolates to beta-lactams and to determine the ESBL-producing strains during 2001, a total of 438 Gram-negative nonfermenters (GNNF) isolates was investigated by semiautomated Mini API System (Bio Merieux, France). Eighty-four A. baumannii non-repeated isolates was studied for ESBL-producing by Double-disk synergy test (DDT) and ATB-BLSE test (Bio Merieux, France). MICs for beta-lactams were determined by E-test (AB Biodisk, Sweden).

Results: A. baumannii (n = 84) showed a multidrug resistance. The isolates were resistant to cefotaxime (79%), cefoxitin (96%), ceftazidime (49%), amoxicillin/clavulanate (76%), piperacillin (72%), aztreonam (84%), imipenem (12%). The 32 (38%) of investigated A. baumannii expressed ESBL activity and originated more frequently from ICU (78%). ESBLs producing strains were isolated from endotracheal aspirate (52%), surgery wounds (29%), blood culture (5.7%).

Conclusions: In general resistance levels were higher in clinical isolates A. baumannii to beta-lactams. The DDT seems to be a practical method for ESBL-screening; ATB-BLSE method is more sensitive. Our study display to be the first report of ESBL-producing A. baumannii strains from our country. Carbapenems seem to be the most active agents against A. baumannii.

Characterization of an extended-spectrum beta-lactamase from Salmonella infantis

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Salmonella infantis, strain 111, was isolated from a newborn baby at Wassila Betagoua Maternity in Tunis. It exhibited high resistance to penicillins, extended-spectrum cephalosporines (ceftaxime, ceftriaxone, ceftazidime, cefpirome) and aztreonam but remained susceptible to cefoxitine and imipenem. Involvement and characterization of enzymatic mechanism in β-lactam resistance were investigated in strain 111. Isoelectricfocusing revealed that this strain produced a β-
lactamase of pl 6. This enzyme had a broad-substrate profile, hydrolyzing amoxicillin, ampicillin, ticarcillin, cephaloridine, cefuroxime, cefotaxime, ceftriaxone, cepirome and cefazidime. The highest specific activity was observed with ampicillin. Cefotaxime was hydrolyzed the most efficiently of the extended-spectrum cephalosporins. The pl 6 extended-spectrum β-lactamase (ESBL) was inhibited by clavulanic acid and sulbactam. No inhibition of the ESBL was observed with 1 mM EDTA. Thus, no metal ion is involved in hydrolysis for this β-lactamase. Resistance due to the production of the pl 6 ESBL was transferred with DNA plasmid into *Escherichia coli*. On the basis of substrate and inhibition profiles and isoelectric point, the pl 6 ESBL was not previously described in *S. infantis* in Tunisia. The presence of such a resistance on a plasmid raises concern for rapid dissemination among bacteria and loss of effectiveness of β-lactams.

**Antivirals**

**Liver biopsy among co-infected HCV and HIV patients** PMI116

Poizot-Martin I, Enel P, Benhaïm S, Vion-Dury F, Dinh T, Drogoü MP, Gastaut J A, Assistance Publique Hôpitaux de Marseille, CIISIH Sud, Pr JA Gastaut, Marseille, France; Assistance Publique Hôpitaux de Marseille, Cellule Santé Publique DMI2, Marseille, France, Assistance publique Hôpitaux de Marseille, CIISIH Sud, Marseille, France

**Objective:** To assess liver biopsy (LB) practices in a cohort of 255 co-infected HCV and HIV patients followed up in an HIV specialized medical unit.

**Method:** Transversal study with questionnaire among patients in pre-therapeutic’s evaluation with PCR + and without LB at 6 months.

**Results:** Among the 255 patients, 28 (11%) are lost of follow up, 159 (62.3%) have had LB, 68 (26.2%) have no LB. The characteristics of these 68 patients are: median age = 38.5 ± 6 years; sex ratio = 2.14, CDC-stage A = 33.3%, B = 47.0%, C = 19.7%; undetectable viral load = 33.3%, median CD4 = 326 ± 204, anti-retroviral therapy = 95.5%, HCV-genotype 1 = 46.7%, 3a = 31.7%, 4 = 21.7%. Causes of non-made LB are: (1) refusal from patients because of biopsy’s fear = 35.1%; (2) contraindications because of HIV infection = 33.8% (clinical events = 16.2% which contraindicate anti-HCV treatment, grade III thrombocytopenia = 8.8% which contraindicate biopsy, non-adherence to previous HIV follow up = 8.8%); (3) other = 30.9% (alcoholism = 13.2%, psychiatric/depressive disorders = 11.8%, decompensated cirrhosis = 5.9%). Drug use or methadone/buprenorphine treatment are not considered as contraindication.

**Conclusion:** One-third of patients are afraid of LB. Alcoholism and psychiatric/depressive disorders are the principal contraindications to anti-HCV treatment. It seems important to improve information of patients about LB and to focus on alcohol and psychiatric/depressive disorders management in such population.

**Human T-Lymphotropic Virus type I (HTLV-I) co-infection accelerates the development of hepatocellular carcinoma (HCC) in patients with chronic hepatitis C virus (HCV) viremia** PMI117

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**Objectives:** To analyze HBV genotype-related clinical differences among patients with chronic HBV infection, all 158 patients were serologically tested for serum alanine aminotransferase (ALT) and hepatitis B e antigen (HBcAg) and followed up for a mean 10.8 (6.4) year period. Genotypes B and C were found in 58 (36.7%) and 100 (63.3%) of the patients, respectively. HBcAg positivity and ALT abnormality rates at the start of the observation period were significantly higher in genotype C patients (66.0 and 84.0%) than in genotype B patients (34.5 and 22.4%). The annual rate of spontaneous HBcAg disappearance in genotype B patients was much higher than in genotype C patients (8.38 versus 2.34%, respectively). Patients with genotype B who were continuously HBcAg negative from entry had significantly higher ALT abnormality (58.8%) than those with genotype B (19.2%). Interestingly, patients with genotype C who became HBcAg negative by interferon treatment had high ALT abnormality (58.8%). All patients with ALT abnormality were serum HBV DNA positive. These findings indicate that HBV genotype C patients are more severe liver deterioration because of the delay of HBcAg disappearance and continued HBV replication after HBcAg disappearance.

**Antiviral and anti-stress activities of ‘gamma’-L-Glutamylhistamine and its derivates** PMI119

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**Objective:** To study the effects of ‘gamma’ L-Glutamylhistamine (Glu-HA) derivates on non-specific immunity (‘alfa’-IFN, ‘gamma’-IFN and NK cell activity) and antiviral activity on the experimental influenza and herpes virus infections in mice. The Glu-VA and its derivates Glu-II were synthesized by peptide chemistry techniques. The Glu-HA and Glu-II were administered i.p. 0.05 and 0.5 mg/kg before and after influenza virus (type A/Aichi) and showed a protective effect even at the high infective dose (100LD50) — the rate of protection = 42–51/60% in the positive/control group. They were not very effective in the protection of IFN-pretreated groups.
in the protection of herpes simplex virus encephalitis in mice. The model of the physico-emotional stress in mice was used to investigate the IFN system and NK cell activity. The production of IFNs and NK cell activity of splenocytes decreased in 2 h after the stress and back to normal level in 7–10 days. It was shown that Glu-HA and Glu-II can protect or substantially prevent the decrease in NK cell activity and IFNs synthesis in post-stress period (so normally did not induce the IFNs’ synthesis).

Conclusions: The Glu-HA and Glu-II showed antiviral effect against influenza virus infection in mice. The immunomodulating activity and ability to normalize the IFN synthesis and NK cell activity depressed the post-stress period and probably play an essential role in the antiviral activity.

No dose adjustment of an anti-influenza prodrug oseltamivir is required in patients with hepatic impairment PM120

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**Background:** Oseltamivir (OSE; Ro 64-0796, Tamiflu\textsuperscript{R}) is an oral ethyl ester prodrug of its active metabolite oseltamivir carboxylate (OC; Ro 64-0802), a potent and selective neuraminidase inhibitor of the influenza virus. The purpose of the study is to evaluate the need for OSE dosage adjustment in hepatic impaired patients (HI).

**Method:** Healthy volunteers (HV) versus HI (Child-Pugh Score 7–9) matched on the basis of age (±10 years), gender and weight (±20%) were compared. Each subject received 75 mg OSE.

**Results:** Based on C\textsubscript{max} (ng/ml) and AUC\textsubscript{inf} (ng h/ml) analysed using nominal times, LS mean ratios and 90% CI between HI and HV were similar. OSE* values in HI were marginally elevated but not sufficiently to require dose adjustment.

<table>
<thead>
<tr>
<th>Mean</th>
<th>Ratio HI/HV (90% CI)</th>
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<tbody>
<tr>
<td>Unpaired (12 HI, 23 HV)</td>
<td>Paired (11 HI, 11 HV)</td>
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<tr>
<td>OSE C\textsubscript{max}</td>
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</tr>
<tr>
<td>OSE AUC\textsubscript{max}</td>
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<tr>
<td>OC C\textsubscript{max}</td>
<td>271 (32)</td>
</tr>
<tr>
<td>OC AUC\textsubscript{max}</td>
<td>3280 (41)</td>
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Conclusions: No OSE dose adjustment is required in HI patients.

Development of perspective antiviral compounds by means of 4D-QSAR PM121

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The aim of this study is to investigate the influence of molecular structure of macrocyclic pyridinophanes and their analogs on anti-influenza and antitherpetic activity of these compounds. We used 4D-QSAR approaches on the basis of simple representation of molecular structure. Such representation for biologically active substances allows the description of the spatial structure of compounds with the complete stereochemical information. It determines spatial structures either promoting or interfering of the concrete biological activity. It is easy to realize the molecular design of compounds with the given level of activity with the help of the combinations of simplexes. Statistic characteristics for QSAR of Partial Least-Squares models are satisfactory (R = 0.92–0.97; CVR = 0.76–0.86). The molecular fragments that increase the antiviral activity were defined and will be demonstrated. This information was used for design and directed synthesis of several novel antiviral agents with predicted high anti-influenza or antitherpetic activities. Predicted activities were confirmed experimentally. 4D-QSAR approaches are useful for development of antiviral compounds.

This work was partially supported by INTAS foundation (grant INTAS 97-31528).

The anti-influenza action of proteolysis inhibitor E-aminocaproic acid (E-ACA) PM122

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The purpose of this study was to research the anti-influenza activity of proteolytic inhibitor E-ACA. It prevents the enhancement of proteolysis during the interaction of virions with cell membranes and decreases penetration of virions into cells. E-ACA brings down proteolytic cleavage of HA-precursor to HA-1 and HA-polypeptides and reduces the infectious virus harvest. It shows the prophylactic and therapeutic action during the experimental influenza reducing the enhancement of alkaline proteases activity in lungs after infection. E-ACA promotes the intensification of specific antibodies production and cell immunity, prevents vessels’ permeability and hemorrhagic phenomena, decreases the destruction of bronchi’s epithelium. It reduces the duration of intoxication, catarrhal instances and hyperthermia in sick children. E-ACA improves the indexes of immunity, non-specific resistance and decreases the rate of bacterial complications. Application of E-ACA for treatment influenza and other ARVI in children is recommended in Ukraine on the base of results of our researches. The higher effects demonstrated as a result of combine usage of E-ACA with specific Ig, or Detiforin, or Unithyol, or Ribavirin. In our opinion, the study of effectiveness of E-ACA combine application with inhibitors of influenza NA is the perspective direction of anti-influenza researches development.

We should we treat immediately all varicella patients with acyclovir if the patient is older than 20 years PM123

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During past 2 years in Institute for Infectious and Tropical Diseases in Belgrade, 89 immunocompetent varicella patients were treated and cured. Among them 32 were older than 20 years (35.95%). X-rays were performed in all patients. Diagnosis of pneumonia was made in 32 patients (35.95%), but in 26 (81.25%) patients older than 20 years. Varicella is a benign, self-limited disease, if it strikes early, i.e. preschool, school children and teenagers. At that time there is no need for specific therapy. But in neonates, immunocompetent adults and in all
immunocompromised patients it can be difficult and life-threatening disease. In immunocompetent adult population pneumonia is a very serious, sometimes fatal complication. Knowing the pathophysiology of primary varicella–zoster infection, specific therapy with acyclovir should be started immediately after making the diagnosis in patients older than 20 years, without waiting for X-ray proof of pneumonia.

Brividin compared to acyclovir for the treatment of herpes zoster: effects on acute disease and posttherapeutic pain  PMI124

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Objective: Comparison of efficacy and safety of brividin 1 x 125 mg and acyclovir 5 x 800 mg, both for 7 days, in the treatment of herpes zoster.

Methods: Randomised, double-blind study on 1227 immunocompetent patients ≥18 years (brividin: n = 613, acyclovir: n = 614). A subgroup of patients ≥50 years (brividin: n = 309, acyclovir: n = 299) was examined for the occurrence of posttherapeutic pain in a poststudy survey. Posttherapeutic pain was defined as any zoster-associated pain, regardless of intensity, after the end of acute zoster.

Results: Brividin was superior to acyclovir in reducing time to last occurrence of new vesicles (RRITT): 1.13 [1.01–1.27], P = 0.01). The advantage of brividin was more pronounced in patients ≥50 years (RRITT): 1.16, [1.01–1.34], P = 0.02). Incidence of posttherapeutic pain was significantly lower with brividin (32.7%) than with acyclovir (43.5%), P = 0.006. Duration of pain was comparable in both treatment groups (RR: 1.11, [0.93–1.32], P = 0.27). Potentially treatment-related adverse events occurred in 7.7% of the brividin recipients and in 10% of the acyclovir recipients.

Conclusions: Brividin 125 mg once daily for 7 days is superior to standard acyclovir in stopping viral replication in acute herpes zoster. In patients ≥50 years, brividin is more effective than acyclovir in reducing the risk of developing posttherapeutic pain. Brividin is as well tolerated as acyclovir.

Antiviral activity of metal complexes of acyclovir PMI126

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We have published that Cu(II) complexes of acyclovir (ACV) are active against HSV infection (MBD, 1996). Here we present data on the activity of ACV complexes of Ni(II), Cd(II), Co(II) and Ag(I) against resistant to ACV HSV 1 strain R-100 in comparison with the effect against ACV sensitive strain Victoria. Selectivity indexes (SI) compared to that of ACV were indicative for activity. The following data were obtained: (i) 1 was 10 times less selective inhibitor of strain R-100 than that of strain Victoria; (ii) under the action of [Cd(ACV)Cl2]2, [Ni(ACV)2(H2O)2]Cl2:2ACV and [Ni(ACV)(NO3)2]·5H2O was up to 90% higher than that in the control; (ii) 2 was 28 times less selective inhibitor than ACV; (iv) SI of 3 was 2 times higher for strain R-100 and five times lower for strain Victoria then that of ACV. These data show that the selectivity of ACV against resistant HSV 1 strains can increase when ACV is bond to a proper metal ion.

Antiviral activity against different types of Herpes simplex viruses, including variant resistant to acyclovir and acute toxicity was determined.

Methods: An antiviral activity against Herpes Simplex virus of the type I (HSV-I/Leningrad/248/88) and variant HSV-1 (VVT/4/00R) resistant to acyclovir was determined using commonly accepted method. Viruses were grown on a continuous culture. Maximal toxic dose was determined by the administration of compounds orally (300 mg/kg) or intraabdominally (100 mg/kg) to white mice that had mass 18–20 g. Condition of the animals was controlled during 72 h. Mice pneumonia model was used for the testing activity in vivo.

Results: Derivatives tested have activity against HSV-1 and HSV-1 resistant to acyclovir. Maximum protection of the cells up to 80% was reached at concentration of compounds 100–10 mg/kg. Tested compounds have low toxicity and animals did not die after intraabdominal and after per oral administration of the substances. Using these compounds led to essential relief of diseases in animals. The number and square of virus specific areas of inflammation in lung was decreased to compare with control untreated group. Tested compounds protected animals similar to acyclovir that was used as control.

Conclusion: Derivatives of carboxalkoxy sulfanilic acids are active against HSV in vitro and in vivo and act on the acyclovir resistant variant viruses.

Denotivir: in vitro, animal model and clinical evidence of its efficacy in Herpes simplex virus infections PMI128

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Background: Denotivir is a 5-benzo amin o-4-chloro-3-methyl-4-isothiazolecarboxanilide anti-inflammatory agent with antiviral and immunomodulatory activities. It possesses also mild antibacterial and antifungal action.

The purpose of the study: The aim of this presentation is to give an overview of recent studies demonstrating denotivir ef ficacy in herpetic infections.

The results obtained: In vitro studies revealed that denotivir in the doses below its cytotoxicity (about 25 μM) significantly inhibited (by 90–99%). Herpes simplex virus (HSV)-1 and HSV-2 replication in fibroblast and kidney cell cultures. Moreover, it was showed that denotivir in the dose of 37 mg/ml markedly inactivated HSV-2 after 30 min incubation at 37 °C. In guinea pigs research, 2% denotivir in 90% DMSO appeared to be superior to 90% DMSO alone and untreated groups in the therapy of animal skin infected by HSV-2. There was no huge difference in edema and oedema scorings between studied groups, however in the group treated with denotivir, in contrast to others, no vesicles developed. Several clinical studies showed usefulness of denotivir in controlling herpetic infections in dermatology.
ophthalmology and otolaryngology. In the majority of studies within few hours after the drug application rich and pain relief was noted and within 1–2 days the vesicular lesions were dried up.

The conclusion reached: In conclusion, denosumab is an effective antitumor agent.

Comparison of therapeutic effects of salicylic acid and fig tree latex on bovine papilloma PM129

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This study was conducted on 12 cows affected with teat papillomatosis. In the first step, each cow was located on one of three groups. The first group contained four cows from 1 to 4 years that were treated with fig tree (Ficus carica) latex. The second group contained four cows from 1.5 to 4 years that were treated with a 10% solution of salicylic acid, and the third group contained four cows as control. In group one and two following treatment with fig tree latex and salicylic acid, superficial necrosis begun from day 5 and all of the warts disappeared by day 30. In the control group, after day 20, there were no changes in number of lesions, but some of them were larger than first observation. On day 25, one of the marked warts disappeared and on day 35 another wart was disappeared but six were present until day 45. Comparison of effects of salicylic acid and fig latex showed similar effects in treatment of udder papillomatosis in cow.

Laboratory markers of skeletal muscle toxicity in HIV-infected patients: a cross-sectional case-control survey of frequency, potential correlation with antiretroviral therapy, clinical significance, and outcome PM130

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To assess skeletal muscle toxicity among ~1000 HIV-infected outpatients (p), the 129 p who had ≥1 altered CPK assay (>195 U/l) between May and November 2001, were compared with 387 p randomly selected among those who had ≥2 laboratory exams in this 6-month interval, in a 1:3 case-control study. Among the 129 p with altered CPK levels only six were females, and 110 received antiretrovirals. The overall frequency of altered CPK among all p who underwent ≥2 laboratory workouts in 6 months was 14.4%. CPK alteration was transient in 98 p, with values ranging from 196 to 3463 (mean 256.2 ± 62.3) U/l, but was recognized ≥2 times in 2–6 months in 31 p (24%), 24 of them showing concomitant high aldolase levels (3.1–10.8 U/l). A myopathy or a rhabdomyolysis were recognized in four p only; a myositis was confirmed in one p by histopathology. In a multivariate logistic regression analysis, when excluding the unexpected prevalence of the male gender (P < 0.0001), no significant difference emerged between p and controls as to age, risk for HIV infection, iv drug use, duration of HIV infection, prior anti-HIV therapy and its length, selected drug combinations, administered nucleoside analogues, HIV disease stage, mean CD4+ count and HIV viremia, signs and duration of lipodystrophy, increased glucose, triglyceride and cholesterol levels, and other therapies. Muscle abnormalities, though frequently asymptomatic, are underestimated HIV disease complications, and the role of metabolic (i.e. mitochondrial) alterations, deserves investigation.

Poor efficacy of non-nucleoside reverse transcriptase inhibitor (NNRTI)-based salvage HAART in HIV-infected patients heavily pre-treated with all other classes of antiretroviral compounds PM131

Manfredi R, Calza L, Chiodo F. Infectious Diseases, University of Bologna, Bologna, Italy

Efficacy and tolerability of atorvastatin in the treatment of hypercholesterolemia in HIV-infected patients receiving HAART PM133

Calza L, Manfredi R, Chiodo F. Division of Infectious Diseases, University of Bologna, Bologna, Italy

Fatal lactic acidosis without elevation of liver-enzymes during the treatment with stavudine, didanosine and efavirenz: a case report PM132

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Nucleoside reverse transcriptase inhibitors (NRTIs) cause various side effects, many of which are thought to be due to their effects on mitochondria.

A 36-year-old HIV positive (HIV RNA: 6000 copies/ml, CD4 cell count: 359/μl), obese (body-mass-index: 40.9), therapy-naïve female patient, who after 7 months of well tolerated and effective antiretroviral therapy (stavudine, didanosine, efavirenz), had slight gastrointestinal discomfort and suddenly developed a lactic acidosis (arterial-pH 7.03 [7.36–7.44], anion-gap 45.8 mmol/l [7–16], serum-lactate 24.8 mmol/l [0.7–2.1]), without clinical and laboratory signs of liver-involvement (bilirubin 0.4 mg/dl [0.1–1], aspartate-aminotransferase 26.0 U/l [15], alanine-aminotransferase 13.0 U/l [17], g-glutamyl- transpeptidase 32.0 U/l [18], alkaline phosphatase 110 U/l [55–170]). She died 4 days later despite intensive care (continuous venous haemodiafiltration, sodium-bicarbonate infusion, high doses of vitamins, respiration). The pathologic examination showed an enlarged liver (2370 g) with yellowish appearance and pasty consistency, which microscopically appeared as a massive macro- and microvesicular fatty degeneration, and only slight signs of terminal pancreatitis.

This reported case gives evidence that a massive lactate acidosis may develop without previously disarranged laboratory parameters for liver or pancreatic function. A fatal outcome may evolve without further accompanying-illnesses.
Introduction: Significant increases in plasma triglyceride and cholesterol levels have been reported in patients treated with HAART, and prolonged metabolic imbalances could significantly act on the long-term prognosis and outcome of HIV-infected persons.

Patients and methods: Fourteen HIV-infected patients on PI-based HAART since at least 12 months and presenting hypercholesterolemia (>290 mg/dl) of at least 6-month duration and unresponsive to a hypolipidemic diet and physical exercise, have been treated with a single daily dose of atorvastatin (20 mg) for 18 months.

Results: One patient was excluded from evaluation due to early drop-out. Ongoing antiretroviral treatment included ritonavir in four cases, indinavir in four, nelfinavir in three, and saquinavir hard-gel in two. At the close of 18-month follow-up of atorvastatin therapy, a decrease of total cholesterol level of 21.9% versus respective baseline value was observed; eight out of 13 patients reached normal values for cholesterol. Mild gastroenteric symptoms were found in only one of the 13 treated patients, while no skeletal muscle and liver toxicity has been observed.

Discussion: In our study, pharmacological treatment with atorvastatin proved certainly effective in the management of diet-resistant hypercholesterolemia, and was associated with a favourable tolerability and adherence profile.

The effectiveness of antiretroviral drug therapy for HIV-1 is associated with HIV-1 proviral DNA level and viral selection

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The effect of combination antiretroviral therapy regimens on HIV-1 proviral DNA level in peripheral blood mononuclear cells (PBMCs) was examined in 12 HIV-1-positive patients, using endpoint dilution PCR and serially cloning and sequencing of the gag region of HIV-1. The major clone was defined as the most numerous of 10 analyzed clones, and observation periods ranged from 8 to 32 months (mean, 19.8 ± 10.2 months). In five patients (one with primary-stage HIV-1 infection) receiving three antiretroviral drugs, HIV-1 RNA levels reduced to undetectable (i.e. < 100 copies/ml). HIV-1 proviral DNA levels and the number of major clones reduced in four of these patients. HIV-1 RNA levels reduced, but remained detectable, in five other patients. In the two remaining patients (both receiving two rather than three antiretroviral drugs) HIV-1 RNA levels increased. These results suggested that the population of the major clones may be affected when HIV-1 RNA levels reduce following combination regimens of antiretroviral therapy.

