patients with new onset of fever, demographic, clinical, and laboratory variables were obtained during the 2 days after inclusion, while microbiological results for a follow-up period of 7 days were collected. Patients were followed up for survival or death, up to a maximum of 28 days after inclusion. MEASUREMENTS AND RESULTS: Of all patients, 95% had SIRS, 44% had sepsis with a microbiologically confirmed infection, and 9% died. A model with a set of variables all significantly ($p<0.01$) contributing to the prediction of mortality was derived. The set included the presence of hospital-acquired fever, the peak respiratory rate, the nadir score on the Glasgow coma scale, and the nadir albumin plasma level within the first 2 days after inclusion. This set of variables predicted mortality for febrile patients with microbiologically confirmed infection even better. The predictive values for mortality of SIRS and sepsis were less than that of our set of variables. CONCLUSIONS: In comparison to SIRS and sepsis, the new set of variables predicted mortality better for all patients with fever and also for those with microbiologically confirmed infection only. This type of effort may help in refining definitions of SIRS and sepsis, based on prognostically important demographic, clinical, and laboratory variables that are easily obtainable at the bedside.

Bottger E.C. *[Mycobacteria and mycobacterioses].* Pneumologie. 1995; 49 Suppl 3 : 636-42.p Abstract: The genus Mycobacterium harbours a number of significant pathogens. The diagnosis of mycobacterial infections has traditionally relied on microscopical and cultural techniques which were compromised by the slow growth of these microorganisms. More recently, molecular methods suitable for use in diagnostic microbiology have been developed and have been demonstrated to significantly improve both our diagnostic capabilities as well as our understanding of this complex genus of microorganisms.

Bouam S. et al. *Development of a Web-based clinical information system for surveillance of multiresistant organisms and nosocomial infections.* Proc AMIA Symp. 1999; 696-700.p Abstract: To optimize the surveillance and control of infections at our hospital, we have developed a clinical information system (CIS) linked to a server providing three kinds of patient-oriented data reports: 1/an automated alert for multiresistant bacteria from a data-driven mechanism; 2/the relevant data for surveillance of hospital-acquired infections; 3/some clinical and educational data for antibiotic prescribing. The new CIS is a Web-based one and now integrated to the Hospital Information System (HIS). In a close collaboration with the experts, we have, first, specified the relevant information for each report. Then, we have linked the system to those HIS DBs containing this information. Finally we have developed a well-secured intranet Web site, on which the concerned practitioners can instantaneously review the latest alerts and/or the summarized/detailed reports. The preliminary results shows that the system is reliable in medical practice and the response time is satisfying.

Bouanchaud D.H. *In-vitro and in-vivo antibacterial activity of quinupristin/dalfopristin.* J Antimicrob Chemother. 1997; 39 Suppl A : 15-21.p Abstract: Quinupristin/dalfopristin is a new water-soluble streptogramin antimicrobial agent comprising quinupristin and dalfopristin in a ratio of 30:70. The in-vitro spectrum of activity includes most multi-resistant Gram-positive aerobes, important Gram-negative aerobes, Gram-positive anaerobes and intracellular bacteria that are causal agents of respiratory, blood and cutaneous infections. Of particular note, quinupristin/dalfopristin is active against multidrug-resistant isolates of Staphylococcus aureus, Staphylococcus epidermidis and Enterococcus faecium, and against penicillin-resistant and/or erythromycin-resistant Streptococcus pneumoniae. The combination is also active against staphylococci showing both constitutive and inducible erythromycin resistance. Bactericidal activity and a prolonged post-antibiotic effect have also been noted for quinupristin/dalfopristin against Gram-positive cocci. Gram-negative bacteria susceptible to quinupristin/dalfopristin include Moraxella catarrhalis, Legionella spp. and Mycoplasma spp. Overall, the spectrum of antibacterial activity indicates a potential role for this combination in the treatment of difficult-to-treat Gram-positive infections, including those caused by multidrug-resistant organisms. Since this activity extends to Gram-negative respiratory bacteria, quinupristin/dalfopristin may also find a role in the treatment of atypical, as well as typical, pneumonia.