Saquinavir hard gel (Shg) as a part of a spontaneous 12–18-month de-intensification anti-HIV regimen following successful highly active antiretroviral therapy (HAART)

Manfredi R, Calza L, Chiodo F. Infectious Diseases, University of Bologna, Bologna, Italy

The induction-maintenance concept was poorly studied in HIV+ patients (p), and Shg was never assessed after prolonged response to potent protease inhibitors (PI)-based HAART. Shg-naïve p who refused indinavir, ritonavir, or nelfinavir-based HAART after achieving long-term viral suppression, and resorted to Shg+2 nucleoside analogues (NA), were followed prospectively. In 60.7% of the 61 p assessed for 12–18 months, ≥1 NA was changed. Prior HAART was interrupted after 8.4 ± 2.9 months, due to adverse events (46 p), or p’s request (15 p), while a viremia < 50 copies/ml was present since 4.7 ± 1.5 months. A viremia of 50–1000 HIV-RNA copies/ml was maintained in 49 p (80.3%), while a higher viral load occurred in 12 p after 5.9 ± 0.6 months, and was related to a pre-HAART viremia > 100 000/ ml, a more frequent >100% recovery of CD4 count, mutations of codons 48–59, and failure to change NA (P < 0.05–0.001). A CD4 drop >20%/150 cells/μL was found after 7.1 ± 0.5 months in only eight p, who also had virologic failure: immunologic deterioration was earlier and deeper when NA were not changed (P < 0.05). All the 37 p who introduced Shg+ novel NA after a successful >6-month induction with a potent PI-based HAART had a stable 12–18-month outcome. A suboptimal HAART including the less effective but better tolerated Shg may be effective for >1 year, especially when novel NA are introduced, and specific mutations are absent. Despite a lower potency, drugs with a good safety and compliance profile may be recovered for simplified regimens.

Quantification of HIV-1 RNA in Cerebrospinal Fluid after the start of dual or triple antiretroviral therapy

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Objective: To evaluate efficacy of antiretroviral therapy (ART) with two or three drugs in the nervous ‘reservoir’.

Patients: Thirteen acute neurological and ART naïve AIDS patients underwent a paired and simultaneous sample from plasma and cerebrospinal fluid (CSF) for a quantitative detection of HIV-1 RNA (Amplicor Roche) before ART. All patients underwent a CT and/or MR of the brain to perform a diagnosis. All of them had an HIV related neurological acute inflammatory disease. After diagnosis all patients received ART: 7/13 received two NRTI and 6/13 received HAART including two NRTI and one protease inhibitor. All patients underwent a paired and simultaneous follow-up from plasma and CSF during the 2nd month of treatment.

Results: In all patients baseline levels of HIV-RNA were higher (P < 0.05) in the plasma (log 10 5.37 ± 0.93) than in the CSF (log 10 4.33 ± 1.379). The 7/13 patients who received dual therapy had undetectable levels (cut-off 200 copies/ml) of viral RNA at the follow-up in CSF, but not in plasma: three of these seven patients had a detectable plasma HIV-1 RNA. All 6/13 patients with HAART had undetectable HIV-1 RNA both in plasma and in CSF at the follow up.

Conclusions: Dual NRTI therapy is rapidly effective in CSF (because of an high penetration of drugs through a more permeable blood–brain barrier and lower HIV RNA baseline levels) but not in plasma. HAART is rapidly and equally effective both in CSF and plasma.

Fulminant hepatic failure after the start of a highly active antiretroviral therapy efavirenz-based regimen in a naive AIDS woman without hepatitis viruses co-infection

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There are no reports of fulminant and fatal hepatic failure after the start of Highly Active Antiretroviral Therapy (HAART) in an HIV subject without chronic viral hepatitis.
Case report: A 30-year-old naive AIDS woman with clinical symptoms due to a PCP was observed. Baseline ALT was increased (0.5 m.n.v.) because of a mild hepatosteatosis and a silent cholelithiasis. Serology for HBV, HDV and HCV was negative; IgG anti-HAV, anti-EBV, anti-CMV and anti-HSV were present. HIV-1 RNA was 5.7 log 10, CD4+ count was 26/µl. During the PCP treatment with co-trimoxazole ALT values increased (>5 m.n.v.); nevertheless, she completed the treatment. Liver enzymes returned to the pre-treatment values over several days. Then she started HAART with stavudine, lamivudine and efavirenz. After 10 days the patient showed an efavirenz-related skin rash that resolved within 5 days, without treatment discontinuation. Fourteen days after the start of HAART jaundice appeared. Laboratory revealed severe ALT increase (>8 m.n.v.) and hyperbilirubinemia (17 mg/dl) and she died because of an acute liver failure syndrome within few days. An HAART efavirenz-based regimen can result highly hepatotoxic when given in presence of a hepatosteatosis, of a recent hepatotoxicity caused by a non-antiretrovirial treatment and of a previous idiosyncratic reaction to efavirenz.

Our experience with Bulgarian herbal extracts for improving the general condition of HIV-positive patients PM138

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Purpose: To investigate the positive effect of Bulgarian herbs on the general condition of HIV-positives.

Methods: We used a combination of 19 Bulgarian herbal extracts and treated six patients, divided into two groups: three with asymptomatic and three with asymptomatic HIV-infection. The all three patients with asymptomatic HIV-infection were treated only with herbal extracts, another three patients with symptomatic HIV-infection were treated with combination of herbal extracts and anti-retroviral therapy. The general status of patients has been evaluated by both subjective and objective surveillance. The immunologic monitoring has been performed by absolute count of CD4+ lymphocytes.

Results: All patients have shown an obvious improvement in their general condition: high spirit and working capacity, good appetite and sleep, a restoration of body weight. The number of CD4+ lymphocytes has been lightly increased or constant.

Conclusion: The combination of Bulgarian herbal extracts has shown significant positive effect on the general condition and improve the quality of life.

Antifungal activity of in vitro and in vivo combinations of voriconazole with 5-fluorocytosine and amphotericin B against Candida andCryptococcus spp PM139

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Purpose: The present study was designed to determine whether the activity of voriconazole (VOR), a novel triazole, was reduced against candidal and cryptococcal infections by the addition of standard antifungal agents, amphotericin B (AMB) and 5-fluorocytosine (5-FC). VOR was tested in combination with standard antifungal agents both in vitro, using a checkerboard MIC determination test, and in vivo in immune normal guinea pig models of fungal infections.

Results: The results indicate that the efficacy of VOR against Candida albicans and C. neoformans was not antagonised by AMB or 5-FC in vitro. Furthermore, in guinea pig models of systemic candidiasis and intracranial cryptococcosis, no antagonism was observed between the lower doses of VOR and either AMB or 5-FC on the basis of reductions in tissue fungal loads. At the highest doses of VOR, both AMB and 5-FC showed some antagonism, but the combinations were still effective in significantly reducing fungal tissue loads compared with vehicle-treated control animals.

Conclusion: These results suggest that VOR may be used in combination with standard antifungal agents, and future studies to elucidate the clinical potential of VOR combination therapies in the management of Candida and Cryptococcus infections are warranted.

Antifungals

Itraconazole in the treatment of pityriasis versicolor PM140

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A comparison of two short-term dose schedules with itraconazole was carried out in 50 patients with pityriasis versicolor. The patients were divided in two groups. Each group consisted of 25 patients who completed the therapy and controls. The clinical diagnosis was confirmed mycologically, by direct microscopic examination. The first group received 400 mg of itraconazole daily for 3 days. The second group received 200 mg daily for 5 days. The patients were controlled clinically and mycologically 15 and 30 days after the initiation of treatment. Erythema, scaling and pruritus was evaluated clinically. Clinically and mycologically cured patients accepted as cured. The cure rate were 76% in the first group and 72% in the second group at day 30. The effects of these two groups are similar. None of the patients reported side-effects.

Fungal urinary infections: emerging species, antifungal susceptibility trends and antibody response PM141

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Objectives: To assess the role of Candida species in 120 patients with urinary tract infections (UTIs) with or without schistosomiasis and/or cancer bladder, to compare chromogenic; CHROMagar (CMA), BIGGY agar; morphologic (corn meal, rice agar-Tween 80) media and biochemical candifast test for identification of Candida species. Susceptibility to antifungal agents using E-test and candidfast and the performance of ELISA test for detection of anticandida antibodies (IgM and IgG) in serum were evaluated.

Results: C. albicans was the most frequent (43.4%) species responsible for fungal UTIs. However, non-albicans species, C. glabrata (23.3%), C. tropicalis (20%) and C. krusei (13.3%) were also isolated. Rice agar-Tween 80 was found to be cheap, available and sufficient to make a final identification (100%). CMA could not identify C. glabrata. BIGGY agar could not adequately differentiate Candida species. Candidfast biochemical identification showed low sensitivity of 83.3%. E-test on Sabouraud dextrose agar (SDA) is simple method for MICs determination and could detect S-DD strains in case of azoles.

Conclusion: The emergence of non-albicans species such as C.
glabrata, C. tropicalis and C. krusei have contributed to complicated UTIs. This necessitates accurate isolation and identification of Candida to the species level. Morphology on rice agar-Tween 80 and antifungal susceptibility using E-test on SDA is a simple rapid scheme for routine identification of clinically important yeasts.

The diagnosis of Allergic Fungal Rhinosinusitis—a case study PM142

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Purpose: Classification of Allergic Fungal Rhinosinusitis (AFR) is based on the immunologic relationship of the host to the fungus. AFR must be differentiated from other fungal rhinosinusitis infections, which include acute invasive, chronic invasive, fungal balls and saprophytic colonization. Although many cases of fungal rhinosinusitis is caused by species of Aspergillus, dermatomycoses moulds have become an emerging pathogen in immunocompetent individuals.

Results: Our case study involved a 36 year male suffering from frontal pain, headache, postnasal drip and loss of smell. He was HIV negative and a nonsmoker. The following laboratory tests were performed: IgE-2331.40 (0.00 – 25.00) IU/ml IgA-2.16 (0.70 – 4.00) g/l IgM-0.61 (0.40 – 2.30) g/l Allergen specific IgE for Alternaria — 20.00 (0.00 – 0.5) kU/l FBC-Normal except eosinophils slightly raised 0.60 (0.00 – 0.50) × 10³ l. CT scans indicated fungus proliferation, bone erosion and extension of disease into adjacent anatomic area. Sinus tissue following debridement was sent for microscopy and culture. Hyphae was microscopically observed and cultures yielded two dermatomycoses fungi, Bipolaris spp and Alternaria spp.

Conclusion: It is important to differentiate these two species from Curvularia, Helminthosporium, Drechleria and Exserohilum, Knowledge of these dermatomycoses fungi is important in directing appropriate antifungal therapy and selecting the correct antigens for postsurgical immunotherapy after initial debridement and irrigation.

Antifungal activity of in vitro and in vivo combinations of voriconazole with 5-fluorocytosine and amphotericin B against Aspergillus fumigatus PM143

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Purpose: A key requisite for a new antifungal drug is to demonstrate that it is devoid of significant antagonism in combination with other agents. Combinations of the new triazole, voriconazole (VOR), and standard antifungal agents (5-fluorocytosine or amphotericin B; 5-FC or AMB) were tested against Aspergillus fumigatus in vitro and in guinea pig models of infections to confirm that antifungal activity was not antagonised by using combination therapies. VOR was studied in combination with AMB or 5-FC in vitro, using a checkerboard MIC determination test, and in vivo, using immune normal and immunocompromised guinea pig models of systemic aspergillosis.

Results: The results indicate that the potency of VOR was not antagonised by AMB or 5-FC in vivo; indeed, at lower concentrations of VOR, significant improvements in reducing fungal burden in both in vivo models were achieved by the addition of AMB. In vitro, no antagonism was found between VOR and AMB, although 5-FC had a significant antagonistic effect on VOR activity.

Conclusion: These results from in vitro and in vivo models of aspergillosis suggest that VOR may be used in combination with standard antifungal agents and, therefore, justify further examinations of VOR combination therapies in a clinical setting.

In vitro activity of caspofungin compared to that of amphotericin B, fluconazole, and itraconazole against Candida species PM144

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Purpose: To evaluate the in vitro activity of caspofungin against various Candida spp. and particularly against isolates with decreased amphotericin B, fluconazole, and itraconazole susceptibilities.

Methods: Susceptibility tests were done by NCCLS M27A microdilution guidelines for 239 clinical Candida strains. The MICs (µg/ml) were read at 24 and 48 h.

Results: Caspofungin MICs at 24 h are shown in the table. MICs at 48 h were similar to 24 h readings. Expectedly, no evidence of cross-resistance was detected between caspofungin and other drugs tested. Caspofungin was similarly active against fluconazole- and itraconazole-susceptible and resistant isolates.

Conclusions: (1) Caspofungin is active in vitro against all Candida spp. tested. (2) Caspofungin MICs are slightly higher for C. parapsilosis compared to other species. (3) Its activity against fluconazole- and itraconazole-resistant isolates is noteworthy. (4) Validation of these data require clinical investigations.

<table>
<thead>
<tr>
<th>Species</th>
<th>n</th>
<th>MIC50</th>
<th>MIC90</th>
<th>MIC range</th>
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<td>107</td>
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<td>–</td>
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</table>

Susceptibility of clinical strains of Candida parapsilosis to triazoles PM145

Śwoboda-Kopec E, Wroblewska MM, Sulik-Tyszka B, Cupak A, Luczak M. aCentral Clinical Hospital, Microbiology Laboratory, Warsaw, Poland, bDepartment of Medical Microbiology, Medical University in Warsaw, Warsaw, Poland

The purpose of the study: Analysis of the patterns of susceptibility to triazole antifungal agents of the clinical isolates of Candida parapsilosis, cultured from patients hospitalised in the years 1998–2000 in different wards of the Central Clinical Hospital (1200 beds) of the Medical University in Warsaw, Poland. The strains were cultured from urine samples, blood, ear swabs and wound swabs.

Results: In total 63 isolates of C. parapsilosis were cultured (28— from internal medicine wards, 27—from surgical wards and eight from the intensive care unit patients). Isolates from wound swabs comprised 14 strains (22.22%), ear swabs—13 strains (20.64%), urine—13 strains (20.64%), blood—10 strains (15.86%) and other specimens—13 strains (20.64%). Susceptibility to fluconazole was detected in 56 strains (88.88%), while resistance—in seven strains (11.12%). Testing
of susceptibility to itraconazole revealed 47 (74.61%) strains susceptible and 16 (25.39%) resistant to this agent.

Conclusions: (1) We report a high frequency of C. parapsilosis isolations from blood culture specimens (15.87%). (2) The isolated strains showed a higher frequency of susceptibility to fluconazole than to itraconazole.

Patterns of susceptibility to triazoles of Candida tropicalis strains from clinical specimens PM146

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The purpose of the study: Estimation of susceptibility to triazoles of the clinical isolates of Candida tropicalis, cultured from sputum, urine, throat swabs, wound swabs, drain swabs, stool, peritonium and other specimens from patients hospitalised in the different wards of the Central Clinical Hospital (1200 beds) of the Medical University in Warsaw, Poland in the period 1998 – 2000.

Results: Out of 52 strains of C. tropicalis, 31 were cultured from internal medicine wards, 17 from surgical wards and four from the intensive care unit patients. There were 11 (21.15%) strains isolated from sputum, six (11.53%) from urine, four (7.69%) both from drain swabs as well as throat swabs, three (5.76%) from stool specimens and 24 (46.18%) from other samples. Twenty-three strains (44.23%) showed susceptibility to fluconazole, while resistance—29 strains (55.77%).

Aspergillosis in high risk groups of patients is still associated with high mortality rate (30–90%). Aspergillus fumigatus is the primary pathogen, while other opportunistic Aspergillus species are emerging. Amphotericin B (AB), itraconazole (IT), voriconazole (VO), and terbinfine (TE) minimum inhibitory concentrations (MIC) were determined by modifying the NCCLS M38-P microdilution method. Stock drug solutions were prepared in RPMI 1640, dimethyl sulfoxide (DMSO), and polyethylene glycol (PEG 400). Inocula, of the A. fumigatus group (7), A. flavus group (6), A. parasiticus, A. versicolor, A. niger group (9), A. tenuis, A. heteromorphus, A. pulvinulenta, A. furtii, A. awamori, and A. carbonarius, the A. terreus group (2) and the M38-P quality control strains were prepared according to, and by modifying, the NCCLS guidelines. Plates were incubated at 30 and 35 °C and read at 24 and 48 h.

PEG 400 effectively dissolved IT and VO, while either DMSO or PEG dissolved TE. Low 30 and 35 °C and read at 24 and 48 h.

PEG 400 effectively dissolved IT and VO, while either DMSO or PEG dissolved TE. Low 30 and 35 °C and read at 24 and 48 h.
MICs (0.062–0.5 mg/l) were recorded. *A. terreus* (1) and *A. parasiticas* (2) were resistant to AB.

Certain clinical isolates demonstrate clinical and in vitro resistance. Standardization of susceptibility testing would offer reliable assistance in selecting and monitoring antifungal therapy.

**Investigation of identification and antifungal susceptibility from clinical specimens**  
**PM150**

Otag F, Aslan, G, Ozturk C. *Microbiology Department, Faculty of Medicine, Mersin University, Mersin, Turkey*

Rates of opportunistic fungal infections have risen markedly. Because some of these species have potential resistance to antifungal agents, rapid presumptive species level identification is crucial in allowing for directed antifungal therapy. In this study, 55 isolated yeasts from the clinical specimens were identified by ATB ID 32 C (BioMerieux, France). The number of identified yeasts were, respectively; 33 (60%) *Candida albicans*, six (10%) *C. glabrata*, five (9.1%) *C. tropicalis*, three (5.4%) *C. parapsilosis*, two (3.6%) *C. krusei*, two (3.6%) *C. kofyr*, one (1.8%) *C. guillermondi*, one (1.8%) *C. dubliniensis*. Twenty-one of 55 strains were investigated for antifungal sensitivities by ATB Fungus kit (BioMerieux, France). The results are as follows: 100% sensitivity was detected to myconasol, 94% to fluotoxin, nystatin and econasol, 95% to amphotericin B and ketoconazol. It is important to achieve empiric treatment of the opportunistic *Candida* infections and the following of resistance to antifungals.

**Microbiology**

**PCR as a diagnostic tool of syphilis in unclear cases**  
**PM151**

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At the present stage in Russia with a background of a high case rate of syphilis, it becomes necessary to exclude biological false positive serological tests. Because the serodiagnosis of syphilis has significant limitations, the direct detection of *T. pallidum* in suspect blood may serve as an alternate diagnostic strategy. Polymerase chain reaction (PCR) has been the most widely used amplification method. The study of 56 patients receiving examination related and treatment for syphilis in STD clinic and persons directed from other hospitals where routine serologic examination revealed doubtful results. PCR reaction was carried out with nested primer pairs based on the DNA sequence of the 47–1 and 47–2 kDa gene of *T. pallidum*. PCR was utilized with whole blood. A complex of serological tests: FTA-abs and TIT was used as the *d relegated* gold standard[1]. As a result the sensitivity of PCR was 91.2% and specificity 90.9%. Selective comparison of PCR results with VDRL, the FTA-abs and treponemal immobilisation test (TIT) has shown concurrence 96.8%. In conclusion, the preliminary results of PCR in whole blood in syphilis detection revealed its high sensitivity and specificity; possibility to obtain rapid results in unclear cases.

**Chlamydia pneumoniae: molecular basis of pathogenesis**  
**PM152**

Caronzo D, Lucini V, Pannacci M, Fraschini F, Scaglione F. *University of Milan of Pharmacology, Milan, Italy*

*Chlamydia pneumoniae* (Cp) is an atypical pathogen whit intracellular location, whose eradication is very difficult. In the past years it has been objects of many studies that lead to the demonstration of a relationship between its presence and the development of widespread multifactorial pathologies such as atherosclerosis and asthma. The lack of its eradication can become an important clinical and social problem. The study objective is the comprehension of pathogen–host interaction mechanism, to characterize therapeutics protocols that cold lead to complete eradication of Cp from organism. The research had been principally made on the studying the molecular mechanisms that are at the root of pathogen permanence inside host cell. Using proliferation and apoptosis tests we underlined a different behaviour of infected cells towards control cells. In presence of PI (20 mg/ml), i.e. a peptide that can inhibit the proliferation and induce apoptosis in vitro inhibiting NF-kB, uninfected cells proliferation decreased of 35% in comparison whist the controls, while the one of infected decreased only of about 15%. Moreover, using various apoptosis-inducers, the infected cells showing apoptosis were about 10% while the uninfected were about 40%. The caspase III activity increased significantly in uninfected cells. In conclusion, Cp could delay its elimination from the host inhibiting the apoptosis via NF-kB activation.

**Broad-range polymerase chain reaction (PCR) fungal identification in diagnosis of fungal superinfection of bacterial endocarditis**  
**PM153**

Hryniewiecki T, Gzył A, Rawczynska-Engiert I, a Department of Acquired Vascular Heart Disease, National Institute of Cardiology, Warsaw, Poland, b Department of Sera and Vaccines, National Institute of Hygiene, Warsaw, Poland

Infective endocarditis (IE) frequently causes problems in diagnosis, especially where blood cultures are negative and with fungal etiology (also as a fungal superinfection in bacterial IE). *The purpose of the study*: The purpose of the study was to evaluate the usefulness of broad-range fungal PCR in diagnosis of fungal superinfection of bacterial IE. Twenty-five blood samples were taken for analysis from patients with infective endocarditis. IE was diagnosed according to Duke criteria including positive blood cultures. Suspicion of fungal superinfection was established on serological investigation in five patients, confirmed by blood culture in two patients. Control group consisted of 15 patients without infection. DNA was isolated using the commercially available S.N.A.P. kit. Amplification products were analyzed by gel electrophoresis stained with ethidium bromide. The results obtained: fungal DNA was found in two patients with fungal superinfection of bacterial IE confirmed by culture. In the remaining patients with IE and controls no fungal DNA was found. *The conclusion reached*: Broad-range fungal PCR is a fast and inexpensive tool for the detection of fungal DNA, but it is more prone to contamination than species-specific PCR. The method may be valuable in the identification of fungal superinfection of bacterial IE or diagnosis of fungal IE.

**Use of ELISA with TT virus (TTV) to detect anti-TTV antibodies in human sera**  
**PM154**

Rivanaer D, Lilli D, Lozzi MA, Piunno M, Mancini C. *Microbiology, Science and Public Health, Rome, Italy*

Aim: The aim of this study was to evaluate the EIA method for detection of antibody to TTV virus (TTV) and to investigate the anti-TTV virus prevalence in patients with hepatitis B (HBV) virus, hepatitis C (HCV) virus, in group of `high risk`subjects to hepatitis and in healthy subjects. The Elisa methods (Nuclear laser Vienna Lab) using TTV S and NS antigens: ORF1 (770 aa) and ORF2 (202 aa) was applied to detect anti-TTV; the serological screening was performed from 250 samples to Italian subjects.
Results: The positive rates of anti-TTV antibodies were 11.29% in 62 patients with hepatitis B–C and 14.06% in 119 ‘high risk’ hepatitis patients. The anti-TTV was also found in 7.56% in 69 healthy people.

Conclusions: The anti-TTV were detected in all groups studied, however, its positive rate was similar in patients with hepatitis B–C and in ‘high risk’ hepatitis respect to healthly people. Our results shown that TT virus is frequent in Italy both in patients infected by others transmitted viruses and in general population. The positivity found in healthy adults included in our studies suggests that the virus might be transmitted non-parenterally. The study of pattern of antibody to TTV may be an infectious marker of TT virus similar to that of anti-HCV.

A stress test on a miniaturized identification system designed for Neisseria and Haemophilus  PM155
Rich M*, Bannatyne RM*, Memish ZA*, King Fahad National Guard Hospital, Division of Microbiology, Riyadh, Saudi Arabia, King Fahad National Guard Hospital, Infection Prevention and Control, Riyadh, Saudi Arabia

We report an incident that occurred in our laboratory when the BBL Crystal Identification System for Neisseria and Haemophilus was used to identify a Haemophilus-like-organism. The numerical profile generated was not in the system database. Conclusions: We subjected two numerical profiles were obtained, 1740616606 and 1740616607, neither of which are listed in the system database. Brucella species have been misidentified as Moraxella species, Moraxella phyllolympica, and as Haemophilus influenzae biotype IV in various identification systems. Two cases of laboratory-acquired brucellosis have been attributed to misidentification. To its credit the BBL Crystal Identification System for Neisseria and Haemophilus neither generates a profile number with a misidentified organism nor assigns a confidence level. To refer to the database where they would be of considerable assistance in areas where brucellosis is widespread.

Cloning and characterization of AFLMP1 in Aspergillus flaus  PM156
Chong TK, Woo PCY, Leung ASP, Yuen KY. The University of Hong Kong, Microbiology, Hong Kong, Hong Kong

Purpose of the study: To clone and characterize an antigenic protein for serodiagnosis of infection caused by Aspergillus flaus which is the commonest Aspergillus species causing aspergilloma (AO) and invasive aspergillosis (IA) in Asia.

Result obtained: We cloned the AFLMP1 gene, which encodes the first antigenic cell wall protein in A. flaus. AFLMP1 codes for a protein, AFLmp1p, of 273 amino acid residues, with sequence features that are present in Mp1p and AFlmp1p, the antigenic cell wall mannoprotein in Penicillium marneffei and Aspergillus fumigatus that we described previously. It contains a serine- and threonine-rich region for O-glycosylation, a signal peptide, and a putative glycosyl-phosphatidylinositol attachment signal sequence. Specific anti-AFLmp1p antibody was generated with recombinant AFLmp1p protein purified from Escherichia coli to allow further characterization of AFLmp1p. Indirect immunofluorescent staining indicated that AFLmp1p is present in the cell walls of the hyphae and conidia of A. flaus. Furthermore, it was observed that patients with AO and IA due to A. flaus develop a specific antibody response against AFLmp1p.

Conclusion reached: This suggested that the recombinant protein and its antibody may be useful for serodiagnosis in patients with AO or IA, and the protein may represent a good cell surface target for host humoral immunity.

Integrins in clinical isolates of Enterobacteriaceae  PM157
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Purpose: To investigate the basis for increasing resistance to trimethoprim and sulphamethoxazole. Methods: PCR screening for integrons of 105 clinical urinary tract isolates was performed. Isolates were tested for resistance to 12 antibiotics. Integrons in 14 isolates were sequenced. Results: Integrons of class I were found in 43 isolates and class 2 integrons were found in 10. Eight isolates in the study were resistant to five antibiotics or more and not shown to carry any integron. Nineteen of 69 isolates resistant to trimethoprim did not carry integrons. Only one of these isolates was shown to carry sul1 and is thus probably also carrying an integron. None of the 19 isolates were shown to carry dfr/s, one of five trimethoprim resistance genes known to exist outside integrons. Three isolates were resistant to sulphonamides but were not shown to carry neither sul nor sul2. Only dfr and aad gene cassettes were found in the sequenced integrons. Conclusions: Resistance to trimethoprim in 19 of 69 trimethoprim resistant isolates is mediated by genes not detectable, as in the case with three sulphonamide resistant isolates. Sequenced integrons that contain dfr genes do not carry any gene cassettes mediating resistance to modern antibiotics.

Unusual diagnosis tool for an unusual presentation of alveolar echinococcosis: report of two cases of local progression after an animal bite  PM158

Introduction: The classical human contamination route for alveolar echinococcosis (AE) is ingestion of eggs. Two exceptional human cases are reported with extensive local evolution of AE after a bite.

Case no. 1: Between 1954 and 1972, a patient underwent surgery seven times for a muscle growing tumour which developed after a bite. The diagnosis of muscle AE was assessed on histopathological examination. In 1980, serological tests were in accordance with Echinococcus sp infection.

Case no. 2: In 1985, a man presented ‘cat-scratch fever’ with a right supraclavicular tumefaction following a cat bite. Between 1986 and 2000, five recurrences occurred. Different surgical explorations indicated multiple abscesses of the cervical muscles. In 2000, serological tests were in favour of Echinococcus sp infection and the pathologist described a parasitic wall suggesting hydatidosis, but specific PCR from histological samples prompted the diagnosis of AE.

Conclusion: In these exceptional observations, the liver which is the most usual location of AE was lesion-free. The chronic inflammatory AE lesions have developed in the local lymphatic chain area of the bite
Antibiotic resistance in foodborne *Salmonella* is an emerging public health concern. Integrons are now recognized as the main genetic vehicles of antibiotic resistance in Gram-negative bacteria, including in *Salmonella*. The purpose of the present study was to investigate the presence of class I integrons in resistant isolates of several serotypes of *Salmonella* isolated from poultry products and to determine their association with multidrug-resistance phenotypes. A total of 20 isolates of *Salmonella* belonging to seven different serotypes were tested. The most frequent multiresistant phenotype, found alone or together with other resistances, was to streptomycin and tetracycline. All but seven were resistant to three or more antimicrobial agents, including quinolones and amoxicillin. PCR analysis with the 5′CS and 3′CS primers detected the presence of class I integrons of 1.5 kb in one isolate, with the multiresistant phenotype: amoxicillin, chloramphenicol, streptomycin, trimethoprimsulphametoxazol and tetracycline. Our findings suggest that the uncontrolled use of the antimicrobial agents in food animals may have contributed to the development of the pattern of resistance observed in *Salmonella* isolates. Also the presence of integrons in low prevalent human *Salmonella* serotypes but associated with food animals underscores the public health problem of antibiotic resistance acquisition and spread.

**Prevalence and antimicrobial resistance of *Campylobacter jejuni* and *C. coli* isolated from broilers and pigs in France**

**PM160**

Avrain L*, Humbert F*, Sanders P*, Kempf P*. *AFSSA, UMB, Ploufragan, France, b AFSSA, HQPAP, Ploufragan, France, c AFSSA, LERMVD, Fougères, France*

In 1999, 620 caeca from standard, export or free-range broilers and in 2000, 600 fecal samples from pigs, were collected in French slaughterhouses. Prevalence of *Campylobacter jejuni* and *C. coli* strains was 56.6% in standard, 51.3% in export and 80% in free-range broilers. In standard and export productions, the most often isolated strains was 56.6% in standard, 51.3% in export and 80% in free-range in 2000, 600 fecal samples from pigs, were collected in French production. 53.8% samples collected from pigs contained *C. coli* isolated from broilers and pigs in France PM161 Campylobacter jejuni of antibiotic resistance acquisition and spread. associated with food animals underscores the public health problem of integrons in low pre

The enzyme DHPS (dihydropteratoate synthase) participates in the folate synthesis pathway, and is well recognized as the target for sulphonamides. The enzyme preceding DHPS in this pathway, PPPK (dihydropterin pyrophosphokinase), is another interesting candidate drug target. The metabolic role of PPPK is to provide one of the substrates for DHPS. Earlier studies have suggested that PPPK and DHPS enzymes need to have physical contact with each other for full enzyme activity. Studies of potential interactions between the enzymes have been initiated. So far, indication of a weak interaction has been detected in gelfiltration experiments and the two-hybrid system. To confirm these results, we are currently developing a method to study substrate channeling, as interfering with such interactions could lead to impaired growth and thus be used as inhibitory drugs. We have also cloned and sequenced the operons coding for the enzymes in the folate biosynthesis from different clinical isolates of *Streptococcus pyogenes*. Comparisons revealed some isolates with a mosaic structure in the operon, suggesting that horizontal transfer of genetic material has occurred.

**Multi-resistance gene cluster on a plasmid in a clinical isolate of *E. faecium***

**PM163**

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**Purpose:** Strain UW786 was isolated from an urine sample of a patient with a permanent catheter. The purpose of our study was to identify and localize the resistance determinants in this isolate.

**Results:** Isolate UW786 was resistant to the following antibiotics: penicillin, ampicillin, gentamicin (high-level), streptomycin (high-level), erythromycin, clindamycin, vancomycin, teicoplanin, ciprofloxacin, moxifloxacin, nourseothricin, rifampicin, and fusidic acid (low-level, MIC = 4 mg/l); but showed susceptibilities to oxytetracycline, phosphomycin, chloramphenicol, trimethoprim/sulfamethoxazol, linezolid, and quinupristin/dalfopristin. Hybridization, PCR and sequencing experiments localized a cluster consisting of several resistance genes in a composite element on a plasmid. The cluster included genes and transposons Tn1546 (vanA–Tn917 (ermB)–Tn1505 (aadE−sat4−aphA-3)). The plasmid itself was not transferable in filter-matings into a fusidic acid high-level resistant Enterococcus faecium recipient while selecting either for erythromycin or vancomycin resistances. After transposing a Tn916-related determinant into UW786, determinants became mobilizable with the help of the conjugative transposon. Transconjugants were, besides others, high-level resistant to fusidic acid, but susceptible to penicillin and ampicillin. PFGE of transconjugants demonstrated a pattern almost identical to the recipient but clearly different from the donor.

**Conclusion:** Resistance genes in *E. faecium* could be arranged in a cluster and are mobile via mobilizable/transferable plasmids.

**Dual infection with hepatitis G virus (HGV) and hepatitis C virus (HCV) in relation to different HCV genotypes**

**PM164**

Lilli D, Rivarera D, Barbacini IG, Lozzi MA, Mancini C. *Department of Science and Public Health, University La Sapienza, Microbiology, Rome, Italy*

**Aim:** Hepatitis G virus (HGV), a new RNA virus that is parenterally transmitted has frequently been found in patients with chronic hepatitis C infection but its role in chronic liver disease is unknown. The aim of this study was to determine the prevalence of HGV infection in patients infected with HCV.
Characterization of extended-spectrum beta-lactamase (ESBL)-mediated resistance in Salmonella spp. from Durban, South Africa PM165

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Background: Gastroenteritis is a common condition among the paediatric population presenting to King Edward VIII Hospital in Durban, South Africa. From July 2001, we noticed that the susceptibility of the Salmonella spp. isolated from stool samples among these children were resistant to multiple antibiotics.

Aim: To characterize the phenotype of the resistance mechanisms involved.

Methods: Minimum inhibitory concentrations (MICs) of ampicillin, azithromycin, ciprofloxacin, cefepime, cefuroxime, cefotaxime, ceftazidine, ceftriaxone, cefoxitin, chloramphenicol, cotrimoxazole and gentamicin were determined by means of the agar dilution method. Isolates were subjected to the E-test for extended-spectrum beta-lactamase (ESBL) production. Isoelectric focusing was performed as a preliminary step in enzyme characterization.

Results and conclusion: Thirty isolates of multiresistant Salmonella spp. were obtained. Antibiotic typing revealed six different resistance phenotypes. All isolates depicted ceftazidime/ceftriaxone –clavulanate ratio of > 8 and were considered putative ESBL-producers. Isolates expressed 1–3 beta-lactamasases each with pH values ranging between 5 and 8.2 indicative of TEM-, SHV- and/or CTX-M-related ESBLs. Nine isolates expressed two beta-lactamasases each and two isolates expressed three beta-lactamasases each. There was evidence of the simultaneous expression of both TEM- and SHV-derived ESBLs as well as the simultaneous expression of multiple TEM- or SHV-derived ESBLs in single isolates, a phenomenon reported in ESBL-positive Klebsiella pneumoniae isolated at the same hospital.

Neutrophils exhibit reduced chemiluminescence response to serum opsonized Klebsiella pneumoniae producing extended spectrum beta-lactamasases (ESBL) PM166

Sixty-eight patients infected with HCV were evaluated for the presence of HGV RNA. The HCV genotypes distribution was 30 genotype 1b, 10 genotype 1a, 5 genotype 3a and four genotype 4c/4d. HCV RNA and HGV RNA were detected by RT-nested PCR.

Results: Infection with hepatitis G virus was detected in 21 (21.4%) patients and 77 (78.6%) were HGV RNA negative.

None of our patients with genotypes 1a and 4c/4d results HGV RNA positive. Prevalence of HGV infection was 10% in patients infected with HCV genotype 1b and 33.3% with genotype 3a.

Conclusions: Infection with HGV occurred frequently (21.4%) in children were resistant to multiple antibiotics.

Comparision of Dio-Bacit, asitracin-SXT and latex agglutination in group A beta-hemolytic Streptococcus definition PM168

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Comparison of Mueller Hinton (MHA) and Iso Sensitest Agar (ISA) using aura PM169

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Objective: Variation in different batches of MHA can influence susceptibility testing markedly, whereas variation in composition of ISA is minimal. Inhibition zone size (IZS) was determined on MHA and ISA.

Method: Agar diffusion technique as recommended by DIN 58940 was used to determine IZS (read using AURA and manually) for 178 Staphylococci and 22 Enterobacteriaceae. Variations in automated measured zone sizes of ±3 mm to the manual readings were considered to be within acceptable range.

Results: Six thousand and fifty-two zone sizes were determined for Staphylococci and 748 for Enterobacteriaceae. MHA displayed tendency to smaller zone sizes in automated readings than ISA, as well in Staphylococci and Enterobacteriaceae. On the other side automated readings presented on ISA more precise results than MHA. Overall less major discrepancies (<3 mm) were found on ISA. IZS were generally smaller on MHA.

The tables below show differences in manually and automated measured zone sizes across media and species.

Evaluation of the E-test and agar dilution method for testing antibiotic susceptibility of Helicobacter pylori strains to metronidazole and clarithromycin PM170

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Purpose: To assess the in vitro susceptibility of Helicobacter pylori to antimicrobial agents with agar dilution method (AD) and E-test.

Results: Forty-one H. pylori strains isolated from patients with peptic ulcer disease were tested by AD. The E-test (AB Biodisk, Sweden) results and strains were gathered from the previous study. The strains were frozen to −80 °C and then used again for our study. Resistances to metronidazole and clarithromycin were defined as MIC values ≥8 and ≥2 μg/ml. The results are presented in the table.

Comparison of two methods for detection of ESBL producers PM171

Rokosz A*, Sawicka-Grzelak A*, Meszaros Jb, Luczak Ma. *Department of Medical Microbiology, The University Medical School, Warsaw, Poland; bDepartment of Bacteriology, State Institute of Hygiene, Warsaw, Poland

Purpose: To identify ESBL-positive strains and to compare two methods applied for the detection of extended-spectrum beta-lactamases (ESBLs).

Methods: Two hundred and sixty strains of Gram-negative rods were cultured from clinical specimens from hospitalized patients. Identification of strains was performed in the automatic ATB system (bioMérieux, France). These strains were identified as ESBL-positive on the basis of the double-disc synergy test (DDST according to Jarlier et al., 1988) results. All strains were also determined using a novel method of ESBL detection (DD, diagnostic disc) according to Appleton (1999). Two discs were applied in this test: CPD (cefepoxide) and CD 01 (cefepoxide/clavulanic acid) (Oxoid, England).

Results: Consistent results of two methods (DDST and DD) were observed se.

### Table: Comparison of Mueller Hinton (MHA) and Iso Sensitest Agar (ISA) using aura PM169

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Range (μg/ml)</th>
<th>Resistance</th>
<th>MIC50 (μg/ml)</th>
<th>MIC90 (μg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD E-test</td>
<td>AD E-test</td>
<td>AD E-test</td>
<td>AD E-test</td>
<td>AD E-test</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>0.016 – 256</td>
<td>0.016 – 256</td>
<td>0.064 – 256</td>
<td>0.016 – 256</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>0.25 – 256</td>
<td>0.016 – 23</td>
<td>0.12 – 256</td>
<td>0.12 – 256</td>
</tr>
</tbody>
</table>

We discovered seven more cases of resistance in the case of metronidazole. We did not have such experience with clarithromycin.

Conclusion: Our results show that E-test is comparable to AD for clarithromycin, but for metronidazole our findings confirm NCCLS recommendation. Classical AD is time consuming for every day use in the laboratory. The use of screening agar plate with 8 μg/ml of metronidazole to detect possible resistance could be the solution.

### Table: Comparison of two methods for detection of ESBL-producers PM171

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Range (μg/ml)</th>
<th>Resistance</th>
<th>MIC50 (μg/ml)</th>
<th>MIC90 (μg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPD/CD01</td>
<td>CPD/CD01</td>
<td>CPD/CD01</td>
<td>CPD/CD01</td>
<td>CPD/CD01</td>
</tr>
<tr>
<td>Cefepoxide</td>
<td>0.016 – 256</td>
<td>0.016 – 256</td>
<td>0.064 – 256</td>
<td>0.016 – 256</td>
</tr>
<tr>
<td>Clavulanate</td>
<td>0.25 – 256</td>
<td>0.016 – 23</td>
<td>0.12 – 256</td>
<td>0.12 – 256</td>
</tr>
</tbody>
</table>

Staphylococci on Mueller Hinton | Staphylococci on Iso Sensitest
---|---
Range mm | 3 | 3 | 3
Amount % | 36.73 54.26 09.01
Enterobacteriaceae on Mueller Hinton | Enterobacteriaceae on Iso Sensitest
---|---
Range mm | 3 | 3 | 3
Amount % | 29.61 66.91 03.48

Enterobacteriaceae on Mueller Hinton | Enterobacteriaceae on Iso Sensitest
---|---
Range mm | 3 | 3 | 3
Amount % | 12.32 80.46 07.22
Conclusions: The novel method of ESBL-producers detection (DD) is more objective and easier for interpretation than the double-disc synergy test (DDST). Diagnostic disc test should be used as the basic one or to confirm the results of DDST in difficult cases.

Assessment of E-test for determining penicillin resistance in pneumococci PM172

Sener B, Yenijehirli G, Ercis S, Hasçelik G. Department of Clinical Microbiology, Hacettepe University Medical Faculty, Ankara, Turkey

There is a greater need for susceptibility testing methods that distinguish between susceptible and resistant pneumococci. An alternative method could be the E-test, which is compared with the reference agar dilution method in this study.

Penicillin susceptibility of a total of 149 pneumococci was determined by E-test and agar dilution methods. Streptococcus pneumoniae ATCC 49619 and Enterococcus faecalis ATCC 29212 were used as controls.

The results were given in the table. Penicillin MIC50 values were 0.125 µg/mL for both methods, while MIC90 was 1 µg/mL for agar dilution and 0.75 µg/mL for E-test.

<table>
<thead>
<tr>
<th>Reference penicillin determinations (no)</th>
<th>Penicillin E-test determinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.002 – 0.094 µg/mL</td>
<td>0.125 – 1.0 µg/mL</td>
</tr>
<tr>
<td>Susceptible (66)</td>
<td>65</td>
</tr>
<tr>
<td>Intermediate (73)</td>
<td>3</td>
</tr>
<tr>
<td>Resistant (10)</td>
<td>–</td>
</tr>
</tbody>
</table>

*By agar dilution.

Overall agreement between agar dilution penicillin MIC and E-test was 0.89 (P < 0.05). Three penicillin intermediate isolates were interpreted as susceptible by the E-test. The E-test MIC’s agreed within 1 log2 dilution of the reference method for 134 (92.41%) of the isolates.

Effect of anoxic conditions on the minimum inhibitory concentration of metronidazole in Helicobacter pylori PM173

de la Obra Sanz P, Lomas E, Roman JL, Alarcon T, Lopez-Brea M. Hospital de la Princesa, Microbiology, Madrid, Spain

The objective of this study was to determine the effect of incubation under anoxic conditions on the metronidazole resistance of Helicobacter pylori.

Methods: A total of 35 clinical isolates were used in this study. MICs were determined by an agar dilution method using Mueller-Hinton agar plus 7% lysed horse blood. Three plates series contained twofold dilutions of metronidazole from 256 to 0.008 mg/ml were prepared. The first one was incubated under microaerophilic conditions (Oxoid) for 3 days; second and third series were incubated anaerobically (anaerobic system, Oxoid) for 8 and 18 h, respectively, and were then transferred to the microaerophilic environment up to complete 3 days of incubation.

Results: With microaerophilic incubation, 12 of 35 strains were resistant (MIC50 and MIC90 were 0.5 and 4, respectively). With 18 h anaerobic preincubation, 1 of 35 strains was resistant (MIC50 and MIC90 were 0.25 and 1, respectively).

Conclusions: Anaerobic preincubations cause an increase in sensitivity to metronidazole, the extent of which was dependent on the length of the anaerobic period.

Microbiological aspects of mixed purulent–septic infections PM174

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The purpose of the research was the investigation of microbiological features of tissue infections in surgical and otolaryngological patients. The prospective microbiological investigations had been conducted in 690 patients and 918 bacterial strains were isolated, 568 (61.9%) of them were in mixed culture. The commonest associations were formed by *Staphylococcus epidermidis* or *Staphylococcus aureus* with the following microorganisms: *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Enterobacter spp.*, *Micrococcus spp.*, *Corynebacterium spp.*, *Klebsiella* spp. Mixed cultures were isolated in high numbers more often than pure cultures: 59.8 ± 0.5 and 37.6 ± 0.6%, respectively (P < 0.01). In the surgical department the percentage of multiantibiotic resistant strains from mixed cultures was 68.1 ± 0.1% and in otolaryngological department—76.9 ± 0.3%, while in monocultures the respective was found, respectively in 31.9 ± 0.18 and 23.08 ± 0.05% (P < 0.01). Microbial associations play a significant role as causative agents of purulent–septic infections in surgical and otolaryngological patients. Components of associations are often multiantibiotic resistant strains and occur in high concentrations.

Antimicrobial susceptibility patterns of *Moraxella catarrhalis* PM175

Kanellopoulou M, Skarmoutsou N, Martoukou M, Charalabopoulou A, Mylona E, Koukis P, Papafrangas E. Sismanoglio General District Hospital of Attica, Laboratory of Clinical Microbiology, Athens, Greece


Methods: The susceptibility to antibiotics was performed by microdilution method according to NCCLS guidelines. The production of β-lactamase was tested by nitrocefin sticks (Oxoid).

Results: The MICs50/MICs90 (µg/mL) appeared, respectively: ampicillin 1.5, amoxicillin/lovulanic 0.06/0.12, cefazolin 0.06/0.5, erythromycin 0.12/0.25, azithromycin ≤ 0.03/0.06, clarithromycin 0.120/0.12, ciprofloxacin 0.03/0.06, imipenem ≤ 0.015/0.06, tetracycline ≤ 0.25/≤ 0.25, trimethoprim/sulfamethoxazole 0.25/0.25.

β-Lactamase was detected in 98.5% of the strains.

Conclusions: (1) *M. catarrhalis* isolates were uniformly susceptible to all tested antimicrobials except ampicillin. (2) The production of β-lactamase was responsible for ampicillin resistance (98.5%). (3) *M.
**Fungal isolates from diarrhoeic faecal samples submitted for detection of Clostridium difficile and its toxins**  PM176

Rokosz A, Sawicka-Grzelak A, Luczak M. Department of Medical Microbiology, The University Medical School, Warsaw, Poland

*Purpose:* To isolate, identify and determine the drug-susceptibility of fungal strains cultured from faecal samples routinely submitted for detection of *Clostridium difficile* and its toxins in cases of antibiotic-associated diarrheal (AAD).

*Methods:* One hundred faecal samples from hospitalized patients were examined (May–October 2001). *C. difficile* toxins A/B were detected directly in stools with C. DIFFICILE TOX A/B II test (TechLab®, USA). Fecal specimens were inoculated on CCCA and *Candida* ID (bioMérieux, France) media. *C. difficile* and fungi were identified with standard microbiological procedures. Susceptibility of fungal strains to anti-fungal agents was determined (ATB FUNGUS, bioMérieux, France).

*Results:* *C. difficile* toxins were detected in 38 and *C. difficile* strains were isolated from 23 of examined specimens. Sixty-two fungal strains of 8 genera were cultured from 50 stool samples (24 *C. albicans* isolates). Massive fungal growths were observed on primary plates in all cases. Fifty-five fungal strains were susceptible to nystatin, 53- to 5-fluorocytosine, 52- to amphotericin B, 45- to ketoconazole, 43- to miconazole and 39- to econazole.

*Conclusions:* In some cases of antibiotic-associated diarrheal fungal strains are responsible for symptoms of this disease. Certain persons having AAD should be treated with anti-fungal agents.

**Streptococcus pneumoniae** resistant to penicillin and erythromycin in Southern European Countries (ARISE Project)  PM177


*Purpose:* To describe the resistance to penicillin and erythromycin among *S. pneumoniae* strains isolated from adult patients with respiratory tract infections in four Southern European countries (Portugal, Spain, Italy and Greece) a multicenter study was carried out between September 2000 to March 2001.

*Results:* A total of 291 isolates (33.2%) were penicillin non-susceptible (intermediate and resistant) and 308 (35.1%) were erythromycin non-susceptible. Non-susceptibility to both antibiotics was found in 183 (20.9%).

*Conclusions:* If penicillin administration eliminates all penicillin susceptible strains, the prevalence of penicillin non-susceptible strains will increase as well as the erythromycin non-susceptible ones. This means that the proportion of erythromycin non-susceptible strains should increase from 35.1 to 62.9%.

At the same time, if erythromycin eliminate all susceptible strains to this antibiotic, the prevalence of penicillin non-susceptible strains would increase from the initial 33.2 to 59.4%. These data can explain the co-selection results observed in different surveillance studies.

**Antimicrobial susceptibility and capsular types/groups of Streptococcus pneumoniae isolates causing pneumococcal diseases in Bulgaria**  PM178

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A prospective study of pneumococcal infections was performed in cooperation with five clinical microbiology laboratories in Bulgaria. MICs values to 12 antimicrobials and serotype/serogroup distribution were determined for 242 strains of *Streptococcus pneumoniae*. Pneumococcci were isolated from patients with systemic or respiratory infections. The incidence of penicillin G-intermediate and penicillin G-resistant isolate was 27.3 and 10.3%, respectively. The rates of resistance to other antimicrobials were: cefotaxime/ceftriaxone—6.2%; erythromycin—21.5%; clindamycin—7.8%; tetracycline—24%; chloramphenicol—26.4%; trimethoprim/sulfamethoxazole—38%; ciprofloxacin—10.7%; rifampicin—3.7%. The *S. pneumoniae* isolates belonged to 19 capsular types/groups.

The most common serotypes/serogroups in Bulgaria are 1, 3, 5, 6, 9, 14, 19 and 23.

**Serotype distribution and antimicrobial resistance of Streptococcus pneumoniae**  PM179

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We aimed to determine the pneumococcal antibiotic resistance rates and the serotypes of those resistant isolates in our hospital.

The MIC values of 212 isolates (year 1996–2001) were determined by agar dilution method. Serotyping was performed by using 12 pooled antisera of the Pneumo-test.

The results were as follows (n = 212).