Boubaker A. et al. *[Investigation of the urinary tract in children in nuclear medicine].* Rev Med Suisse Romande. 2000; 120(3) : 251-7.p Abstract: The early detection of urologic abnormalities by antenatal sonography has resulted in the investigation of many infants and neonates for suspicion of either obstructive uropathy or reflux nephropathy. Nuclear medicine techniques allow to assess renal parenchyma integrity, to detect pyelonephritic scars and to measure absolute and relative renal function; these methods are easy to perform and reproducible, without any sedation, repeated venous punctures or bladder catheterization. Furthermore, the use of dynamic tubular tracers and frusemide test is a very usefull method which can differentiate between upper and/or lower urinary tract obstruction and determine the degree of obstruction (severe or incomplete) in order to plan for surgery or conservative treatment. The detection of vesicoureteric reflux may be difficult as it is an intermittent phenomenon: the use of the indirect radionuclide cystography (IRC), that is to say after completion of a dynamic renography, allows to detect reflux with a high sensitivity because images can be recorded continuously until the child voids, without any bladder catheterization and at low radiation dosis. In case of discordant results between micturating cysto-urethrography and IRC or of concomittant obstructive uropathy, the direct radionuclide cystography (DRC) is indicated for appropriate treatment. Nuclear medicine techniques do not give morphological information about the urinary tract and should be considered as complementary to radiological investigations in first evaluation of children with recurrent urinary tract infections or hydronephrosis.

Boucher B.A. *Role of aztreonam in the treatment of nosocomial pneumonia in the critically ill surgical patient.* Am J Surg. 2000; 179(2A Suppl) : 45S-50S.p Abstract: In 1995 the American Thoracic Society issued an official consensus statement on the treatment of hospital-acquired pneumonia (HAP). Classes of antimicrobials included in the list of antimicrobials deemed to be suitable for the empiric treatment of severe HAP were the aminoglycosides, quinolones, antipseudomonal penicillins, carbapenems, and beta-lactam/beta-lactamase inhibitor combinations. Aztreonam, a monobactam, was also listed and is unique among these agents based on its spectrum of activity being limited to the gram-negative bacillary bacteria combined with an excellent safety profile. This review focuses on the role of aztreonam in the treatment of nosocomial pneumonia in the critically ill patient. A review of the literature was performed using PubMed and secondary literature sources as to the clinical efficacy of aztreonam in the treatment of lower respiratory tract infections as well as its pharmacokinetic and safety profiles. An analysis of aztreonam's potential pharmacoeconomic advantages compared with other agents was also performed. Numerous studies have documented that aztreonam has effectiveness that is equal or superior to that of other suitable antibiotics in the treatment of nosocomial pneumonia. Its excellent safety profile makes it a particularly attractive agent compared with the aminoglycosides. Considering the potential costs of bacterial resistance from the use of broader-spectrum alternatives, a case can be made that aztreonam is a pharmacoeconomically sound choice as well.

Boulesteix J. et al. *Acute otitis media in children: a study of nasopharyngeal carriage of potential pathogens and therapeutic efficacy of cefixime and amoxicillin-clavulanate.* Infection. 1995; 23 Suppl 2 : S79-82.p Abstract: We conducted a large, multicenter, randomized, open-label study throughout France comparing the efficacy and safety of cefixime suspension (8 mg/kg/day, b.i.d., for 10 days) versus amoxicillin-clavulanate suspension (80 mg/kg/day, t.i.d., for 10 days) in 510 chil-

dren (ages 6 to 36 months) with acute otitis media. The most frequent microorganisms colonizing the nasopharynx at the start of treatment were Streptococcus pneumoniae (51.5%), Haemophilus influenzae (45%) and Moraxella catarrhalis (30.2%). Rates of beta-lactamase positivity were 32.1% and 95.3% for H. influenzae and M. catarrhalis, respectively. Decreased susceptibility of S. pneumoniae to penicillin was found in 39.7% of isolates. Clinical efficacy was 87.8% (223/254) for cefixime and 87.0% (215/247) for amoxicillin-clavulanate. At the 5-week follow-up visit, relapse had occurred in 15.7% (31/197) of cefixime-treated patients and in 15.6% (32/205) of those treated with amoxicillin-clavulanate. We conclude that these two regimens are equally effective in acute otitis media in children.