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Susceptible (%)</th>
<th>Intermediate (%)</th>
<th>Resistant (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin G</td>
<td>109 (51.4)</td>
<td>88 (41.5)</td>
<td>15 (7.0)</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>203 (95.8)</td>
<td>4 (1.8)</td>
<td>5 (2.4)</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>175 (82.5)</td>
<td>2 (0.9)</td>
<td>35 (16.5)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>212 (100.0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>207 (97.6)</td>
<td>–</td>
<td>5 (2.4)</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>163 (76.9)</td>
<td>9 (4.3)</td>
<td>40 (18.9)</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>188 (96.5)</td>
<td>3 (1.5)</td>
<td>4 (2.0)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>193 (99.0)</td>
<td>0 (0)</td>
<td>2 (1.0)</td>
</tr>
</tbody>
</table>

*Were tested in 195 strains.

Cefadroxil MIC₅₀ was 0.5, MIC₉₀ was 4 μg/ml. The rates of resistance in penicillin intermediate and resistant strains (n = 103) were cefotaxime 26.7%, erythromycin 26.7%, chloramphenicol 13.3%, tetracycline 26.7%, rifampicin 3.9%, ciprofloxacin 1.9%. Among these resistant isolates the most frequent serotypes were 19, 23, 9, 6, 14.

The prevalence of the penicillin resistant pneumococci, particularly the intermediate ones, is high in Turkey. These penicillin resistant strains also show multiple resistance to other antimicrobials.

**Antimicrobial susceptibility of clinical isolates of Pseudomonas aeruginosa. Evolution of resistance in 4 years**  PM180

Cesteros R, Guerrero C, Miranda A, Menasalvas A, Bláñezquez R, Segovia M. *Hospital Morales Meseguer, Servicio de Microbiología Clínica y Unidad de Enfermedades Infecciosas, Murcia, Spain*

*Objectives:* To assess the antimicrobial susceptibility of clinical isolates of *Pseudomonas aeruginosa* obtained from 1997 to 2000 and to monitor trends in antimicrobial resistance.

*Methods:* MICs were determined by microdilution testing according to NCCLS. The antibiotics tested were: ceftazidime (CAZ), aztreonam (ATM), imipenem (IMP), gentamicin (CN), tobramycin (TB), amikacin (AK) and ciprofloxacin (CIP).
Antimicrobial susceptibility testing of clinical isolates of *Bordetella pertussis*: report on 27 isolates from Rouen, France  
**PM181**

Lemee L<sup>a</sup>, Nouvellon M<sup>a</sup>, Caron F<sup>b</sup>, Lemeland JF<sup>a</sup>, *CHU* Rouen, Bactériologie, Rouen, France; *CHU* Rouen, Maladies Infectieuses et Tropicales, Rouen, France

Reports of an increased clinical incidence of pertussis and the development of resistance by *Bordetella pertussis* to erythromycin prompted the collection and antimicrobial susceptibility testing of recent clinical isolates from patients, who were hospitalized in Rouen between 1991 and 1999. MICs of nine antimicrobial agents (erythromycin, josamycin, spiramycin, roxithromycin, ketolide HMR 3647, ciprofloxacin, rifampicin and amoxicillin) were measured by agar dilution method on Mueller-Hinton agar containing 5% sheep blood. MBCs of erythromycin and rifampicin were also determined against four isolates of *B. pertussis*. All isolates were fully susceptible to the nine antimicrobial agents tested. MICs 90 (mcg/ml) were 0.03 for erythromycin, ketolide HMR 3647 and ciprofloxacin, 0.06 for josamycin, 0.25 for spiramycin, roxithromycin and rifampicin, 0.52/0.5 for crotomoxazole, and 1 for amoxicillin. MBCs (mcg/ml) were 0.125–0.5 for erythromycin and 0.5–1 for rifampicin. In conclusion, our isolates of *B. pertussis* remain extremely susceptible to all antimicrobial agents tested, especially macrolides. No resistance was detected. Finally, if erythromycin remains the molecule of choice, other macrolides (C14 and C16) also confirm their good in-vitro activity. In addition, the good in-vitro potency of rifampicin, together with its great diffusion within the respiratory tract, suggests that rifampicin has potential clinical efficacy in pertussis too.

### Fluoroquinolones resistance phenotypes in 252 Streptococcus pneumoniae strains  
**PM182**

Roussel Delvallez M<sup>a</sup>, Morel E<sup>a</sup>, Cattoen C<sup>b</sup>, Hendricx S<sup>a</sup>, Verhaeghe A<sup>a</sup>, Wallet F<sup>a</sup>, Delpierre F<sup>a</sup>, Varon E<sup>a</sup>, Courcol RP<sup>a</sup>, Laboratoire de Bactériologie, Hôpital Calmette, Lille, France; Laboratoire de Bactériologie, Hôpital de Valenciennes, Valenciennes, France; Laboratoire de Bactériologie, Hôpital de Douai, Douai, France; Laboratoire de Bactériologie, Hôpital de Dunkerque, Dunkerque, France; Centre National de Référence des Pneumocoques, HEGP, Paris, France

The emergence of *Streptococcus pneumoniae* (Sp) with diminished susceptibility to penicillin G (PSDP) suggests the use of other antibiotics such as newer fluoroquinolones (FQ). The resistance phenotypes of 252 consecutive pneumococcal strains isolated from patients of four hospitals (Observatoire Régional des Pneumocoques du Nord-Pas de Calais) were studied: 39 strains were susceptible to penicillin G and 213 were PSDP. Reference strains provided from the Centre National de Référence des Pneumocoques were added to the study. The activity of pefloxacin, ciprofloxacin, norfloxacin, sparfloxacin, levofloxacin and moxifloxacin was studied. Reserpine was used to detect the efflux phenotype. Methods used were performed according to the recommendations of the Comité de l’Antibiogramme de la Société Française de Microbiologie. For each strain, the resistance phenotype to FQ was deduced by comparison of MICs or diameters obtained with those obtained with the reference strains of known phenotypes. FQ resistance phenotypes were not correlated to β-lactam agent susceptibility. Wild type phenotype was observed among 76.9 and 77.5% of the susceptible and PSDP strains, respectively. A ‘wild efflux’ mechanism, deduced by addition of reserpine to norfloxacin, represented the predominant phenotype. It was detected among Sp susceptible to penicillin G (23.1%) as well as among PSDP (17.4%).

<table>
<thead>
<tr>
<th>Department</th>
<th>n strains</th>
<th>Constitutive R</th>
<th>Inducible R</th>
<th>Efflux R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpes-Maritimes</td>
<td>439</td>
<td>303 (69%)</td>
<td>27 (6.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Doubs</td>
<td>459</td>
<td>235 (51.2%)</td>
<td>111 (24.9%)</td>
<td>0</td>
</tr>
<tr>
<td>Nord</td>
<td>364</td>
<td>251 (68.9%)</td>
<td>59 (16.2%)</td>
<td>2 (0.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>1262</td>
<td>789 (62.5%)</td>
<td>197 (15.6%)</td>
<td>2 (0.16%)</td>
</tr>
</tbody>
</table>

Macrolide resistance is a well known phenomenon in France and is confirmed by our study. These results show that the constitutive phenotype is predominant as in other parts of Europe and the frequency of efflux mechanism is lower than that observed in the USA and Canada.
Developing antibiotic resistance surveillance of _Helicobacter pylori_ in England and Wales  PM1184

Elviss NC, Owen RJ. Central Public Health Laboratory, Laboratory of Enteric Pathogens, London, UK

*Purpose*: _Helicobacter pylori_ antibiotic resistance is a key contributing factor in ~10% of infected patients failing drug treatment. Our aim was to survey rates of primary in-vitro resistance at different locations, and links to disease severity, Antral gastric biopsies/cultures were received from PHLs in Chelmsford, mid-Essex (1115 isolates 1995–2001); London (103 isolates 1999–2000); and Bangor, north Wales (165 isolates 1999–2001). Susceptibilities to metronidazole (Mtz), clarithromycin (Cl), tetracycline (Tet) and amoxicillin (Amx) were tested by disc diffusion and also by E-test for Cl and Mtz.

*Results*: Overall resistance rates (1383 isolates) were 38% for Mtz and 8% for Cl. All were susceptible to Amx and Tet. Dual resistance rate was 5%. Breakdown by location showed some marked differences. Mtz resistance was highest in London (63%) compared to 37% in Chelmsford and 20% in Bangor. By contrast Cla rates were 11% for London, and about 5% for Bangor and Chelmsford. In London, the majority of Mtz resistant isolates were from non-UK borne individuals (75% non-UK vs 25% UK). Comparison of duodenal ulcer-associated isolates with those from non-ulcer patients indicated similar rates of Mtz resistance (28%).

*Conclusion*: Resistance rates may vary significantly between locations depending on the local population with non-UK birth being a key risk factor for primary resistance with a Mtz resistant strain. Local resistance rates should be taken into account in test and treat strategies.

Effects of a major _Escherichia coli_ efflux pump alterations on intrinsic and plasmid-borne antibiotic resistance  PM1185

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*Purpose of the study*: Because of their ability to extrude a wide range of compounds, multidrug efflux pumps have recently become an important issue in combating bacterial infections. AcrAB-ToIC is the major efflux system of _Escherichia coli_. We investigated the effect of AcrA on plasmid-borne and intrinsic chloramphenicol, tetracycline and ampicillin resistance.

*Results and conclusions*: Recently, we reported a chloramphenicol sensitivity of _E. coli_ mutant expressing cat, the chloramphenicol resistance gene. The strain was shown to bear a nonsense mutation in the _acrA_ gene. Our studies indicate that this mutation is, at least in part, responsible for the observed chloramphenicol sensitivity phenotype. The mutation seems also to influence the strain’s susceptibility to ampicillin and _tetA(C)_-mediated (plasmid-borne) tetracycline resistance. Although the TetA(C) protein retained its biological function, there was a considerable growth impairment of the mutant strain when cultured in tetracycline containing medium. Deletion of the _acrAB_ locus prevented any growth in the presence of tetracycline. Upon the addition of ampicillin, the mutant underwent lysis more rapidly than the control strain. Such was also observed in _acrAB_ deletion derivatives of other _E. coli_ strains. We are trying to elucidate the role of the _acrA_ gene product in the phenomena described above.

Existence of efflux pumps in wild type isolates of drug-resistance bacteria  PM1186

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Efflux pumps possessed by the bacterial cells of different kinds of bacteria had presented as a newer mode of drug resistance in many organisms. The capacity of bacterial cells to cause outward flow of noxious agents was known, however, for a considerable time with respect to tetracycline. Recently, interest in the efflux pump system has brought to light some previously ill-understood mechanisms of drug resistance, involving noxious agents, toxins or poisons. We have found high level of resistance in pseudomonads towards cetrimide and other germicides for which no definite chromosomal/plasmid-mediated genes/mechanisms could be identified. Likewise, occurrence of non-antibiotic sensitive vibrios, staphylococci and pseudomonads in the background of their high level of resistance to most of the common antibiotics suggest a mechanism of interference with the efflux pump, which accounts for such sensitivity in such cases. Involvement of multiple resistance of marine isolates of _V. parahaemolyticus_ to numerous clinically used antibiotics to which they have never been exposed also suggests a possible role of efflux pumps in determining such resistance—that these can simultaneously develop against multiple marine toxins/poisons and other noxious agents.

Interaction between oxacillin and glycopeptides in a teicoplanin-resistant mutant of _Staphylococcus epidermidis_ with reduced susceptibility to vancomycin  PM1187

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We selected a laboratory-generated mutant of _Staphylococcus epidermidis_ capable of growing in the presence of 256 mg/l of teicoplanin (353b TM256), from a methicillin-resistant (MIC > 256 mg/l), teicoplanin-sensitive (MIC 4 mg/l) and vancomycin-sensitive (MIC 2 mg/l) clinical isolate of _S. epidermidis_ (353b SO). In a previous work, we studied the different phenotypic characteristics acquired by the teicoplanin-resistant mutant 353b TM256 (20th Interdisciplinary Meeting on Anti-Infectious Chemotherapy, December 2000, poster sessions, 82/P1). In this work, we examined the interaction between oxacillin and glycopeptides against this teicoplanin-resistant mutant of _S. epidermidis_ with reduced susceptibility to vancomycin. To study the combined antibiotic activity of oxacillin and glycopeptides, we used different methods: a modified disk diffusion test, the E-test, time-kill assays and population analysis profiles. The synergistic activity of glycopeptides in combination with oxacillin against the teicoplanin-resistant mutant 353b TM256 was demonstrated with a bactericidal effect. No synergy was seen against the parental strain 353b SO. Moreover, the synergy between glycopeptides and oxacillin occurred with suppression of the subpopulation with the highest level of glycopeptides resistance. We concluded that combination of glycopeptides and oxacillin may be a possible alternative in the treatment of infections caused by methicillin-resistant, teicoplanin-resistant _S. epidermidis_.

Compositional changes in microcosm biofilms induced by application of minocycline: a preliminary study  PM1188

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The aim of the study was to observe the effect of application of minocycline upon microcosm dental plaques. The plaques were cultivated in a Constant Department Film Fermentor (CDIFF), which produces biofilms under conditions mimicking those present in vivo. The composition of the biofilms was determined by viable counting on selective and non-selective media. The proportion of antibiotic
resistant genera within the biofilm was determined by viable counts utilising media containing minocycline (16 µg/ml).

Before commencing antibiotic pulsing, the biofilms had a total viable anaerobic count of $1.26 \times 10^{10}$ CFU per biofilm, with negligible (6 CFU/biofilm) minocycline-resistant bacteria. However, 24 h after introduction of the antibiotic, the total count had been reduced to $1.02 \times 10^6$ CFU/biofilm whilst the number of minocycline-resistant bacteria had risen to $1.23 \times 10^6$ CFU/biofilm. At the final sampling time point (192 h) the total viable anaerobic count was $5.82 \times 10^8$ CFU/biofilm whilst the number of minocycline-resistant bacteria was $1.12 \times 10^5$ CFU/biofilm.

Hence, there is a very low basal level of inherent resistance to minocycline within microcosm dental plaques, but this increases considerably once the biofilms are exposed to minocycline.

**Mechanism of resistance to aminoglycosides (AMG) E. coli isolated from children with community-acquired urinary tract infections (CAUTIs)**  PM189


**Background:** Urinary tract infections are one of the most frequently infections in children. *Escherichia coli* is one of the leading bacterial pathogens causing CAUTIs.

**Methods:** During the 2000–01 years nine centers took part in the study. The MICs of antimicrobials were determined by the agar dilution method as described in the NCCLS guidelines.

**Results:** A total of 710 consecutive urine isolates from 692 children aged 1 month to 18 years with CAUTI were collected. The most frequently isolated species from children with CAUTI was *E. coli* (52.3%), followed by *Escherichia coli* spp. (8.0%) and *Serratia* spp. (7.6%).

The difference in R between E-β-L and A-L-I are: (1) piperacillin, piperacillin/tazobactam: between 10 and 30% of R for most isolated, except for *Escherichia coli* (45%); (2) piperacillin/tazobactam; between 10 and 30%; (3) cefoperazone, cefoperazone/sulbactam: between 5 and 25%; (4) amoxicillin, ampicillin/sulbactam: between 10 and 30%; (5) cefazolin, cefazolin/sulbactam: between 5 and 25%. How is expected gramnegative rods resistance to β-lactams with a β-L-I is lower than the β-lactam alone; furthermore the difference between both series, grows higher with time. These results are relevant and they were not expected, since β-L-I have been shown to be β-lactamase inducers.

**Trends in the Resistance (R) to β-lactams and others antimicrobials in *P. aeruginosa* in Venezuelan medical centres. Nosocomial (Nos) and communitarian resistance**  PM191

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In order to approach the infection produced by resistant bacteria, it is convenient to consider the hospital and the community as two separate ecosystems. The hospital ecosystem has special relevance in the infection and R of gramnegative aerobic bacilli. Today, they are the main responsible of Nos infection, with special reference to *Pseudomonas aeruginosa*. Infection by resistant bacteria is a world wide problem, specially related to Nos. Since 1988, The Venezuelan Group of Bacterial Resistance, with 29 health institution in the country; identify, analyse and publish data on bacterial R to antimicrobials: β-lactams, quinolones and aminoglicosides of isolates from patients with bacterial infection coming from hospitals and the community. It was used diffusion disk, according NCCLS. The software program WHONET (WORLD HEALTH ORGANIZATION NET) was used. We follow the trends of R of gram-negative rods to β-L and with β-L-I during the decade 1988–1998. Statistical analyses were made by evaluating the differences among percentages of resistance between the two series ($P \leq 0.05$).

**Results and discussion:** The difference in R between β-L and β-L-I is: (1) piperacillin, piperacillin/tazobactam: between 10 and 30% of R for most isolated, except for *Escherichia coli* (45%); (2) *Pseudomonas aeruginosa* spp. (60%); (2) amoxicillin, ampicillin/sulbactam: between 10 and 30%; (3) cefazolin, cefazolin/sulbactam: between 5 and 25%; (4) amoxicillin, ampicillin/sulbactam: between 10 and 30%; (5) cefazolin, cefazolin/sulbactam: between 5 and 25%. How is expected gramnegative rods resistance to β-lactams with a β-L-I is lower than the β-lactam alone; furthermore the difference between both series, grows higher with time. These results are relevant and they were not expected, since β-L-I have been shown to be β-lactamase inducers.
Susceptibility to antibiotics of Enterobacter cloacae and Citrobacter freundii from drinking water PM192

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The increased use of antimicrobials in farming, together with the practice of raw sewage discharge into receiving waters, has resulted in a significant increase in the number of antibiotic resistant bacteria present in aquatic environment. Our objective was to determine the antimicrobial susceptibility, with focus on β-lactam resistance, among Enterobacteriaceae strains isolated from raw drinking water samples. Several isolates (n = 107) of Enterobacter cloacae and Citrobacter freundii obtained from drinking waters were screened for antibiotic susceptibility patterns, using the agar diffusion technique, according to NCCLS’s procedures. Only 55% of E. cloacae strains, as well as 37% of C. freundii strains show resistance to amoxicillin and amoxicillin/clavulanic acid. A reduced incidence of resistance to several others antibiotics was also observed. The obtained results suggest that strains isolated from raw drinking water have greater susceptibility to antimicrobial agents than pathogenic strains from hospital or outpatient infections. The ‘natural’ antimicrobial resistance phenotypes, usually described for C. freundii and E. cloacae, only seem to apply to strains isolated from human infections. Notwithstanding the high susceptibility of the tested isolates to β-lactams, the role of environmental bacteria as a reservoir of resistance genes justify its periodical monitoring as a valid index for resistance spreading.

A snapshot of the soil. Using bacterial communities for tracing the evolution of metal-resistance PM193

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It is well known that pathogenic bacteria, specially those resistant to antimicrobial agents and heavy metals poses public health risks of great concern, and its detection, namely in soils is generally related to pollution. In this study, the heavy metal resistance patterns of the microflora isolated from polluted (dump area) and unpolluted soil environments were examined. The plate growth covering percentage in the soil samples was determined using Mueller-Hinton plates supplemented with different heavy metal (Al3+, Cd2+, Cu2+, Pb2+, Hg2+ and Zn2+) concentrations. Parallelly, using ICP-AES, it was possible to ascertain the real heavy metal concentration for each soil sample. We found that the percentage of plate growth covering from the used samples was closely linked to the level of chemical pollution measured for each location. Moreover, using ANOVA, we found significant differences between locations. The dump site showed the highest tolerance to all the tested metals (Newman–Keuls test). This pattern of results was consistent when using the data from the ICP-AES. Furthermore, it was possible to observe that Pseudomonas spp., with a relatively high MIC for the studied metals, might become a relevant model for both public health issues and eco-toxicological studies.

Biochemical characteristics of environmental isolates of Listeria monocytogenes PM194

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Purpose: The investigations were carried out to study the biochemical reactions of Listeria monocytogenes isolated from different sources in the environment.

Results: A total of 12 isolates of L. monocytogenes were obtained from 230 samples of agricultural soil, faecal matter of animals and sewage. All the isolates were Gram-positive, small rods, catalase positive, oxidase negative, motile with tumbling motility in hanging drop at 22–25 °C, aerobic, facultative anaerobic, fermentative and produced acid from glucose. All the isolates of L. monocytogenes were beta haemolytic and positive for CAMP reaction with Staphylococcus aureus. All the isolates were negative for phenyl alanine deaminase, ornithine decarboxylase, lysine decarboxylase, malonate utilization and beta galactosidase tests. These were also negative for acid production from arabinose, r-xylene, mannitol, soluble starch and sucrose but acid was produced in rhadose, salicin, and trehalose. Hydrogen sulfide production was recorded in triplicate soy broth with lead acetate paper strips but negative with triple sugar iron agar. All the isolates were found to hydrolyse aesculin. Out of 12 isolates of L. monocytogenes only two produced acid from lactose. In serotyping all the isolates were serotype 4b.

Conclusion: We can conclude that L. monocytogenes serotype 4b at least in fermentation of lactose shows different reactions.

Incidence of multi-resistant enterococci in enteric flora of healthy human volunteers from Portugal PM195

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Objective: To evaluate the occurrence of antibiotic resistant enterococci isolated from faeces of healthy human volunteers from Portugal (January–June 2001).

Methods: The samples were pre-enriched in BHI broth with and without vancomycin (6 mg/l) and then plated onto M-Enterococcus agar with and without antibiotics: vancomycin (6 mg/l), gentamicin (125 mg/l), kanamycin (500 mg/l), and streptomycin (1000 mg/l). Representative colonies of each morphology were isolated and identified as Enterococcus sp as previous described. PCR was used to identify E. faecium and E. faecalis and to characterise vancomycin resistant genotype. API20Strep was also used in the identification. Susceptibility testing to 11 antibiotics was performed by an agar dilution method (NCCLS).

Results: Three hundred and fifty-three enterococci were isolated from 92 of a total of 99 faecal samples (93%, n = 92/99). The majority of enterococci were identified as E. faecium, E. faecalis and Enterococcus sp. Resistance to almost all antibiotics studied was observed: vancomycin—3.0%; teicoplanin—3.0; ampicillin—21.2%; tetracycline—81.8%; erythromycin—86.9%; ciprofloxacin—78.8%; chloramphenicol—54.5%; gentamicin—17.2%; streptomycin—78.8%; kanamycin—77.7%; linezolid—0%. The vancomycin resistant enterococci presented a vanA genotype.

Conclusion: Resistance to several common antibiotics used in therapy was observed among enterococci isolated from healthy human from community. Many of these isolates presented multi-resistance. Of concern is the presence of vanA genotype among these populations that may constitute a reservoir of vancomycin resistant genes.

Antimicrobial resistance in tetracycline-resistant oral bacteria PM196

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Mercury release from dental amalgam may select for mercury-resistant oral bacteria. Mercury resistance is often associated with multiple antibiotic resistances. The aims of this study were to determine whether tetracycline-resistant oral bacteria from children with and without amalgam fillings were also resistant to: (a) mercury; and (b) multiple antibiotics. Tetracycline-resistant organisms were isolated on Iso-Sensitest/blood agar containing tetracycline (8 μg/ml). The MIC of HgCl₂ and several antibiotics were determined using agar dilution (BSAC). One hundred and three organisms were isolated from patients without amalgam. Ninety-one were Streptococcus species, seven Neisseria species, three Veillonella dispar and two Rothia species. Fifty-seven percent exhibited resistance to at least one antibiotic, 12% were mercury-resistant, 42% were penicillin-resistant, 11% were ampicillin-resistant and 23% erythromycin-resistant. Fifty-two organisms were isolated from patients with amalgam. Forty-five were Streptococcus species, five Neisseria species, one V. dispar and one Staphylococcus aureus. Sixty-three percent exhibited resistance to at least one antibiotic, 23% were mercury-resistant, 38% penicillin-resistant, 11% were ampicillin-resistant and 31% showed erythromycin-resistance. Statistically, the results showed that in tetracycline-resistant, 11% were ampicillin-resistant and 31% showed erythromycin-resistant. Fifty-two percent of the responding ICUs furnished microbiological testing data, of which three quarters indicated the incidence of chemoresistance of the isolated strains. Fungal infections were less frequent than bacterial, the most commonly isolated agent being Candida spp. In conclusion, the sample of ICUs examined showed adequate and reasonable use of antimicrobial agents, with heavy reliance on medium-high dose combination therapy due to the elevated incidence of resistant isolates found.

Prevalence of antibiotic-resistant oral bacteria in children not receiving antibiotic therapy PM197


The purpose of this study: To determine the prevalence of antibiotic-resistant oral bacteria in children who had not received antibiotics during the 3 months prior to sampling. Plaque samples were obtained from 16 children aged 4–6 years and plated onto media containing: penicillin, ampicillin, tetracycline, erythromycin and vancomycin. Resistant isolates were enumerated, sub-cultured and frozen for subsequent identification. The process was repeated 6 and 12 months later.

The results obtained: Bacteria resistant to each of the antibiotics were present in all of the children at each sampling time (except in the case of ampicillin and penicillin at 0 months). The proportion of antibiotic-resistant bacteria in the oral microflora ranged from ≥13.7 (erythromycin) to ≤0.5% (ampicillin). The proportions of bacteria resistant to a particular antibiotic remained reasonably constant over the 12-month sampling period. In only two cases (penicillin and ampicillin) was there a statistically significant change in the proportions of resistant bacteria at different time periods.

The conclusion reached: The results of the study have revealed that bacteria resistant to a wide range of antibiotics may be isolated from children who have not been administered these agents during the 3 months prior to sampling. Furthermore, in many cases the proportion of bacteria resistant to a particular antibiotic remains constant over a 12-month period.

Pharmacology

Antimicrobial use in the intensive care unit: results of a pharmacoepidemiological study in Italy PM198

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A retrospective survey of antimicrobial chemotherapy use in 560 Intensive Care Units in Italy was carried out in 1999 using a computerized questionnaire under the auspices of the Journal of Chemotherapy. Of the ICUs contacted, 43.4% replied, being mainly general or post-surgical and pediatric units having a mean of 10 beds, nine doctors and 20 nurses. The antimicrobial agents used in these wards were almost always polychemotherapy with prevalent use of beta-lactams, aminoglycosides and glycopeptides or as empirical treatment during the first 72 h after hospital admission. The continual use of medium-high dose combinational antimicrobial chemotherapy was justified by microbiological testing, which revealed that more than one-third of bacterial pathogens were resistant. Approximately, 60% of Gram-positive bacteria were methicillin-resistant, whereas about 13% of Gram-negative strains were resistant to at least one of the tested antibiotics. Forty percent of the responding ICUs furnished microbiological testing data, of which three quarters indicated the incidence of chemoresistance of the isolated strains. Fungal infections were less frequent than bacterial, the most commonly isolated agent being Candida spp. In conclusion, the sample of ICUs examined showed adequate and reasonable use of antimicrobial agents, with heavy reliance on medium-high dose combination therapy due to the elevated incidence of resistant isolates found.

Plasma concentrations (P), urinary excretion (U) and bactericidal activity of gatifloxacin (GAT) 400 mg versus ciprofloxacin (CIP) 500 mg in 12 healthy volunteers after a single oral dose PM199

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Twelve volunteers received a single oral dose of 400 mg GAT versus 500 mg CIP to assess P up to 36 h, U (by HPLC), and urinary excretion (U) and bactericidal activity between 1:8 and 1:1024 for the first 12 h, and between 1:16 and 1:1024 for the five Gram-positive strains. The median UBTs measured within the first 6 h for gatifloxacin were between 1:16 and 1:1024 for the five Gram-negative strains. The median UBTs for ciprofloxacin were between 1:64 and 1:1024 for the Gram-negative strains (incl. P. aeruginosa) and between 1:5 and 1:1024 for the five Gram-positive strains. The median UBTs for ciprofloxacin were between 1:64 and 1:1024 for the Gram-negative strains (incl. P. aeruginosa) and between 1:1.5 and 1:768 for the five Gram-positive strains. For the UBTs up to 12 h, GAT was significantly superior to ciprofloxacin in all Gram-positive strains, not different in the two E. coli strains, and inferior in the Klebsiella, Proteus and Pseudomonas strains. For the UBTs at 12–24 h, GAT was generally superior to CIP, but showed no difference in the Proteus and Pseudomonas strains. GAT showed overall comparable urinary bactericidal activity as CIP. This is in agreement with a clinical study performed previously.

Comparison of quinine therapeutic drug monitoring to 96 patients admitted in Intensive Care Unit or Infectious Medical Department in Bichat Hospital during 2001 PM200

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Malaria is one of the most prevalent endemic infectious disease affecting humans. In Bichat hospital 111 cases of malaria acute illness were reported during 2001. Among them, 96 patients were hospitalised and intravenously treated by quinine. This retrospective study consisted of comparing the therapeutic drug monitoring (TDM) of quinine distinguishing, respectively 36 and 60 patients cured in Infectious Medical Department (IMD) and Intensive Care Unit (ICU) where a standardised quinine regimen was established (62 and 47% malaria attacks, respectively). In ICU, the treatment consisted of an infused loading dose 16 mg/kg/4 h of quinine diluted in 5% glucose 47% malaria attacks, respectively (ICU) where a standardised quinine regimen was established (62 and 47% malaria attacks, respectively). In ICU, the treatment consisted of an infused loading dose 16 mg/kg/4 h of quinine diluted in 5% glucose followed by 24 mg/kg/day. Plasma quinine maximal concentrations were assessed after selective liquid–liquid extraction and spectrophotometry detection. Statistical analysis was performed using t-test. Results showed that patients had comparable weight (71.4 ± 19.7 and 70.8 ± 17.9 kg) but quinine doses and plasma concentrations were significantly different in ICU and IMD, respectively (20.2 ± 6.5 versus 22.7 ± 3.7 mg/kg/day, P < 0.001 and 11.4 ± 3.3 versus 10.3 ± 3.2 mg/l, P < 0.01). In ICU and IMD, respectively: 57 and 49% were in the therapeutic range (10–15 mg/l) with 29 and 43% below the requested therapeutic concentration (10 mg/l) and 13 and 8% above the limit of toxicity (15 mg/l) conveying the importance of TDM in intravenous quinine treatment to avoid infra-therapeutic or toxic concentrations.

Simultaneous central nervous system distribution using microdialysis and pharmacokinetic–pharmacodynamic modelling of the electroencephalogram effect of norfloxacin in rats PM201

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Purpose: To investigate the epileptogenic activity of norfloxacin by a pharmacokinetic–pharmacodynamic (PK–PD) modelling approach and to assess the contribution of distributional processes across the blood–brain barrier (BBB) to the delayed effect.

Methods: Rats (n = 10) received an IV bolus dose of norfloxacin (150 mg/kg). Convulsant effect was quantified by electroencephalogram (EEG) recording during 9 h post-dose. Arterial blood samples were collected for drug assays in plasma. Unbound norfloxacin concentrations were monitored in brain extracellular fluid (ECF) using microdialysis with in vivo calibration of the probes by retrodialysis with ciprofloxacin.

Results: The EEG effect reached its maximum between 70 and 190 min post-dose. A PK/PD effect compartment model was successfully fitted to these data. The relationship between effect and concentration at the effect site was best described by a spline function. Norfloxacin concentrations in brain ECF were relatively low compared to plasma levels (ECF/plasma under curve (AUC) ratio equal to 9.7 ± 2.8%), but central distribution was rapid. Therefore, the effect versus brain ECF concentrations curves still exhibited a marked hysteresis.

Conclusion: The delay observed between plasma concentrations and norfloxacin convulsant effect cannot be explained by a slow distribution of norfloxacin across the BBB.

CSF kinetics of Vancomycin (Van) and Fusidic acid (Fu) PM202

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CSF kinetics of Van and Fu were studied in 57 patients who underwent short urological surgery under spinal anesthesia. Patients were excluded if they were already receiving an antibiotic or were suffering from renal and hepatic dysfunction. Van was administered at 1 g over 1 h infusion. Serum and CSF samples were collected post-dose and the mean serum levels were as follows: 30 min–1 h: 21.1 µg/ml (five patients), 1–2 h: 10.1 µg/ml (five patients), 2–4 h: 8.5 µg/ml (six patients), 4–6 h: 6.7 µg/ml (six patients) and 6–8 h: 5.15 µg/ml (seven patients). Fu was administered at 500 mg dose over 1 h infusion. Serum and CSF samples were taken post-dose and the mean serum concentrations were found as follows: 0–30 min: 43.08 µg/ml (six patients), 30 min–1 h: 41.7 µg/ml (six patients), 1–2 h: 33.8 µg/ml (five patients), 2–4 h: 27.8 µg/ml (six patients), 4–6 h: 25.6 µg/ml (five patients). In CSF, both Van and Fu were undetectable. It is concluded that in the absence of meningeal inflammation Van and Fu do not penetrate (with the applied microbiological assay) the CSF barrier.

Comparison of the pharmacology of intravenous and orally given moxifloxacin in an in-vitro model PM203

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Purpose: The intravenous form (IV) of 400 mg Moxifloxacin (MOX), one of the newer fluoroquinolones, has been recently approved by the FDA. During the IV treatment higher peak serum concentrations are achieved in comparison to the oral administration (PO) of the same dose. The antibacterial activity of fluoroquinolones is concentration dependent. We therefore simulated human pharmacokinetics of single PO and IV dosages of 400 mg MOX in an in-vitro model using six different gram-negative and -positive pathogens to elucidate the different effect of these two dosing schedules.

Results: The comparison of the pharmacological parameter AUC/MIC shows an increase (Table 1) that could predict an enhanced antibacterial effect. However, the analysis of the killing curves with the following parameters, ka.max (maximal killing activity) and AAC (area above the killing curve between 0 and 24 h), reveals no major difference between the PO and IV dosage.

<table>
<thead>
<tr>
<th>Strain</th>
<th>AUC/MIC (µg min/ml)</th>
<th>ka.max [log cfu h]</th>
<th>AAC [log cfu h]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PO</td>
<td>IV</td>
<td>PO</td>
</tr>
<tr>
<td>M. catarrhalis</td>
<td>271</td>
<td>396</td>
<td>−6.1</td>
</tr>
<tr>
<td>E. coli</td>
<td>1129</td>
<td>1649</td>
<td>−7.2</td>
</tr>
<tr>
<td>K. pneumonia</td>
<td>565</td>
<td>825</td>
<td>−5.9</td>
</tr>
<tr>
<td>S. pyogenes</td>
<td>135</td>
<td>198</td>
<td>−3.6</td>
</tr>
<tr>
<td>S. pneumonia-PEN6</td>
<td>135</td>
<td>198</td>
<td>−3.9</td>
</tr>
<tr>
<td>S. pneumonia-PEN6</td>
<td>271</td>
<td>396</td>
<td>−5.1</td>
</tr>
</tbody>
</table>

Conclusion: The serum concentration after oral administration is already sufficiently high to show the optimal bactericidal effect of MOX that can only be slightly increased by higher peak concentrations and higher AUC/MIC ratios. Thus the concentration dependence is not linear but ends already at concentrations achievable by oral dosing and documents that AUC/MIC calculations cannot easily be translated into dosing schedules.

Effect of Quinolones against slowly growing E. coli PM204

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Background: Bacteria growing in vivo multiply much more slowly than in vitro. Whether the bactericidal activity of quinolones may be affected by an increase in generation time (g) was studied in batch cultures.

Methods: By limiting the nutrient supply, generation times were lengthened from approximately 0.45 to 1.5 h up to 3.9 h. Alternatively, the quinolones were added to the bacterial cultures during the lag-, exponential- and stationary phase. Recent clinical isolates of Escherichia coli were exposed to multiples of the MICs of ciprofloxacin or norfloxacin. The ‘killing rates’ were calculated in analogy to the growth rate.

Results: The bactericidal activity of the quinolones tested against E. coli was minimally influenced by the reduced generation time. Ciprofloxacin concentrations of $\geq 2 \times \text{MIC}$ eliminated the test strains within $\leq 2$ h from the test system if added during the lag or exponential growth phase; four times higher concentrations were needed to reduce CFUs by 99% within 2 h, if added during the stationary phase. Norfloxacin was significantly less active.

Conclusion: In contrast to norfloxacin, the bactericidal activity of ciprofloxacin is minimally affected by the generation time or growth phase of the bacteria.

Pharmacology of intravenous moxifloxacin in an in-vitro model PM205

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Purpose: Moxifloxacin (MOX) is one of the newer fluoroquinolones, now available for parental application. The pharmacology of an intravenous once-daily dose (OD) of 400 mg MOX was determined with five gram-negative and -positive pathogens (Streptococcus pneumoniae, Moraxella catarrhalis, Escherichia coli, and Klebsiella pneumoniae). A twice-daily dose (BID) of 400 mg MOX was studied with the gram-positive species in order to increase the bactericidal effect.

Results: To determine the efficacy, killing curves were analyzed, and following parameters were calculated: $\text{ka}_{\text{max}}$: maximal killing activity [log cfu]; $\text{ka}_{\text{1 h}}$: reduction of viable cells after 1 h [log cfu]; $\text{AAC}$: area above the killing curve between 0 and 24 h [log cfu h] (Table 1).

<table>
<thead>
<tr>
<th>Strain</th>
<th>OD</th>
<th>BID</th>
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<tbody>
<tr>
<td></td>
<td>$\text{ka}_{\text{1 h}}$</td>
<td>$\text{ka}_{\text{max}}$</td>
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<tr>
<td>M. catarrhalis</td>
<td>$-5.1$</td>
<td>$-6.9$</td>
</tr>
<tr>
<td>L. coli</td>
<td>$-7.2$</td>
<td>$-7.3$</td>
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<tr>
<td>K. pneumoniae</td>
<td>$-6.5$</td>
<td>$-6.9$</td>
</tr>
<tr>
<td>S. pyogenes</td>
<td>$-0.8$</td>
<td>$-2.7$</td>
</tr>
<tr>
<td>S. pneumoniae</td>
<td>$-0.9$</td>
<td>$-3.5$</td>
</tr>
</tbody>
</table>

Conclusion: An intravenous once-daily dose of MOX is active against all tested pathogens. The gram-negative species are rapidly killed ($\text{ka}_{\text{1 h}}$ similar to $\text{ka}_{\text{max}}$). There is no pronounced initial effect on the two gram-positive species but a general slow reduction in the viable cell count ($\text{ka}_{\text{max}}$ is reached after 24 h). The efficacy of MOX (measured as AAC and $\text{ka}_{\text{max}}$) on S. pyogenes and S. pneumoniae is to some extent increased after the second dose. However, the analysis of the killing curves reveals no major difference between OD and BID. Even the OD nearly gives the maximal bactericidal activity of MOX against gram-positive pathogens.

Dose proportionality and pharmacodynamic (PD) breakpoint of amoxicillin PM206

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Objectives: To evaluate the dose proportionality of amoxicillin and to compare the respective PK/PD parameters of two dosage regimens.

Methods: The dose proportionality of amoxicillin was evaluated using linear regression of mean AUC$_{0-\text{inf}}$ and C$_{\text{max}}$ data of 13 different bioequivalence studies ($N = 477$ volunteers) performed with formulations containing various amounts of amoxicillin alone or in combination with clavulanic acid. The volunteers received a single oral dose in the range of 250–1000 mg. Amoxicillin plasma concentrations were determined by HPLC/UVR or LC/MS/MS methods. Time above MIC (TMIC) expressed in% of dosing interval was calculated with three target MIC values (0.5, 1.0 and 2.0 mg/l) for 500 mg 8-hourly and 1 g 12-hourly dosage regimens.

Results: The absorption of amoxicillin (AUC$_{0-\text{inf}}$) showed a linear dependence with a correlation coefficient of 0.975. The correlation coefficient of the linear regression for the C$_{\text{max}}$ dependence on the actual dose was 0.909. The respective TMIC for both dosage regimens were very similar, with largely overlapping confidence intervals, supporting a PD breakpoint of 2 mg/l for the 1 g 12-hourly regimen (TMIC $\geq 2$ mg/l: 42.8%, 95% CI 38.6, 46.9%).

Conclusion: This analysis shows the dose proportionality of amoxicillin over the dosage range of 250–1000 mg and supports the pharmacodynamic rationale for a 1 g bid dosage regimen.

Piperacillin/tazobactam concentration profile after high dose administration pattern in nosocomial pneumonias due to mechanical ventilation PM207

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The piperacillin (P)/tazobactam (T) antibacterial spectrum covers the largest part of bacteria responsible for pneumonias due to mechanical ventilation. But, due to important bacterial inoculum and pharmacokinetic parameter modifications in intensive care patients, high doses of beta-lactamines seem to be necessary to obtain antibiotic concentrations above suspected bacteria’s MIC (Minimal Inhibitory Concentration). This led us to compare, in patients with pneumonia due to mechanical ventilation, two intermittent administration patterns: 4 g three times a day (usual pattern) versus 4 g four times a day (high dose pattern). This study is carried out in collaboration with intensive care unit, bacteriological department and pharmacy where antibiotic concentrations are determined. Twenty-three takings of blood are executed within a 48 h period, in addition to two bronchial secretion samples. Concerning P seric concentrations, the high dose pattern seems to be more adapted because of relatively high residual concentrations (> 20 µg/ml). Three hours after each injection, T seric concentrations are lower than the 4 µg/ml activity threshold. First and second day residual bronchial concentrations of P seem to be sufficient although T concentrations are below activity threshold. These results are to be correlated with the MIC determined by the bacteriological department, and only this correlation will make us able to conclude the better efficacy of the high dose pattern in intensive care patients.

Anti-inflammatory drugs interference in absorption and tissue penetration of amoxicillin PM208

Del Fiol FS, Menon SZ, Carames TH, Celotto TF, Lopes RAS.

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Antibiotics and anti-inflammatory agents are frequently associated in clinical practice. There is some concern about the quantity of antibiotic that reaches the infection sites, which may be reduced in the presence of an anti-inflammatory drug. The purpose of the present study was to investigate how steroids (dexamethasone (DEXA)) and AINES (celecoxib (CELE)) influence the penetration of amoxicillin into inflamed tissues. Thirty female rats (Rattus norvegicus) were used with surgically implanted PVC sponges on their backs to form granulomatous tissue. One week later the animals were divided into three groups. One group received only AMOX (40 mg/kg), another received AMOX (40 mg/kg) plus CELE (6.0 mg/kg) and the last received AMOX (40 mg/kg) plus DEXA (0.3 mg/kg). One hour later the animals were sacrificed and the concentration of amoxicillin in the serum and tissue was estimated. Thirty female rats (Rattus norvegicus) were used with surgically implanted PVC sponges on their backs to form granulomatous tissue. One week later the animals were divided into three groups. One group received only AMOX (40 mg/kg), another received AMOX (40 mg/kg) plus CELE (6.0 mg/kg) and the last received AMOX (40 mg/kg) plus DEXA (0.3 mg/kg). One hour later the animals were sacrificed and the concentration of amoxicillin in the serum and tissue was investigated.

There was no difference among the groups in the quantity absorbed (AMOX = 18.87 ± 2.05 μg/ml; AMOX + CELE = 18.20 ± 1.89 μg/ml and AMOX + DEXA = 18.13 ± 2.28 μg/ml). There was a reduction in the tissue concentration of amoxicillin (P < 0.01 Tukey-Kramer) for the group that received the drug with dexamethasone. For the other groups, there was no difference in the tissue concentration of amoxicillin.

The results indicated that in inflamed tissue, a significant reduction of antibiotic penetration was induced by simultaneous dexamethasone therapy.

Prediction of the optimal amoxicillin dose regimen based on coupling of pharmacokinetic data and bactericidal activity PM209

Galmiche H, Tod M, Drugeon H, Rouveix B. Service de Pharmacologie Clinique, Hopital, Cocchin, Paris, Service de Pharmacie, Hopital Avicenne, Bobigny, Service de Microbiologie, Hopital Laennec, Nantes, France

Background: Given its short half-life, amoxicillin (AMX) should be administered at least three times a day to patients with acute exacerbations of chronic bronchitis, in order to achieve serum concentrations well above the MIC of the responsible pathogen. However, several authors have recommended twice-daily administration of a higher dose for a shorter period. We assessed the relationship between AMX sputum concentrations and antibacterial activity following two treatment schedules in healthy volunteers.

Subjects and methods: Twelve healthy volunteers were randomized to receive AMX for 4 days at a dose of either 1 g bd or 500 mg bd. Serum and sputum were collected every day, 3 h after the morning administration, and again 2 days after the last dose. AMX concentrations were determined by HPLC with fluorometric detection. Sputum killing activity was determined against Haemophilus influenzae, Streptococcus pneumoniae and Moraxella catarrhalis.

Results: Mean serum concentrations measured 3 h after the morning administration were 1.5 (500 mg bd) and 1.95 mg/l (1 g bd), and were above the MICs of three microorganisms. In contrast, sputum concentrations were always below 0.5 mg/l. In terms of sputum killing activity, 1 g bd was more effective than 500 mg bd against S. pneumoniae and M. catarrhalis, whereas no sputum samples were active on H. influenzae.

Conclusion: The optimal amoxicillin treatment schedule cannot be established on the basis of serum pharmacokinetics only.

Cysteine based mucolytics inactive amoxicillin PM210

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Background: Cysteine-based mucolytics are commonly used in combination with antibiotics to treat patients with acute exacerbations of chronic bronchitis (AECB). They are also used to allow in vitro MIC determination in sputum specimens. We conducted an in vitro and ex-vivo compatibility study designed to detect a possible interaction between mucolytics and antibiotics.

Methods: Serial samples of bronchial secretions were collected from AECB patients and from healthy volunteers who received 1 g of amoxicillin twice a day for 4 days. Two mucolytics were used to fluidify sputum specimens: 2,3-dihydroxy-1,4-dithiolbutan (Digest-EUR®) and acetylcysteine (10% solution). Amoxicillin was assayed using a chromatographic system with fluorometric detection. Each sample was also tested in a microbiological assay. Results: Amoxicillin could not be detected in the presence of the mucolytic agents.

Conclusions: This mucolytic–amoxicillin interaction may be explained by amoxicillin fixation to fluidified mucoproteins, and should be taken into account when assessing antibiotic efficacy in vivo.

Influence of milk in macrolides absorption and distribution PM211

Del Fiol FS*, Ferro CB, Albuquerque ET, a*University of Sorocaba, Pharmacy, Sorocaba, Brazil, bUniso, School of Pharmacology, Sorocaba, Brazil

Physicians frequently recommend that macrolides should be administered with milk to decrease the discomfort they cause. Thus the objective of this study was to verify the interference of milk in the absorption and distribution of erythromycin (ERYT); clarithromycin (CLAR); roxithromycin (ROXI) and azithromycin (AZIT). Forty female rats (Rattus norvegicus) were used with surgically implanted PVC sponges on their backs for granulomatous tissue formation. One week later the animals were divided into groups that received the drugs ERYT, CLAR, ROXI and AZIT with and without milk (3.5 ml/kg [Ca+++] = 1.1 mg/ml). The animals were sacrificed and the serum and tissue concentration of the drugs was investigated.

There was no reduction (P < 0.05 Tukey-Kramer) in the serum and tissue concentration in the presence of milk for AZIT and CLAR. There was a 27% reduction for ROXI in the serum concentration in the presence of milk (11.84 ± 1.35 and 8.63 ± 1.34 μg/ml), but no alteration in the tissue concentration. There was a 33% reduction for ERYT (P < 0.05), in the serum concentration in the presence of milk (10.20 ± 1.06 and 6.83 ± 0.88 μg/ml) and a 40% reduction in the tissue concentration.

The milk decreased the effectiveness of treatments with erythromycin and roxithromycin and the bioavailabilities of this macrolides were affected by co-administration with milk.

Milk influence in tetracycline absorption and distribution PM212

Del Fiol FS*, Souza GP*, Duzzi MR, a*University of Sorocaba, Pharmacy, Sorocaba, Brazil, bUniso, School of Pharmacology, Sorocaba, Brazil

The degree to which tetracyclines are absorbed differs greatly. This absorption is impaired by the concurrent ingestion of dairy and trivalent cations. Thus the objective of this study was to investigate the interference of milk in the absorption and distribution of tetracycline (TETR), oxytetracycline (OXYT), minocycline (MINO) and doxycycline (DOXY). Forty female rats (Rattus norvegicus) were used with surgically implanted PVC sponges on their backs for granulomatous tissue formation. One week later the animals were divided into groups that received the drugs: TETR; OXYT; MINO; and DOXY with and without milk (3.5 ml/kg [Ca+++] = 1.1 mg/ml). The animals were sacrificed and the drug concentrations in the serum and tissue were determined.
There was no reduction (P < 0.05 Tukey-Kramer) in the serum and tissue concentrations in the presence of milk for MINO. There was a 25% reduction (P < 0.05) for DOXY in the serum concentration in the presence of milk (11.24 ± 0.61 and 8.40 ± 0.41 µg/ml) and 32% in the tissue concentration. For OXYT, there was a reduction of 34% (P < 0.05) in the serum concentration in the presence of milk (14.57 ± 1.51 and 9.54 ± 1.51 µg/ml) and 16% in the tissue concentration. The TETR results show a 35.4% reduction (P < 0.05) in the serum concentration in the presence of milk (13.46 ± 3.39 and 8.69 ± 3.03 µg/ml) and 40% in the tissue concentration.

Milk decreased tetracycline bioavailability and effectiveness.

Isotopic studies with oxine labelled platelet. Platelet kinetics in thrombocytopenic malaria patients PM213

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Introduction: Thrombocytopenia is a common feature in human malaria (1). Excessive splenic platelet pooling has been suggested to play a role in uncomplicated cases of malaria, but a moderately shortened platelet life span during the period with decreasing parasitemia seems the most plausible cause of the frequently observed thrombocytopenia (2, 3). Consumption coagulopathy, eventually manifested as disseminated intravascular coagulation, has been described in malaria (4). In uncomplicated malaria, however disseminated intravascular coagulation is rarely found (3).

Results: In malaria patients the sequestration was not different to normal. Platelet half-life was reduced in patients with P. falciparum malaria to 10–17 h (normal ~ 8 days). In one patient with P. vivax malaria Platelet half live was 59.5 h.

Conclusion: No significant differences in the sequestration of platelets when compared to healthy individuals could be detected by 111In-labelled platelet scintigraphy. Especially, no enhanced splenic sequestration, as previously expected, was the cause of the thrombocytopenia. Therefore, other mechanisms than sequestration are responsible for the dramatically reduced life span of the platelets during acute malaria.

Characteristics of DNA condition from male generative cells under doxycycline and macrolides using PM214

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Aim: The studying of chromatingeterogenous test (CT) results in sperm of subjects taking doxycycline (D) and some macrolides (Erythromyclic (E), Jozanycin (J), and Azymytricyn (A)) in moderate therapeutic doses.

Methods: Forty healthy volunteers (20–23 years) were studied. Daily dose of D was 0.2; E was administered in dose 0.25 four times per day 10 days; J—0.5 before meals twice daily 10 days; A—0.25 before meals once daily 5 days. CT for evaluation of DNA condition in human spermatozois was performed before treatment (twice), on the 5th and 10th days of treatment, as well as after 1 and 2 months after treatment course completing.

Results: CT data analysis revealed that the mean amount of defective spermatozois before treatment was 18.5 ± 3.5%. By the 5th day of D treatment the index of de-natured DNA was 63.4 ± 6.5% (P < 0.001), by the 10th day—80.4 ± 7.2% (P < 0.001). One and 2 months after the D treatment course the amount of generative cells with denatured DNA was 54.5 ± 4.6 and 42.5 ± 3.8%, respectively (P < 0.001 in both case). Under E treatment the amount of defective spermatozoids changed as 38.2 ± 4.2 (5th day), 42.4 ± 2.7 (10th day), 35.6 ± 2.5 (after 1 month), and 30.5 ± 4.2% (after 2 months) (P < 0.05 in any case). Under A using the CT results at the same control points were 39.5 ± 4.7, 46.5 ± 3.2, 40.2 ± 3.5, 25.6 ± 3.2% (P < 0.05 in any case); and under J treatment—18.2 ± 2.5, 20.3 ± 2.5, 17.2 ± 3.2, 15.2 ± 4.2%, respectively (P > 0.05 in any case).

Conclusions: The data obtained permit to conclude that D demonstrates the high level of toxicity to male generative cells. This effect preserves during 2 months after the course of D treatment.

Hospital-acquired infections

An outbreak of multi-resistant Acinetobacter baumanii (MR-Ab) in an intensive care unit (ICU) PM215

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Objective: To study the effect of aggressive isolation and decontamination measures to control an outbreak of multi-resistant Acinetobacter baumanii (MR-Ab) in an ICU.

The outbreak: The index case was transferred from a Mediterranean hospital, directly into an open-plan 10-bedded ICU, with severe injuries to his head and thorax. He died shortly after admission. Sputum, Bronchoalveolar lavage fluid, blood cultures and a chest drain swab grew MR-Ab, resistant to ampicillin, co-amoxiclav, aztreonam, amikacin, ceftazidime, cefotaxime, cefuroxime, ciprofloxacin, gentamicin, meropenem, piperazobactam, tobramycin and sensitive only to colistin. Within 10 days, MR-Ab was isolated from two further ICU patients. All isolates demonstrated identical antimicrobial susceptibility profiles. The ICU was closed to admissions and thoroughly cleaned. All patients were isolated and their contacts screened. The ICU was reopened, however, MR-Ab was isolated from a fourth patient. This patient was isolated, the ICU closed, for a second time, thoroughly cleaned, and all contacts isolated until discharge. All subsequent patients screened were negative for MR-Ab

Conclusion: This illustrates the importance of aggressive isolation measures and thorough supervised cleaning in control of an outbreak, and the need to screen patients for resistant bacteria before admission to the intensive care unit in a General hospital.

Extended spectrum beta-lactamase-positive bacteria isolated in neonatal intensive care unit PM216

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Extended-spectrum beta-lactamasises hydrolyse all penicillins, cephalosporins, including third-generation cephalosporins and aztreonam. ESBL are predominantly produced by Klebsiella spp. but may be presented in other Enterobacteriaceae, too. The aim of present study was to investigate the occurrence of ESBL-producing bacteria isolated from patients hospitalized at the neonatal Intensive Care Units (ICU). Fifty Escherichia coli and 35 Klebsiella spp. were isolated from rectum of patients hospitalized at the neonatal ICU. The MICs of antimicrobial agents were determined by the standard agar plate dilution method according to the NCCLS guidelines. For screening of ESBL production we investigated strains showing reduced susceptibility
**Isolation of staphylococci from wound swabs and their susceptibility to antibiotics**  
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**Purpose:** To determine percent of staphylococci from wound swabs and to establish their susceptibility to antibiotics.

**Material and method:** The wound swabs have been evaluated with standards microbiological techniques. Bacteria have been identified with strips from the 'ATB EXPRESSION' system. The susceptibility testing has been performed with strips with dilution technique, read by the same system.

**Results:** During the last 5 years (01 01 1997 – 25 02 2002), a total of 1978 wound swabs have been evaluated in the Military Hospital in Skopje. Positive bacterial finding have been determined in 1345 (68%) swabs with 1575 isolated bacterial species, from which 587 (37.3) were staphylococci: *Staphylococcus aureus* 460 (29.2%) isolations (173 methicillin resistant *S. aureus*); *S. epidermidis* 79 (5.0%); *S. haemolyticus* 21 (1.3%); *S. hominis* 11 (0.7%); *S. chromogenes* and *S. lugdunensis* nine (0.6%); *S. intermedius, S. lentus, S. sciuri* and *S. warneri* all with seven (0.4%) isolations. The susceptibility of *S. aureus* was to: penicillin 2%, ampicillin 15%, amoxicillin/clavulonic acid 67%, cefazidine 66%, gentamicin 29%, tetracycline’s 28%, erythromycin 61%, lincomycin 44%, ciprofloxacin 95%, cotrimoxazol 82%, vancomycin 100%, fusidic acid 96%, cefixime 57%, and Azitromicin 78%.

**Conclusion:** In our study most frequently isolated bacteria from the wound swabs were staphylococci, especially *S. aureus*. Susceptibility, except for the penicillin (2%), was high to other antibiotics.

**Antimicrobial susceptibility of MRSA at Maribor Teaching Hospital — a comparison of the years 1999 and 2000**  
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The study went on from January 1999 to December 2000. At Maribor Teaching Hospital, 2288 *Staphylococcus aureus* isolates were collected. In 1999, 114 (10%) and in 2000, 73 (6.4%) were MRSA. MRSA were recovered from routine clinical material and from surveillance swabs (nose, throat, skin). For isolation, conventional culture media were used and for surveillance swabs MRSA-screening plate (manitol salt agar with 6% oxacillin) and Trypticase soy broth with 6.5% NaCl were added. *S. aureus* was identified by catalase, DNA-se and tube-coagulase test. Antibiotic susceptibility was determined by the disk-diffusion method according to NCCLS guidelines. All 187 MRSA isolates were tested for sensitivity to the following antimicrobials: gentamicin, netilmicin, ciprofloxacin, erythromycin, chloramphenicol, tetracycline, cotrimoxazol, vancomycin and clindamycin. It was found that all MRSA isolates were sensitive to vancomycin and partially or totally resistant to the rest. There were no important differences between the years 1999 and 2000. Our MRSA isolates were completely (100%) susceptible to vancomycin, but resistant to the other antimicrobials in use to some extent. Although the monitoring of MRSA susceptibility to antimicrobials once a year did not show any important change in antimicrobial resistance, the periodical monitoring of MRSA susceptibility to antimicrobials and revaluation of current treatment regimens of MRSA infections is necessary.

**Abstracts**

*Staphylococcus aureus* strains with reduced susceptibility to vancomycin among clinical isolates in University hospital in Warsaw  
Mlynarczyk A, Mlynarczyk G, Luczak M. Department of Medical Microbiology, Medical University of Warsaw, Warsaw, Poland

The appearance of VISA (vancomycin intermediate *Staphylococcus aureus*) or h-VISA (hetero-VISA) strains could explain occasionally occurring failures of therapy of MRSA infections with vancomycin. The VISA and especially h-VISA are very difficult to be found in the routine laboratory. In our investigations we examined 1011 of *S. aureus* strains isolated and stored in our laboratory for several last years (1997 – 2001). Most strains were isolated in 2000, and some in 2001. For all staphylococcal strains MRSA as well as MSSA the MICs of vancomycin were performed by the standard dilution method. Among strains isolated in the last year three strains were recognized as VISA (MIC values were 8 mg/l). The frequency of VISA was 0.3%. In the aim of founding the h-VISA strains the population analysis was used. For this analysis all strains growing on the concentration 4 mg/l of vancomycin from the inoculum 10^6 were chosen. It was 54 strains, but only 32 of them were recognized as h-VISA. The frequency of h-VISA among investigated strains was about 3%. Most but not all of the h-VISA and all VISA strains were methicillin resistant.

In vitro activity of vancomycin, teicoplanin and oxacillin against staphylococci isolated from patients of surgical intensive care unit  
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**Objectives:** Oxacillin-resistant staphylococci have emerged as a major infection control problem in our hospital. The aim of this study was to evaluate the in vitro activity of vancomycin, teicoplanin and oxacillin against staphylococci.

**Material and methods:** This study was performed between January 2000 and December 2001, at University of Istanbul, Institute of Cardiology. The antimicrobial susceptibilities of 179 staphylococci isolates for vancomycin, teicoplanin and oxacillin have been investigated by E-test according to NCCLS guidelines.

**Results:** Fifty-five (30.73%) of 179 clinical isolates were *Staphylococcus aureus*. One hundred and twenty-four (69.27%) of 179 clinical isolates were coagulase negative staphylococci (CNS). None of 179 staphylococci isolates were resistant to vancomycin. But three of CNS isolates were intermediate and six of CNS isolates were resistant to oxacillin. Ninety (72.60%) of 124 CNS isolates were completely (100%) susceptible to vancomycin, but resistant to the other antimicrobials in use to some extent. Although the monitoring of MRSA susceptibility to antimicrobials once a year did not show any important change in antimicrobial resistance, the periodical monitoring of MRSA susceptibility to antimicrobials and revaluation of current treatment regimens of MRSA infections is necessary.

Oxacillin-resistant staphylococci have emerged as a major infection control problem in our hospital. The aim of this study was to evaluate the in vitro activity of vancomycin, teicoplanin and oxacillin against staphylococci.

**Material and methods:** This study was performed between January 2000 and December 2001, at University of Istanbul, Institute of Cardiology. The antimicrobial susceptibilities of 179 staphylococci isolates for vancomycin, teicoplanin and oxacillin have been investigated by E-test according to NCCLS guidelines.

**Results:** Fifty-five (30.73%) of 179 clinical isolates were *Staphylococcus aureus*. One hundred and twenty-four (69.27%) of 179 clinical isolates were coagulase negative staphylococci (CNS). None of 179 staphylococci isolates were resistant to vancomycin. But three of CNS isolates were intermediate and six of CNS isolates were resistant to teicoplanin. Twenty-eight (50.9%) of 55 *S. aureus* were resistant to oxacillin. Ninety (72.60%) of 124 CNS isolates were also resistant to methicillin.

**Conclusions:** Nosocomial staphylococcal infections, especially in intensive care units increase day by day. Staphylococcal infections are a major problem in many hospitals. According to our experiences the rate of oxacillin resistant staphylococci isolates in our hospital has also increased.
Activity of linezolid against nosocomial strains of *Staphylococcus aureus* in Russia: results of multicentre study PM221

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**Purpose:** To determine the susceptibility of nosocomial strains of *Staphylococcus aureus* to linezolid in different regions of Russia.

**Results:** A total of 879 clinical strains of *S. aureus* isolated in 2000–2001 from patients hospitalized in 17 medical institutions in different parts of Russia—four in Central region (Moscow, Ryazan, Smolensk), two in North-Western region (St.-Petersburg), three in Southern region (Krasnodar, Stavropol), two in Volga region (N. Novgorod, Kazan), three in Ural region (Ekaterinburg, Ufa), three in Siberia (Krasnoyarsk, Novosibirsk, Tomsk), were included in the study. Antimicrobial susceptibility testing was performed by agar dilution method in accordance with the NCCLS recommended. All tested strains including 295 MRSA strains (33.6% of all strains) were found to be susceptible to linezolid with the MIC ranged from 0.5 to 4 mg/l. Both MIC50 and MIC90 were 2 mg/l.

**Conclusions:** Linezolid had excellent in vitro activity that was not affected by resistance to other classes of antimicrobials, so it has a potential as an option for the treatment of nosocomial infections caused by *S. aureus* including MRSA.

Susceptibility to antiseptics of MRSA isolated in Japan during 1998–1999 PM222

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is a clinically significant pathogen because MRSA is resistant to many kinds of antibiotics and causes nosocomial infections around the world. The antiseptics are used for prevention of infections by MRSA. Antiseptic-resistant MRSA strains have been isolated from clinical specimens. Antiseptic resistance genes confer resistance to many kinds of drugs structurally and the resistance mechanism is the energy-dependent drug efflux system. In addition, the fluoroquinolone (FQ)-resistance gene, *norA*, confers also resistance to many kinds of antiseptics. We studied the relation of the susceptibility to antiseptics and FQs of MRSA strains isolated in Japan. A total of 420 strains of MRSA were isolated from 14 hospitals in Japan from 1998 to 1999. Acriflavine (AF), acrinol, benzethonium chloride, benzalkonium chloride and chlorhexidine digluconate were used as the antiseptics. Norfloxacin and acrinol, benzethonium chloride, benzalkonium chloride and chlorhexisolated from 14 hospitals in Japan from 1998 to 1999. Acrifla

Synergistic action of methicillin and vancomycin against methicillin resistant *Staphylococcus aureus* strains PM223

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The drug of choice in treatment of serious infections caused by MRSA was still vancomycin, however sometimes failures were observed, especially in monotherapy. Some conflicting are present in literature about an effect of combined action of vancomycin and beta-lactams. In the present work, the common effect of vancomycin and methicillin against chosen *Staphylococcus aureus* strains was examined. The investigated strains were characterized as VISA, h-VISA and clones obtained from h-VISA in population analysis. Two methods were performed: E-tests with methicillin and vancomycin placed on the media supplemented with the second antibiotic and the chessboard micro-analysis with increasing concentrations of both antibiotics. The FIC indexes were calculated for different combinations of concentrations. On the basis of the FIC indexes it was shown that the simultaneous action of vancomycin and methicillin was synergistic in all examined strains VISA and h-VISA, but only in appropriate concentrations. In different combinations the observed effect was addition or indifference. Antagonism was never observed. The synergetic effect was not observed in the case of standard *S. aureus* strain sensitive to methicillin. Supplementation of media with 4% of NaCl substantially decreased the observed effect.

Incidence of antibiotic resistance in *Staphylococcus aureus* strains in Hungary with special reference to MRSA PM224

Ghidán A, Maródi C, Csukás Z, Kamotsay K, Szabó D, Ostorházi E, Rozgonyi F. Institute of Medical Microbiology, Semmelweis University, Budapest, Hungary

Between January 1997 and December 2000, a total of 3109 *Staphylococcus aureus* strains isolated from patients admitted to the clinics of the Semmelweis University were examined for antibiotic sensitivity with the disc diffusion test. Resistance to individual antimicrobials was as follows: penicillin 84%, oxacillin 25%, erythromycin 31%, ciprofloxacin 15%, amikacin 12%, netilmicin 8%, tobramycin 10%, gentamicin 20%, clindamycin 22%, mupirocin 4%, tetracyclines 34%, chloramphenicol 9%, teicoplanin 2% and vancomycin 0%. All MRSA were β-lactamase producer. They showed co-resistance to erythromycin (53%), ciprofloxacin (36%), amikacin (29%), netilmicin (23%) and mupirocin (10%). Multiple resistant MRSA strains to mupirocin+tetracyclines+chloramphenicol amounted to 0.9%. Triple resistance to oxacillin+ciprofloxacin+netilmicin was 14%. The detection of *mecA* gene by PCR in randomly chosen MRSA qualified with 1 μg oxacillin disc resulted in only 15% mecA positivity indicating that the traditional disc diffusion test overestimates the frequency of MRSA strains particularly in such an environment where the usage of penicillins and cephalosporins is so liberal as in Hungary. Consequently, the selective pressure for β-lactam-resistance and β-lactamase induction exists everywhere. This conclusion is coherent with the relatively low frequency of multiple resistant MRSA strains and urge the need of a routinely available genetic method to apply for MRSA detection.

Final results from the antibiotic resistance surveillance at the St. Elizabeth Cancer Institute in Bratislava after 2 years (1999–2000) PM225

Babela R1, Krcmery V1, Kovacićova G1, Lovasová M1, Svetlansky P1, Gogova M*, 1School of Public Health, University of Trnava, Trnava, Slovakia, 2Department of Clinical Pharmacology, St. Elizabeth Cancer Institute, Bratislava, Slovakia

**Objectives:** The main objectives of this study were to monitor antibiotic resistance, identify new/emerging resistance mechanisms at an early stage, prevent their dissemination, early detection and prevent the outbreaks.

**Methods:** Our laboratory used antibiotic disc sensitivity testing methodology (NCCLS 1993). Zone sizes were measured objectively using a BIOMIC automated radius zone reader. Results: Throughout 2 years (January 1999 till December 2000) we have surveyed 3190 organisms collected from Outpatient Departments (1145, 35.8%), Radio-Oncology Department (992, 31.1%), Medical Department (765, 23.9%), OBG Department (217, 6.8%), Surgical-Oncology Non
ICU Department (207, 6.5%), ICU Department (175, 5.5%). From 1543 (100%) strains of Enterobacteriaceae 68 (4.4%) were resistant to 4th generation fluoroquinolone and 44 (2.9%) strains were ESBL positive. From 416 (100%) strains of Staphylococcus aureus were only five (1.2%) strains resistant to methicillin (MRSA). We collected 370 (100%) strains of enterococci, whereabout only two (0.5%) were resistant to glycopeptides (VRE). From 235 (100%) strains of Pseudomonas aeruginosa, 97 (41.2%) were resistant to aminoglycosides.

Conclusions: National restrictive antibiotic policy hand in hand with local hospital antibiotic policy and regular rotation of antibiotics used in prevention and treatment on all departments is leading in our case in positive situation in antibiotic resistance in comparing with other Slovakian and European centers.

Antimicrobial resistance of nosocomial strains of Staphylococcus aureus PM226

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Purpose: To determine the antimicrobial resistance of Staphylococcus aureus causing nosocomial infections in Smolensk Regional Hospital.

Results: A total of 140 S. aureus strains isolated during 2000–2001 were studied. Antimicrobials tested included oxacillin (OXA), erythromycin (ERY), clindamycin (CLJ), gentamicin (GEN), vancomycin (VAN), linezolid (LNZ), tetracycline (TET), chloramphenicol (CHL), rifampicin (RIF), fusidic acid (FU), trimethoprim/sulfamethoxazole (TS), ciprofloxacin (CIP), mupirocin (MUP), quinupristin/dalfopristin (QD). Susceptibility testing and its interpretation were performed by agar dilution according to NCCLS guidelines where applicable.

Results are presented in the table.

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>L/R (%)</th>
<th>MIC&lt;sub&gt;50&lt;/sub&gt;/MIC&lt;sub&gt;90&lt;/sub&gt; (mg/l)</th>
<th>MIC ranges (mg/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OXA</td>
<td>0/55</td>
<td>16/64</td>
<td>0.25/128</td>
</tr>
<tr>
<td>ERY</td>
<td>0/50.7</td>
<td>256/256</td>
<td>0.25–256</td>
</tr>
<tr>
<td>CLI</td>
<td>0/43.6</td>
<td>0.125/256</td>
<td>0.125–256</td>
</tr>
<tr>
<td>GEN</td>
<td>0/47.9</td>
<td>0.5/128</td>
<td>0.25–128</td>
</tr>
<tr>
<td>VAN</td>
<td>0/0</td>
<td>1/2</td>
<td>0.5–4</td>
</tr>
<tr>
<td>LNZ</td>
<td>0/0</td>
<td>0.02/0.6</td>
<td>2.0–2.0</td>
</tr>
<tr>
<td>TET</td>
<td>0/0</td>
<td>0.04/0.6</td>
<td>0.25–128</td>
</tr>
<tr>
<td>CHL</td>
<td>0/76.3</td>
<td>64/128</td>
<td>4–128</td>
</tr>
<tr>
<td>RIF</td>
<td>0/98.7</td>
<td>0.03/0.03</td>
<td>0.15–128</td>
</tr>
<tr>
<td>FU</td>
<td>0/0</td>
<td>0.125/0.125</td>
<td>0.06–0.125</td>
</tr>
<tr>
<td>TS</td>
<td>0/0.4</td>
<td>0.06/0.06</td>
<td>0.03–16</td>
</tr>
<tr>
<td>CIP</td>
<td>0/0.5</td>
<td>0.5/0.15</td>
<td>0.25–16</td>
</tr>
<tr>
<td>MUP</td>
<td>0/0.25</td>
<td>0.25/0.25</td>
<td>0.125–0.25</td>
</tr>
<tr>
<td>QD</td>
<td>0/0</td>
<td>0.5/1.0</td>
<td>0.5–1.0</td>
</tr>
</tbody>
</table>

Conclusions: The most active antimicrobials were vancomycin, linezolid, quinupristin/dalfopristin, fusidic acid, mupirocin, followed by co-trimoxazole, rifampicin. Beta-lactams, macrolides, lincomycin, tetracyclines and chloramphenicol should not be used for the treatment of nosocomial S. aureus infections.

Nosocomial infections due to Staphylococcus aureus in neonates PM227

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We investigated all staphylococcal infections within 2 years among 246 neonates hospitalized for infection in the neonatal ICU in a tertiary neonatal referral center. Univariate analysis, to assess risk factors for neonates infected with Staphylococcus aureus (121) vs. without S. aureus (125) was performed. From the total number of 246 cases, in 121 cases S. aureus was isolated from various samples; in 16 cases from blood cultures, in 36 cases from urine, in 18 cases from eye swabs and in 29 cases from gastric content (no significant differences in comparison with control group). Colonization with S. aureus, was a predictor of infection: nasal swabs, throat swabs, ear swabs, skin swabs and umbilical swabs were significantly more commonly observed in neonates infected with S. aureus, than with other infections. Etiological analysis showed that co-pathogens Escherichia coli and viridans streptococci were significantly more frequently associated with neonatal infection caused by S. aureus, in comparison to other organisms. According to localization of infection site, conjunctivitis and thrush stomatitis was the commonest S. aureus neonatal infections. Outcome was similar to other infections and without any significant differences between both groups. Mortality was similar to other infections, probably because: initial therapy in our centre contains an antistaphylococcal active agent (cefuroxime or cefotaxime plus aminoglycosides).

Nosocomial infections caused by Enterococcus spp. PM228

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Purpose is to study the role of Enterococcus spp. in the aetiology of nosocomial infections among the patients of the childrens clinical hospital and susceptibility of these strains to antibiotics.

Methods: The strains of enterococci were isolated from 66 patients with hospital infections in 2000–2001.

Results: The aetiological structure of Enterococcus-infections showed the predominance of skin and soft tissue infections (39.4%), urinary tract infections (33.3%), bloodstream infection (10.6%), pneumoniae (4.5%), infection of central nervous system, gastrointestinal tract, eye, surgical wound infections were of rare incidence (3–1.5%). Various nosological forms of infections were caused more often by E. faecalis than E. faecium (72.7, 27.3%). The antibiotic resistance to ampicillin and other beta-lactams occured in 100% of E. faecium isolates, but all strains of E. faecalis were susceptible to these drugs. High-level gentamicin resistance demonstrated E. faecalis isolates—29.0%, E. faecium—100%; and high-level streptomycin resistance showed E. faecalis—67.7%, E. faecium—88.8%. All the E. faecalis were active against fluoroquinolones, but E. faecium were resistant in 22.0%. There were no vancomycin resistant enterococci.

Conclusion: E. faecalis predominated in the aetiological structure of nosocomial infections due to Enterococcus spp. Antibiotic resistance patterns for two species of enterococci were different, all the strains were susceptible to vancomycin.

Evaluation of antimicrobial resistance of Enterococcus spp. experience of 6 years (1996–2001) PM229

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Abstracts

Objective: Determination of quantitative changes in antimicrobial resistance of Enterococcus isolated from clinically significant not urinary samples of patients remitted to the Laboratory of Microbiology during a 6 years period (1996–2001).

Material: The period of the study was COMPRISED between 1996 and 2001. The samples has been processed for the isolation of Enterococcus following conventional methods. Were isolated 3424 enterococci strains. The identification and susceptibility to antibiotics have been performed in automated system MicroScan(c) Dade Behring(c) through panels Combo CGP. The data were processed by the statistical system Statgraphics Plus 4.1.

Results: Of the 3424 Enterococcus, have been identified 3298 E. faecalis and 126 E. faecium. The resistance is shown in Table 1.

Conclusions: The resistance to Va and Tei of E. faecalis remains through last 4 years (2–3%). The high resistance to erythromycin and tetracillin (>70%) and the resistance (30–31%) to quinolones, antibiotics all of them used in community-acquired infections justify the susceptibility testing to the clinical strains isolated of this group of microorganism. In E. faecium the antimicrobial resistances was high and increasingly to imipenem, meropenem, erythromycin and quinolones.

Characteristics of strains E. faecium colonizing the neutropenic patients PM230

Abbassi MS, Achour W, Gréco A, Ben Hassen A. Laboratory of Bone Marrow Transplant Center, Tunis, Tunisia

Digestive colonization by Enterococcus faecium in the neutropenic patients under gut decontamination is important. Seventeen multi-resistant strains of E. faecium isolated from stools of seven neutropenic patients were the target of an epidemiological analysis through the determination of the MICs of amoxicillin, gentamicin, vancomycin, the transferability gentamicin resistance to the recipient strain E. faecalis JH12-2 by filter-mating assay, analysis of plasmid profiles of E. faecium-strain and of transconjugants and the amplification by PCR of the gene aac(6’)-aph(2”) coding for the bifunctional enzyme by using primer M13771 who gives a fragment of 174 kb. Among the seventeen strains, eleven had the same antibiotic A1, 12 had a gentamicin MIC >4096 mg/l. The MIC90 of the amoxicillin was of 128 mg/l. All the strains were sensitive to vancomycin. Ten strains harbored a plasmid of 70 kb transfered at a frequency of 6.10–5, also found in gentamicin-resistant transconjugants. However, strains belong to nine distinguished plasmids profiles. All high-level gentamicin resistant-strains had a positive PCR amplification of the aac (6’)-aph (2”) gene. The features of the studied strains establish their endogen origin, specific for every patient, sharing only high-level resistance to gentamicin. Gut decontamination treatment with gentamicin enhance either the spread and the preservation of easy-transferable plasmid carrying genetic transposable element.

Frequency and antibiotic resistance of bacteria isolated from patients suffering infectious complications following the implantation of prosthetic devices PM231

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For patients with indwelling joint prosthesis, early recognition and prompt therapy for infection in any location may be critical to reduce the risk of seeding the joint implant hematogenously. A year period (2001) a total of 2440 swabs of aspiration from patients with infectious complications following the implantation of prosthetic devices were cultured. Cultivation and identification of the strains were performed by conventional methods and by VITEK system (bioMérieux) and susceptibility testing by disc diffusion. Potentional pathogens were recovered in 324 cases (13.27%). Gram positive cocci, in particular Staphylococcus spp. proved to be the most commonly isolated bacteria. Coagulase-negative Staphylococcus (CNS) was isolated more frequently (48%), followed by S. aureus (28%), Enterococcus faecalis and E. faecium (11%), Gram-negatives (3%), anaerob isolates (7.5%). Resistance to individual antimicrobials of S. aureus and CNS were as follows: methicillin 8 and 47%, clindamycin 4.5 and 21.7%, fluoroquinolones 0 and 18%. Mupirocin resistant strains of S. aureus were not found, while 7.7% were among the CNS strains. Our results could be essential for the rational selection of treatment at our orthopedic wards.

Emergence of vancomycin-resistant Enterococcus faecium isolated from blood cultures of haematological patients hospitalised in a Central Clinical Hospital of the Medical University in Warsaw in 2001 PM232

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Purpose of the study: In the year 2001 the first strains of vancomycin-resistant enterococci (VRE) have been reported at a university-affiliated hospital in Warsaw (1200 beds). The aim of the study was to investigate the frequency of enterococcal isolates in haematological patients in 1999–2001, estimation of the percentage of VRE in 2001 and characterisation of VRE strains.

Results: In the analysed period the percentage of isolated Enterococcus sp. strains among all non-repetitive clinical isolates in 1999, 2000 and 2001 was 3.9, 3.1 and 51%, respectively. Cultured strains were identified as E. faecalis, E. faecium, E. gallinarum and E. avium. The most prevalent was E. faecium strains, isolated with a frequency of 75, 62 and 75%, respectively. Vancomycin-resistant strains were all identified as E. faecium and in 2001 they comprised 17% of all isolates of this species.

Conclusions: (1) The frequency of isolation of Enterococcus sp. in blood cultures of haematological patients remained relatively stable in 1999–2001. (2) The predominant enterococcal species isolated from these patients was E. faecium. (3) In 2001 we recorded for the first time an emergence of vancomycin-resistant E. faecium, which comprised 17% of all isolates of this species.

Epidemiology of Pseudomonas aeruginosa strains isolated in immuno-compromised patients PM233

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From April 1998 to June 2000, 47 non-repeated strains of Pseudomonas aeruginosa were isolated from 42 immunocompromised patients. Thirty-six percent of strains were isolated from abscess, 27% from blood culture and 11% from urine. Susceptibility to antibiotic was studied by the routine disk diffusion method (CA-SFM). MICs were determined using agar dilution to 11 antibiotics (5b-lactams, four aminosides and two fluoroquinolones). Serotyping of the different strains was performed using antisera to the International Antigenic Typing Systems Serotypes. The study showed 80% of resistance to
Infectious complications sustained by Stenotrophomonas (Xanthomonas) maltophilia in HIV-infected patients: a ten-year surveillance study PM234

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Introduction: Stenotrophomonas maltophilia is an ubiquitous, aerobic, gram-negative bacillus closely related to the Pseudomonas species, and usually considered an opportunistic, nosocomial pathogen. At present, very little information are available about S. maltophilia infections in the setting of HIV disease.

Patients and Methods: A retrospective survey of clinical and microbiological records of 1374 HIV-infected patients referring to our tertiary care centre between 1991 and 2000 was performed, in order to identify all episodes of S. maltophilia infections, and analyze its epidemiological, clinical, and microbiological variables.

Results: Sixty-one episodes of S. maltophilia infection were observed in 59 patients: sepsis/bacteraemia in 48 cases (78.7%), lower airways infection in five, urinary tract infection in four, pharyngitis in two, lymphadenitis and liver abscess in one case each. Forty-seven out of 61 episodes of S. maltophilia infections (77%) occurred as nosocomial disease, generally in association with advanced immunodeficiency, neutropenia, instrumentation, and prior antimicrobial therapy. Bacterial isolates showed an elevated resistance profile against many beta-lactam compounds, aztreonam, imipenem, and aminoglycosides.

Conclusion: S. maltophilia represents an emerging opportunistic pathogen in HIV-infected patients, responsible for a broad range of clinical manifestations, and often resistant to multiple beta-lactam and aminoglycoside compounds.

Extended spectrum beta-lactamases producing germs in intensive care units PM235

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The purpose of the study: We collected 226 bacteriological samples from adult and neonate patients who were admitted in intensive care units (ICU). The aim was to observe the colonization status with microbes that may have a nosocomial potential and to establish circulating phenotypes in ICUs. The results obtained from a total of 226 samples 61 strains of gram negative bacteria (Enterobacteriaceae family) were isolated. Fourteen strains showed extended spectrum beta-lactamases (ESBL) phenotype (eight strains of Klebsiella pneumoniae, three of Escherichia coli, two of Klebsiella ornithinolytica, one of Klebsiella oxytoca). We used both disc diffusion test (extended antibiotic susceptibility test and synergy test to visualize ‘champagne stopper’ pattern) and mini API® system.

The conclusion reached: We put in evidence a massive colonization with germs that may have a nosocomial potential especially microbes that produce ESBL (22.9% from all enterobacteriaceae isolated) which implies a rational policy in prescribing antibiotics in hospitals from western part of Romania.

Carbapenem activity against nosocomial Gram-negative rods PM236

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Purpose: To determine a susceptibility of nosocomial Gram-negative rods to carbapenems.

Methods: Two hundred strains of Gram-negative rods were cultured from clinical specimens from hospitalized patients (July-November 2001). Identification of strains was performed in the automatic ATB system (bioMerieux, France). Susceptibility of strains to carbapenems: imipenem and meropenem was determined with disc diffusion method according to NCCLS recommendations. ESBL-producing strains were detected with double-disc synergy test (DDST according to Jarlier et al., 1988) or a novel method of ESBL detection (DD, diagnostic disc) according to Appleton (1999). Two discs were applied in this test: with cefpodoxime (CPD) and with cefpodoxime/clavulanic acid (CD 01) (Oxoid, England).

Results: One hundred and ten strains of enteric rods and 90 strains of non-fermenting rods were cultured. Twenty eight (14%) ESBL-positive strains were detected. Carbapenem were active against 96% of enteric rods. The percentage of non-fermenting rods susceptible to imipenem was 70 and to meropenem—60.

Conclusions: Carbapenem: imipenem and meropenem demonstrated high activity against clinical strains of enteric rods. However, the antibiotics were less active against nosocomial strains of non-fermenting rods.

Inhaled antibiotics against multiresistant bacteria in bronchial secretions of ICU patients: a preliminary report PM237

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Purpose: The aim of this study was to assess the effectiveness of aerosolized ampicillin/sulbactam, ceftazidime and colistin, in ICU patients with multiresistant Acinetobacter baumannii or Pseudomonas aeruginosa colonization of the respiratory tract.

Methods: Fifty-three intubated, mechanically ventilated patients participated in the study. Multiresistant A. baumannii, sensitive only to ampicillin/sulbactam, or P. aeruginosa, sensitive to ceftazidime or colistin, were isolated from the bronchial secretions (103–106 CFU/ml). All 53 patients were subsequently treated with intravenous ampicillin/sulbactam, ceftazidime or colistin, whereas 27 of them were also given the same antibiotic in aerosolized form.

Results: A decrease in the number of colonies by 103–106 CFU/ml was observed, following 2–4 days of combined treatment with both
intravenous and inhaled antibiotic. None of the 27 patients developed VAP. In the 26 patients who only received the antibiotic intravenously, the decrease ranged from zero to 10^3 CFU/ml, after 7 days of treatment. Two of 26 patients developed VAP.

Conclusions: Our results suggest that the administration of aerosolized antibiotics represents an effective means of preventing ventilator-associated pneumonia caused by A. baumannii and P. aeruginosa.

Activity of antibiotics against Pseudomonas aeruginosa strains isolated from tracheal aspiration PM238

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Introduction: Pseudomonas aeruginosa is an important nosocomial pathogen. Resistance to certain beta-lactam antimicrobial agents among P. aeruginosa is increasing. Despite the development of new antibiotics multiresistant strains of P. aeruginosa represent an important therapeutic problem. The aim of this study was to investigate the activity of imipenem, amikacin, piperacillin, ciprofloxacin, ceftazidime, against clinical isolates of P. aeruginosa.

Methods: A total of 54 isolates by tracheal aspiration from hospitalized patients, admitted to intensive care units were identified as P. aeruginosa using an algorithm that included: Gram stain, pigment, oxidaze (+/-) and Gram negative identifications Microscan Walkaway-96 (Dade Behring) were used according to the manufactures instructions. Minimal inhibitory concentrations were determined using Walkaway, interpretation based on NCCLSM 100-59, January '99.

Results: The respiratory tract was the single site of isolation for this study. The best activity was showed by imipenem 25%, followed by amikacin 22®, piperacillin, pip/tazobactam, ciprofloxacin had the same sensitivity 11%. Conclusion: A high level resistance to antibiotics was observed to P. aeruginosa isolated from tracheal aspiration. Carbapenems seem to be the most active against P. aeruginosa in this study.

Comparative activity of colistin by agar dilution and disk diffusion against 35 isolates of Acinetobacter baumannii PM239

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Objective: To compare the susceptibility to colistin results by disk diffusion (DD) and agar dilution (AD), using 35 Acinetobacter baumannii strains collected from significant clinical samples of infected and colonised patients admitted to the Hospital Universitario de la Princesa from June to November 2001.

Materials and methods: Clinical samples were collected from patients admitted to this hospital. Only one isolate per patient was included. Antimicrobial susceptibility testing was performed as recommended by the NCCLS. All bacterial isolates were tested by DD and AD to provide a comparison of both test results. Very major error was considered when the strains were resistant (R) by AD and susceptible (S) by DD and major error when S by AD and R by DD. Categories of S and R were stabilised using the breakpoints suggested by Mensura (2000). Colistin R strains was typed by REP-PCR.

Results: Among the 35 strains included in this study 30 (85.7%) were S to colistin and five (14.2%) were colistin R by AD, of this five colistin R strains four (11.4%) were S to colistin by DD and one was R by both methods. All R isolates were similar by REP-PCR.

Conclusions: Most of the AD colistin resistant strains were S when tested by DD indicating that this method is not useful to determine the resistance to colistin. REP-PCR patterns show that the spread of a colistin R clone seems to be involved.

Treatment of bone and joint infections (BJI) due to gram negative bacteria (GNB) by a cefepime (CFP)+fluoroquinolones (FQ) combination PM240

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Objective: To assess the efficacy and safety of CFP combined with ofloxacin (OFL) or ciprofloxacin (CIP) in the treatment of hypercase GNB, BJI.

Methods: GNB were isolated from per-operative biopsies (pob) and/or from articular punction (ap). Patients (pts) received CFP, 2 g bid+OFL, 200 mg tid or CIP, 400 mg bid intravenously for 28 days, followed by a prolonged oral FQ monotherapy. Cure was defined as: resolution of all clinical signs of infection, normalization of the biological inflammatory profile at the end of treatment (EOT) and absence of infection at the same site during the post-treatment follow-up period (PTFU).

Results: All of the 20 studied patients [mean age = 48 years] had hospital acquired BJI. Seventeen/20 had an infected orthopedic device (prosthetic joints = 6, other orthopedic prosthetic devices = 11). Culture of 17 pob and 5 ap yielded to Pseudomonas sp. (11), Enterobacter cloacae (6), others (4). Vancomycin was added for six pts co-infected by GNB-MRSA. Nineteen/20 pts underwent a surgical intervention (debridement = 11, removal-replacement = 7, amputation = 1). After PTFU period of 17 months (range 3–29), the overall success rate was 12/17 (88.2%) without serious adverse events.

Conclusion: CFP–FQ combination was safe and efficient in the treatment of hypercase GNB, BJI.

Treatment of posttraumatic MRSA osteomyelitis of the femur with long-term cotrimoxazole—a case report PM241

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The authors report a case of posttraumatic osteomyelitis of the femur caused by methicillin-resistant Staphylococcus aureus (MRSA), following the shot injury. Relapses of the infection occurred in 3 months interval and were treated by revision, debridement, lavage and vancomycin. Because of laboratory signs of renal insufficiency vancomycin became contraindicated for treatment of the third relapse of infection and the different approach was employed: classic open treatment of bone infection see. Orr was combined with a long-term administration of high-dose cotrimoxazole. The patient was given cotrimoxazole 9600 mg daily divided in four doses (120 mg/kg/24 h) for 2 months, then for gastrointestinal complaints with lowered dose of 5760 g daily for next 6 months. The wound completely healed. During 18 months after the final surgery there was no relaps of infection, but the atrophic pseudoarthrosis of the femur resulted. The patient can walk with a rigid orthosis and two crutches. The whole treatment of the
plasmid dissemination contributed to the concurrent nosocomial infections due to PM243
viable bacteria in Smolensk Regional Hospital (Russia) PM245
Aminoglycoside resistance mechanisms in nosocomial Gram-negative bacteria in Smolensk Regional Hospital (Russia) PM245

Sawicka-Grzelak A, Rokosz A, Lucek M. Department of Medical Microbiology, University Medical School, Warsaw, Poland

Purpose: To identify and determine the drug-susceptibility of ESBL-positive strains isolated from urine samples.

Results: Five hundred and ninety-five strains (83.6%) belonging to Enterobacteriaceae family, 115 strains (16.1%) of non-fermenting rods and two strains (0.3%) of other Gram-negative rods were isolated. Eighty-two ESBL-producing strains (11.5% of all strains) were detected. Fifty-nine ESBL-positive strains were susceptible to nitrofurantoin, 58- to norfloxacin and ciprofloxacin and 54- to fosfomycin.

Conclusions: ESBL-positive strains were detected most frequently among enteric rods (80 strains). Nitrofurantoin and quinolones were the most active in vitro antibacterial agents against examined ESBL-positive uropathogens.

Aminoglycoside resistance mechanisms in nosocomial Gram-negative bacteria in Smolensk Regional Hospital (Russia) PM245

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Purpose: To determine aminoglycoside resistance mechanisms in nosocomial gram-negative bacteria isolated in Smolensk Regional Hospital in 1995–2000.

Results: The mechanisms of resistance were evaluated phenotypically using 12 different aminoglycosides. A total of 257 aminoglycoside resistant gram-negative strains were studied. One hundred fifty-eight strains were collected in 1995–1996, 52 in 1998 and 47 in 2000. The resistant profiles were determined: Enterobacteriaceae—152; Pseudomonas aeruginosa—62; Acinetobacter spp.—43. The most frequently phenotypes were GT (gentamicin, tobramycin)—48% and GTNet (gentamicin, tobramycin, netilmicin)—35%. The GT phenotype due to production ANT(2′)-I enzyme, the GTNet–AAC(3)-V (87 strains), AAC(3)-IV—one strain and AAC(2′)-I—one strain. The resistance to amikacin in 7% strains was due to production AAC(6′)-I (3%) and AHP(3)-VI (4%). The most of examined strains were simultaneously resistant to kanamycin and neomycin caused by production of AHP(3)-I (69%). Only seven strains were resistant to all aminoglycosides due to impermeability of outer membrane. No substantial differences were observed between years.

Conclusions: The main mechanism of aminoglycoside resistance is fermentative modification. The high rate to gentamicin and tobramycin was due to production of ANT(2′)-I and AAC(3)-V. Amikacin and isepamicin were the most active aminoglycosides against gram-negative nosocomial isolates.

Severe nosocomial infections due to *Stenotrophomonas maltophilia* PM243


Objective: To present a variety of severe nosocomial infections due to *Stenotrophomonas maltophilia* in patients hospitalized in tertiary medical units from Cluj.

Results: During the last year nine strains of *S. maltophilia* obtained from patients with severe infections and hospitalized in different wards were isolated. All but one were considered nosocomial infections: four cases of pneumonia, one urinary tract infection, three cases of surgical wound infections and one case of endocarditis under surgical treatment. The cases of pneumonia were either primary occurring in a granulocytopenic patient with leukemia or secondary in patients that underwent surgical treatment. In the case of endocarditis the etiology was established after surgery from the damaged valve in a negative hemoculture patient with a poor outcome under medical treatment. In all cases of surgical wound infection bacteremia occurred diagnosed on clinical basis in the presence of severe sepsis or hematogenous dissemination in the lung. The urinary tract infection occurred in a patient after urinary surgery and having a catheter in place. The immediate evolution was favorable in all cases but treatment was difficult due to the highly resistant strains and to underlying diseases.

Conclusions: *S. maltophilia* should be considered in nosocomial severe infections and prophylaxis by interrupting environmental transmission has to be promoted.

Susceptibility of nosocomial ESBL-positive uropathogens to antimicrobial agents PM244

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Objectives: To determine the frequency of ESBLs and their genetic relatedness among Enterobacteriaceae clinical isolates recovered at the Microbiology Laboratory of TBD. The abilities of different methods to detect these resistant strains were compared.

Methods: One hundred out of 178 isolates that were screened positive for ESBLs were tested with double disk synergy test (DDST), three dimensional test (TDT), E-test-ESBL and Vitek-ESBL test. Pulsed field gel electrophoresis (PFGE) analysis was applied to 13 ESBLs: five Klebsiella pneumoniae and eight Escherichia coli.

Results: Revealed the prevalence of ESBLs in 25.8% of clinical isolates. The sensitivities of the DDST, TDT, E-test and Vitek were 100, 73, 86.9 and 47.8%, respectively. In the DDST, aztreonam was the most sensitive indicator (93.4%). PFGE demonstrated that 80% of K. pneumoniae were derived from a single clone whereas 62.5% of E. coli isolates were derived from two different clones. Non-clonal origin was demonstrated in 20% of K. pneumoniae and 37.5% of E. coli.

Conclusion: There is an increased prevalence of ESBLs. The DDST is the most sensitive, practical and cost effective diagnostic method reliable for routine use in our laboratory. Both clonal spread and plasmid dissemination contributed to the concurrent nosocomial outbreaks caused by ESBL-producing *K. pneumoniae* and *E. coli*. Judicious use of antibiotics and implementation of infection control measures are necessary to limit the prevalence of such outbreaks.

Comparison of different methods for detection of extended spectrum beta lactamases (ESBLs) and their genetic relatedness among enterobacteriaceae clinical isolates in a research medical institute PM242

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Risk factors (RF) of infectious complications (IC) after extensive operations in onco-gynaecologic (OG) patients  PM246

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The aim of the study was to determine RF of IC in OG pts. Total 241 OG pts after extensive hysterectomy (201 pts), extensive vulvectomy (22 pts) and extensive/combined operations for ovarian cancer (18 pts) were analysed. IC developed in 74 pts. One hundred and sixty-seven pts had no IC. Twenty-eight of 50 RF analysed were independent RF of IC. Most important included: age > 50 years (P = 0.0002), grade 2–3 obesity (P = 0.005), diabetes mellitus (P = 0.0002), diagnosis of cervical cancer (P = 0.0001), history of pre-cancer of vulva (P = 0.0001) and its duration > 10 years (P = 0.0094), hypoalbuminemia (P = 0.001), hypoproteinemina (P = 0.007), anemia (P = 0.0154), radiodermatitis (P = 0.004), previous chemotherapy (P = 0.017), if more than five courses of chemotherapy (P = 0.003), leukopenia after chemotherapy (P = 0.014), previous antibiotic therapy (P = 0.0004), duration of operation > 3 h (P = 0.0001), duration of postoperative draining (P = 0.0001), blood loss > 900 ml (P = 0.003), intraoperative antibiotic prophylaxis (P = 0.0004). RF for UTI only were following: pyelocystitis by ultrasound investigation (P = 0.0001), leukocyturia before operation (P = 0.017), bacteriuria before operation (P = 0.016) and duration of urinary catheter using > 10 days (P = 0.0001).

Postpartum endometritis due to group A Streptococcus: a case-control study  PM247

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Aims: To determinate risk markers of an outbreak of postpartum endometritis due to group A Streptococcus.

Design: A case-control study using data collected with a structured form.

Setting: The cases of postpartum endometritis were diagnosed in the department of Obstetric of the Paris hospital network during 5 days (December 1999–January 2000). The group of controls consisted of women delivered in the same department during the same period.

Participants: Cases (n = 3) and controls (n = 59).

Findings: Cases had smoked more often during pregnancy (67 vs. 16%; P = 0.089) and received more often immunosuppressive treatment than controls (33 vs. 0%; P = 0.060). Instrumental delivery had been needed more often for cases than controls (67 vs. 13%; P = 0.062). Cases had been hospitalized after delivery in a ward z of the department more often than controls (100 vs. 23%; P = 0.017). They had been examined after delivery more often by a midwife x (100 vs. 18%; P = 0.009) and a nurse y had provided care to cases and not to controls (33 vs. 0%; P = 0.051).

Conclusion: Smoking, receiving immunosuppressive treatment during pregnancy, and instrumental delivery were significantly associated with postpartum endometritis (P < 0.10). A midwife and a nurse might be involved in the transmission of the infection.

Antibiotic prophylaxis (AP) in extensive operations in onco-gynaecologic (OG) patients  PM248

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The aim of the study was to assess efficacy of perioperative AP. Total 241 pts were included. Two hundred and one pts with cervical cancer (CC) undergone extensive hysterectomy, 22 pts with cancer of vulva (CV)-extensive vulvectomy, 18 pts with ovarian cancer (OC) – extensive/combined operations. Fifty-one pts (group 1) received AP with amoxicillin/clavulanate (AM/CL) 1.8 g IV 30 min prior to operation, then 1.2 g IV thrice per day for 3–5 days. Fifty pts (group 2) received cefotaxime (CTX) 2 g IV 30 min prior to operation, then 1 g four times per day for 3–5 days + metronidazole (MTZ) 500 mg two times per day for the same period. One hundred and forty pts were retrospective control (they received II–III generation cephalosporins or linkosamides only after operation). The rate of SWI in pts with CC, CV and OC was 13.5, 73, 29%, respectively; DWI–16.2, 0 and 21%, respectively; UTI–72, 80, 42.8%, respectively. The AP with AM/CL was more effective compared to CTX+MTZ (SWI–6 vs 18%, respectively, P < 0.05, DWI–9.8 vs 14%, respectively, P < 0.05). The rate of postoperative UTI was equivalent in two groups (62 vs 74%, P = N.S.). Thus, AP with AM/CL is preferable option in extensive operations in OG pts.

Prophylaxis of post-operative hospital pneumonia in elderly surgical patients in the general resuscitation department  PM249

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Fifty-eight patients were randomized into two groups. Group 1, a treatment consisting of 31 patients and Group 2, consisting of 27 patients as a control. The patients were at the age of 67±1.2 and had had different surgical interventions with general anaesthesia from 1 to 3 h and accompanying COPD (89%). Artificial pulmonary ventilation was used in 45 cases. In the early post-surgery period the patients of Group 1 were administered inhalation therapy, including ipratropium bromide with fenoterol (atrovent, berodual) and ambrocol (lazolvan) through a nebulizer. The inhalation therapy was not administered to the patients of Group 2. Under the influence of the inhalation therapy pulmonary ventilation and respiratory metabolism was restored faster in all the resuscitation patients (in Group 1—by the end of the first 24 h, in Group 2—on the 3rd–4th day). The percent rate of PEF1 was 76.7±4.1 and 56.4±4.5, respectively. Artificial pulmonary ventilation ended in 9.2 and 7.3 h, respectively. The time of the patients’ stay in the resuscitation department was 3.2 days in Group 1 and 4.6 days in Group 2. By the end of the 1st week pneumonia developed in one patient from Group 1 and in eight patients in Group 2. Aerosol therapy application accelerates medication delivery to the respiratory tracts, increases the local activity and effects good prophylaxis for surgical hospital pneumonia.

Variation in etiology of early and late onset ventilator associated pneumonia  PM250

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**Purpose:** To compare the distribution of causative microorganisms, their susceptibility to antibiotics and outcome of ‘early’ and ‘late’ VAP in a Greek ICU.

**Methods and results:** Retrospective study of mechanical ventilated (MV) patients (pts) with early and late VAP during a 6-month period. Diagnosis of VAP was made by clinical, radiographic criteria and quantitative cultures of bronchial secretions. VAP was diagnosed in 17 pts (26%) out of 67 consecutive admissions in ICU. All pts before the development of VAP received antibiotics. Three episodes of VAP (17.6%) were developed before the 7th day of MV (early VAP) and were caused: (1) by multi-resistant Acinetobacter; and (2) by antibiotic-susceptible *Pseudomonas aeruginosa*. In this group one pt died from septic shock related to VAP and two pts survived. Fourteen pts (82.4%) developed VAP after the 7th day of MV (late VAP). Five cases were caused by multi-resistant *P. aeruginosa*, two cases by MRSA, two cases by multi-resistant Acinetobacter, two cases by susceptible to antibiotics *Klebsiella pneumoniae*, and three were polymicrobial and caused by multi-resistant microorganisms (MRSA and GNB). Four pts died (28.6%) from septic shock related to VAP, five pts (36%) died because of another cause and five pts (36%) survived.

**Conclusions:** Early and late onset episodes of VAP were caused by ‘potentially drug-resistant bacteria’. *P. aeruginosa* as a cause of early VAP was susceptible. Mortality attributed to early and late VAP was similar.

**Antibiotic prophylaxis in oncological and major reconstructive orthopaedic surgery** PM251

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During last year patients scheduled for oncological surgery or major reconstructive procedures were randomised to either vancomycin or teicoplanin prophylaxis. Prophylaxis was performed with either vancomycin 1 g i.v. twice daily or teicoplanin once daily 400 i.v. Two hundred patients were included. Four patients did not agree the study protocol and were excluded. We treated 98 patients with teicoplanin and 98 patients with vancomycin. Out of the 196 patients 117 were operated for oncological disease, while the remaining 79 underwent major orthopaedic procedures. We experienced 10 cases of red man syndrome, and five cases of moderate hypotension. Five patients had postoperative complications: two deep venous thrombosis, one pulmonary embolism, two postoperative haematoma. In five patients we observed a wound dehiscence; two of these patients showed clinical sign of SSI and microbiological examinations were positive for MRSA. One patient recovered from infection with medical therapy, while the other patient showed a local tumour recurrence and was amputated at the thigh. At last surgery infection was still present clinical and at microbiological examination. In conclusion we had an infection rate of 1.02% which is comparable to the infection rate of a ‘clean’ surgery in patients with normal risk of infection. Teicoplanin showed lower toxicity, has a longer half-life and has a simpler way of infusion and it is our current choice in high risk surgery.

Injuries with contaminated sharp articles in health care workers in General Hospital Celje, Slovenia PM252

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In a prospective study carried out from January 1997 till June 2001, we registered 133 subcutaneous injuries with sharp objects, mostly in nurses and cleaning service workers. In 19% of cases the incident occurred outside the hospital, in persons who were not medical workers. In 69 cases the injury causing object was a needle that had been used in known patients, 14 of which were hepatitis B positive. Fifty-five (48.2%) of the injured health workers had been previously vaccinated against hepatitis B; the protective antibodies to hepatitis B in the blood were found in 35/114 (30.7%) health workers only, while the tests for antibodies to hepatitis C and HIV were negative in all cases. Following the incident, the majority of the injured persons, i.e. 102, were vaccinated against hepatitis B, while 46 persons (34.6%) also received passive prophylaxis with human immunoglobulin against hepatitis B. None of the injured persons have developed the disease or showed evidence of sero-conversion. In the year 2000 the general as well as specific preventive measures practised in our hospital became more rigorous. Thus, approximately 80% of our health workers at risk have already been vaccinated against hepatitis B.

**Multidrug-resistant bacteria infected patients isolation precautions in outpatient and investigation departments in a Paris university hospital: knowledge of medical and paramedical health workers** PM253

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To improve measures preventing dissemination of multidrug-resistant bacteria (MRB), a cross-sectional survey (2000) was conducted to analyse healthcare workers’ (HCWs) isolation precaution knowledge for MRB infection at 21 investigation and outpatient departments excluding four declaring not to be in charge of MRB patients (emergency, obstetrics, nuclear medicine, and bacteriology). Two hundred and eight HCWs answered (67% of the paramedical staff, 28% of the physicians). Thirty-three percent of them reported they do not know frequently or always the patient MRB status. They (82%) wish MRB status to be mentioned on the test form or on the advice request letter. MRB patient visit or test was appropriately timed in 62% answers. Gowns (61%) or masks (58%) use were not systematically reported. Other HCWs (74%) reported better isolation precaution knowledge than physicians (58%) and nurses (81%) than investigation assistants (58%). Physicians declared lower compliance with use of gowns, gloves or draw-sheets than other HCWs. They had also lower education in isolation precautions and were less interested in education programs. This study suggests the necessity to improve MRB infection information. Physicians and investigation assistants seem to be insufficiently aware of hospital infection control. Therefore, education strategies targeted at physicians and investigation assistants working at outpatient and investigation departments should be developed.

**Outbreak of Clostridium difficile-associated diarrhea in Infectious Disease Department: risk factors and hygiene measures assessment** PM254

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Abstracts

The incidence of *Clostridium difficile* associated diarrhea (CDAD) increased in our department from January to June 2001.

**Objective:** To confirm the out break of CDAD, to identify the risk factors and assess the effectiveness of the measures implemented for controlling this outbreak.

**Methods:** CDC definitions were used to identify the cases. The scope of the outbreak was defined. CDAD incidences during the outbreak period and during the same period in 2000 were compared. Risk factors (reduced mobility, antibiotic treatments ... ) were studied for patients from whom length of hospital stay (LHS) was more than 6 days. Contact precautions and environmental cleaning with CIONa implemented were assessed.

**Results:** Seventeen episodes of CDAD were identified. Sex ratio: 1.41, mean age = 58.5, mean LHS = 36 days, mean delay for CDAD occurring = 21 days. One hundred and fifty-two patients involved in the study of risk factors. Relative Risk (R.R.) evaluated were: β-lactams (R.R. = 7.62, IC95%: 1.03 – 56.56), reduced mobility (R.R. = 7.61, IC95%: 1.76 – 32.85). Incidence of CDAD was less than two cases per 1000 hospital days after June 2001.

**Conclusion:** We confirmed the outbreak of CDAD in our department β-lactams and reduced mobility were identified as risk factors for CDAD. Measures implemented to control the outbreak were effectiveness.

Positive heart transport fluid cultures associated with severe infections in heart transplant recipients  PM255

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At the Mount Sinai Hospital in New York City 256 heart transplants were performed between 1986 and June 2000. Cultures were routinely performed on all heart transplant transport fluids. Culture data was available for 204 of these patients. In total 24/204 (11.8%) were positive for bacteria, fungi or both. The organisms isolated included coagulase negative staphylococci (13), *Pseudomonas aeruginosa* (2), *Staphylococcus aureus* (1), *Acinetobacter baumanii* (1), *Serratia marcescens* (1), *Enterobacter cloacae* (1), *Escherichia coli* (1), *Proteus mirabilis* (1), *Enterococcus faecalis* (1), *Viridans Streptococci* (1), and fungi (*Aspergillus fumigatus* (1), *Penicillium species* (1), and *Rhodotorula rubra* (1). Two heart transport recipients had two organisms isolated from the transport fluid. Isolation of resistant gram-negative bacilli in the transport fluid was significant infection in 3/5 patients (60%) with the same organism. The observed infections were pneumonia secondary to *E. cloacae*, sternal wound infection secondary to *P. aeruginosa*, and *bacteremia* secondary to *P. aeruginosa*. It appears prudent to provide prophylaxis against resistant Gram negative bacilli to prevent infections.

Rate and mortality in nosocomial bloodstream infections  PM256

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**Objective:** We studied the trends of nosocomial bloodstream infection and calculated the population-attributable risk for death among hospitalized patients. **Methods:** We perform a 15-year retrospective study for all patients (N = 79160), admitted to our department between 1986 and 2000.

**Results:** Between 1986 and 2000, a total of 1577 patients developed 1763 episodes of nosocomial bloodstream infection. The crude infection rates increased linearly from 7.2 to 25.4 per 1000 discharges (1.11–1.93 episodes per 1000 patient-days) during the 15-year study period. Increases in the infection rates were due to gram-positive cocci, yeasts and essentially explained by infections caused by coagulase-negative staphylococci, *Staphylococcus aureus*, enterococci, and *Candida* species, respectively. Although the crude mortality in patients with nosocomial bloodstream infections decreased from 45% in 1986 to 28% in 2000, the in-hospital population-attributable mortality among infected patients increased from 5.5 deaths per 1000 discharges in 1986 to 8.2 per 1000 discharges in 2000. The etiologic fraction or the proportion of deaths in patients with bloodstream infection to all deaths occurring in the hospital increased from 15.4% in 1986 to 26.4% in 2000.

**Conclusions:** The incidence and the population-attributable risk for death among patients experiencing nosocomial bloodstream infections increased progressively during the last 15 years in our department.

Ventilator-associated pneumonia before and after intensive care unit temporary closure  PM257

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**Purpose:** To evaluate the influence of ICU’s temporary closure on the characters of VAP.

**Results:** We compared the incidence, causative organisms and mortality of VAP in two different time periods. Period 1 June to December 1999. Period 2 June to December 2000. Between those two periods the ICU remained closed for 4 months because of reconstruction works.

**Period 1:** Sixty-seven consecutive patients (pts) were studied with bronchial secretions cultures at least 2 days after Mechanical Ventilation (MV) initiation. The VAP was diagnosed by clinical, radiological and microbiological criteria in 17 pts (26%). Causative organisms included: *Pseudomonas aeruginosa* 8, *Acinetobacter 5, Staphylococcus aureus* 4, *Klebsiella pneum.* 3, *Enterobacter 1*. In three cases VAP was proved polymicrobial. Fourteen (14) episodes of VAP (82%) were developed after 7 days MV (late VAP) and were attributed to multiresistant microorganisms. Mortality of VAP was 29%.

**Period 2:** Among 66 consecutive pts, VAP was diagnosed in 21 (32%). Causative organisms included: *Acinetobacter 10, P. aeruginosa 8, S. aureus 4, K. pneumoniae 3, Escherichia coli 1*. Five (5) cases were polymicrobial and 14 cases were ‘late VAP’ (67%). Causative microorganisms had similar patterns of sensitivity to antibiotics (compared to period one). Mortality of VAP was 38%.

**Conclusion:** Temporary ICU closure had no significant influence on the incidence, distribution of causative organisms, their sensitivities to antibiotics and mortality of the VAP.

A mortality prediction model in acute pyelonephritis  PM258

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**Purpose:** The aim of this study was to derive a scoring system for the prediction of outcome in adult patients with acute pyelonephritis (AP) severe enough to need hospitalization. Therefore, the charts of 225 patients (102 men, median age 67 years) were reviewed.

**Results:** Logistic regression analysis identified in both sexes four independent correlates of in-hospital mortality, the coefficients of which divided by 0.5 and rounded to the nearest integer, resulted in the following integer-based scoring system: Points (men) = 6*
PCT and C-reactive protein (CRP) for differentiation of systemic inflammatory response syndrome (SIRS), sepsis and severe sepsis

Procalcitonin (PCT) and C-reactive protein (CRP) for differentiation of systemic inflammatory response syndrome (SIRS), sepsis and severe sepsis

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Objectives: To evaluate the value of PCT in the differentiation of patients with SIRS, sepsis, severe sepsis and bacteremia in comparison to CRP.

Design: Prospective study including patients who meet criteria for SIRS, sepsis or severe sepsis (Consensus Conference of the ACCP/SCCM) admitted over 18-month period.

Patients and method: A total of 67 patients were included: eight with SIRS, 35 with sepsis and 24 with severe sepsis. Sixteen from 59 patients had bacteremia. PCT and CRP were evaluated in the first 24 h after admission: PCT by BRAHMS PCT-Q test and CRP by turbidimetric assay. The sensitivity, specificity, predictive value of different cutoff points for PCT and PCT were determined.

Results: With a cut off point of 0.5 ng/ml for PCT and 0.6 mg/dl for CRP sensitivity and specificity for sepsis were 73%, respectively 75% (PPV 95.6, NPV 27.3) and 96%, respectively 17% (PPV 87.2, NPV 75). A cutoff point of 2 ng/ml for PCT accurately predict sepsis (sensitivity 80%, specificity 100%, PPV 100). A PCT level of at least 10 ng/ml was a good predictor for bacteremia (sensitivity 86%, specificity 90%, PPV 73.7 and NPV 95).

Conclusion: PCT is a good discriminating marker to characterize the level of inflammation caused by infection and can predict bacteremia.

Assessment of Procalcitonine (PCT) and antigens in the diagnosis and follow-up of systemic fungal infections in neutropenic patients

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Neutropenic patients are at high risk of developing systemic and often fatal fungal infections especially candidiasis and aspergillosis. Signs of infection are often absent or appear late and cultures have low sensitivity.

Our study included 35 patients who were categorized as having proven (9), probable (11), or possible (5) systemic fungosis according to EORTC criteria; 10 showed no sign of infection, and were used as controls. Blood samples were received on the 1st, 3rd, and 5th day from the onset of signs of a fungal infection, and then twice a week. PCT levels were determined by an immunochromilumiminent assay, and Candida and aspergillus antigen levels by ELISA.

In only five patients PCT indicated early signs of infection, albeit at barely detectable limits. Six patients, however, showed significantly increasing titres preceding time of death. Positive antigens titres were observed only in 10 patients who had proven or probable systemic fungosis. Only half of the control group had negative antigen titres; a high rate of false negatives was also observed. Both PCT and antigens titres increased in parallel in 4/6 patients with unfavorable outcome. PCT and antigens titres cannot reliably indicate early diagnosis of systemic fungal infections although may be used as a prognostic tool of severity.

Lactulose, a factor that decreases endotoxaemia, in obstructive jaundice? 

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Bacterial translocation is a process implicated in the pathogenesis of spontaneous peritonitis. In order to evaluate the impact of lactulose administration on systemic endotoxaemia, obstructive jaundice was induced in 11 rabbits by common bile duct ligation. Animals were divided into two groups, group A of five rabbits not receiving lactulose and group B of six rabbits, which received 1.5 ml/kg of lactulose orally by an oral catheter. Blood was collected daily, before and after operation for a total duration of four days. Samples were applied for culture and for determination of endotoxins (LPS) by the LAL QCL-1000 assay. Concentrations of LPS (mean \pm SD) of group A were 1.15 \pm 0.74, 2.24 \pm 0.74, 1.60 \pm 0.81 and 2.34 \pm 0.70 EU/ml on the 1st, 2nd, 3rd and 4th day, respectively. Respective concentrations of LPS (mean \pm SD) of group B were 0.84 \pm 0.28, 0.65 \pm 0.12, 0.81 \pm 0.20 and 0.60 \pm 0.42. All blood cultures were sterile in both groups. Differences...
between concentrations of LPS of the two groups were statistically significant on the 2nd and the 4th day (P < 0.05). It is concluded that the administration of lactulose may decrease systemic endotoxaemia in the field of obstructive jaundice.

Nosocomial infections: a prevalence study in the island of Crete PM263

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Prevalence surveillance is a rapid and inexpensive mode to estimate the problem of hospital-acquired infections (HAIs). To study the problem of nosocomial infections in our hospital, a prevalence study was made from our team in 1999. The study included 265 patients (the total number of hospitalized patients at the time of the study). From these patients 129 were males (49.0%) and 136 females (51.0%). One hundred and ninety-one patients (72.0%) belonged in the groups of age between 50 and 89 years. Fifty-seven patients had a urine catheter (22.3%). One hundred and fifty-five patients (58%) received antibiotics and from these 99 patients received one antibiotic and the remaining 56 patients two or more. A nosocomial infection was found in 13 patients and consequently the prevalence of HAIs was 5.0%. Among these, urinary tract infections were six (46.1%), lower respiratory tract infections were three (23.0%), surgical site infections were three (23.0%), and bloodstream infections was one (7.7%).

The incidence of multiresistant bacteria was primarily Enterococcus spp and secondary, Pseudomonas aeruginosa, Enterobacter spp, Klebsiella pneumoniae, Escherichia coli, Staphylococcus aureus, Enterobacter cloacae. Unfortunately prophylactic chemotherapy of long duration was found despite the suggestions of the infection control committee. Regarding age the highest incidence of HAIs occurred in the third age group.

Bloodstream infections (BSI) in patients with haematological malignancies (HM) PM264

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Objectives: To determine the pathogens and susceptibility to antimicrobials.

Methods: Blood samples were collected from 430 adult PTS (1997–2001). The bacteremic episodes were classified according to the definitions of the CDC. Laboratory detection of bacteremia and fungaemia was performed according to Cumitech 1B (Blood Cultures III. 1997). Susceptibility testing was performed by disk diffusion method (NCCLS).

Results: The total number of blood samples—1371, 249-positive (18.2% episodes of significant bacteremias). BSI was confirmed microbiologically in 137 of 430 febrile PTS (31.9%). The most frequent pathogens were Gram(+) cocci (62.7%) (P < 0.0001), gram(−) bacilli—22.7%, fungi—11.4%. Coagulase-negative staphylococci (CNS) represented 38.9%, Staphylococcus aureus 12.4%, Streptococcus spp. 4.9%, Enterococcus spp. 5.9%, Enterobacteriaceae 15.1%, Pseudomonas aeruginosa 3.2%, other non-fermenting—5.9%, yeast 8.1%, mould 3.2%, anaerobes 2.7%. One hundred percent CNS were resistant to penicillin, 68.4% to oxacillin, 36.6% to clindamycin, 39.5% to cefazolin, 80.3% to cefazidime, 48.7% to ciprofloxacin, 51.3% to gentamicin, and no isolate was resistant to vancomycin.

Conclusion: The predominant pathogens in all types of HM were Gram(+) cocci (mainly CNS). All Gram(+) microorganisms were sensitive to vancomycin.

Isolation of bacterial agents and study of their antibiotic susceptibility in hospitalized patients PM265

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This investigation was carried out in Odessa State Clinical Hospital during 2000–2001. Of the patients with post-operation complications, 60% of 518 Gram-negative cultures were sensitive to cefazidime and 72% to amikacin. Sixty-nine percent of 143 Gram-positive cultures were resistant to penicillin G, but they were sensitive to vancomycin and nitrofurantoin in 100 and 92% of cases, respectively. Sixty percent of 366 isolates of Pseudomonas aeruginosa were sensitive to ceftazidime and 71% to amikacin. Rates of resistance to carbencillin and gentamicin were 60 and 66%, respectively. One hundred and forty-three isolates of Escherichia coli were studied and 65% of them were resistant to ampicillin 67% to cephalothin and 70% to tetracycline. Of the isolates tested against ciprofloxacin, all were sensitive. One hundred and eight isolates of Staphylococcus aureus were studied and they were resistant only to penicillin G (69%). Staphylococcus aureus was sensitive to erythromycin (65%), tetracycline (65%), oxacillin (83%) and vancomycin (100%). All 34 isolates Enterococcus faecalis were sensitive to nitrofurantoin and 70% to ciprofloxacin. The majority of S. aureus and E. faecalis isolates were susceptible to most other antibiotics, but the majority of E. coli isolates were resistant to the studied antibiotics expect ciprofloxacin.

Campylobacter fetus bacteraemia in an immunocompromised patient: a case report PM266

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A 33-year-old woman was admitted for recurrent fever. The patient underwent a liver transplantation and splenectomy in 1985. She had followed immunosuppressive therapy until 1995 when tacrolimus was added for chronic rejection. In 1999 non-Hodgkin lymphoma was diagnosed and chemotherapy was started. Six months later because of the presence of two metastatic encephalic foci affecting the optic chiasm, a new chemotherapy course was started with the regression of lesions. In January 2000 she was treated with steroid recycle and cyclosporine–azathioprine–prednisone reintroduction. Fever occurred after 2 months and Cytomegalovirus (CMV) infection was diagnosed. Treatment with Ganciclovir was started with clinical remission. In November 2000 CMV infection recurred and blood cultures were positive for a bacterium that was identified as Campylobacter fetus. The patient was successfully treated with intravenous ciprofloxacin. Bacteremia frequently occurs in cancer patients. Bacteremia due to C. fetus are rare, occurring mainly in immunocompromised patients. C. fetus expresses a proteinaceous surface layer that confers serum resistance. In our patients steroid and immunosuppression may have contributed to the development of lymphoma. All of these factors and chemotherapy have contributed to CMV infection and all have made the patient susceptible to bacteremia with this infrequently found
bacterium. The clinical microbiologist should be aware of this infection in immunocompromised host.

Cefepime (CEP) versus ceftazidime (C) plus aminoglycosides (A) in the treatment of patients with fever and granulocytopenia  PM267

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C+A is the standard regimen as empirical therapy for febrile neutropenia (FN). Activity of C against g+ bacteria and g− bacteria, producing chromosomally-mediated b-lactamases (e.g. AmpC) is suboptimal. CEP is active against a broad range of g+ and g−, including AmpC producing bacteria. The purpose of the study was to compare the efficacy of two regimens in the treatment of FN.

Methods: Patients with FN received either CEP (2 g/8h) or C (2 g/8 h) plus Amikacin (15 mg/kg/day) or Netilmicin (5 mg/kg/day). Data were collected prospectively.

Results: A total of 35 pts with 41 episodes (35/41) of FN were included. Fifteen/19 in CEP group and 20/22 in C group. The median duration of neutropenia grade 4, distribution of age, sex and underlying disease were comparable in both arms. MDI was in 37 and 24%, CDI in 21 and 18% FUO in 57 and 63% in FEP and C+A groups correspondingly. Response to the initial empirical regimen according in the treatment of patients with febrile neutropenia (FN). Acti in 13.5%, Enterobacter spp. in 8.1%, Providencia spp. in 2.7%. Of the Klebsiella spp. isolates 25% were resistant to amikacin, 85% to cephalosporins, 87% to piperacillin/tazobactam. All were sensitive to imipenem. Of the A. baumannii isolates 100% were resistant to amikacin, aztreonam, cefepom, cefotaxime, ceftriaxone, piperacillin; 60% to ampicillin-sulbactam, 80% to ceftazidine, and 40% sensitivity to imipenem. The resistance rate of Providencia was 100% for all antibiotics.

Conclusion: A high level of resistance to antibiotics was observed in bacteria isolated from blood cultures in our hospital.

Antimicrobial activity of selected pharmacopoeial antiseptics analysed according to European standards  PM270

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PURPOSE: There are some substances described in Pharmacopoeias, which might be used as antiseptics for skin disinfection. European Committee for Standardisation approved several European Standards (EN), describing test methods establishing, whether an antiseptic has or does not have a bactericidal or fungicidal activity under the laboratory conditions defined by EN. The aim of the study was to investigate, if some chemical compounds in concentrations recommended by Polish Pharmacopoeia for skin disinfection comply European Standards requirements.

Methods: Basic bactericidal (EN 1040) and fungicidal (EN 1275) activity were investigated as well as bactericidal activity of products for hygienic and surgical handrub and hand wash used in human medicine (prEN 12054). All methods and used neutralizers were validated. Standard strains: Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, E. herae, Candida albicans and A. niger were used, when EN standards were evaluated. Results: Ethanol, isopropanol and n-propanol caused viable microbial count reduction required by ENs in pharmacopoeial concentrations. Benzalkonium chloride 0.1%, benzoic acid 0.1%, chloramine 1%, resorcin 3%, hydrogen peroxide 3%, showed to be effective antiseptics. Boric acid 6%—in double pharmacopoeial concentration, showed biocidal activity. Chlorhexidine digluconate 0.1 and 0.2% was effective against bacteria and fungi, respectively. Potassium permanganate 0.1% was fungicidal while 1.6% bactericidal.