Bouletreau A. et al. *Comparison of effectiveness and required time of two surveillance methods in intensive care patients.* J Hosp Infect. 1999; 41(4) : 281-9.p Abstract: The intensive care unit (ICU) standardized protocol of the NNIS (National Nosocomial Infections Surveillance) system is a surveillance method of hospital acquired infections (HAI), which provides device-associated infection rates. The aim of this study was to assess the effectiveness and the required time for data collection and analysis of a selective surveillance method (SSM) derived from the NNIS ICU surveillance protocol, and to compare its data with that of a reference surveillance method (RSM). The sensitivity, specificity and the positive predictive value (PPV) of the RSM were 87.5, 100 and 100%, respectively. The sensitivity, specificity and the PPV of the SSM were 59.4 97.6 and 79.2%, respectively. Considering device-related infections only (ventilator-related pneumonia, catheter-related urinary tract infections, central line-related sepsis), the sensitivities of the RSM and the SSM were 80.9 and 90.5%, respectively. The SSM required only one third of the time of the RSM (1.1 h and 3.4 h per 10 beds per week with the SSM and the RSM, respectively). We conclude that the SSM has a very high sensitivity for detecting device associated infections, but is not sensitive enough for surveying all types of HAI.

Bourbeau P. et al. *Use of the BacT/Alert blood culture system for culture of sterile body fluids other than blood.* J Clin Microbiol. 1998; 36(11) : 3273-7.p Abstract: Studies have demonstrated that large-volume culture methods for sterile body fluids other than blood increase recovery compared to traditional plated-medium methods. BacT/Alert is a fully automated blood culture system for detecting bacteremia and fungemia. In this study, we compared culture in BacT/Alert standard aerobic and anaerobic bottles, BacT/Alert FAN aerobic and FAN anaerobic bottles, and culture on routine media for six specimen types, i.e., continuous ambulatory peritoneal dialysate (CAPD), peritoneal, amniotic, pericardial, synovial, and pleural fluids. Specimen volumes were divided equally among the three arms of the study. A total of 1,157 specimens were tested, with 227 significant isolates recovered from 193 specimens. Recovery by method was as follows: standard bottles, 186 of 227 (82%); FAN bottles, 217 of 227 (96%); and routine culture, 184 of 227 (81%). The FAN bottles recovered significantly more gram-positive cocci ($P < 0.001$), Staphylococcus aureus ($P = 0.003$), coagulase-negative staphylococci ($P = 0.008$), gram-negative bacilli ($P < 0.001$), Enterobacteriaceae ($P = 0.005$), and total organisms ($P < 0.001$) than the routine culture. There were no significant differences in recovery between the standard bottles and the routine culture. The FAN aerobic bottle recovered significantly more gram-positive cocci ($P < 0.001$), S. aureus isolates ($P < 0.001$), coagulase-negative staphylococci ($P = 0.003$), and total organisms ($P < 0.001$) than the standard aerobic bottle, while the FAN anaerobic bottle recovered significantly more gram-positive cocci ($P < 0.001$), S. aureus isolates ($P < 0.001$), Enterobacteriaceae ($P = 0.03$), and total organisms ($P < 0.001$) than the standard anaerobic bottle. For specific specimen types, significantly more isolates were recovered from the FAN bottles compared to the routine culture for synovial ($P < 0.001$) and CAPD ($P = 0.004$) fluids. Overall, the FAN bottles were superior in performance to both the standard bottles and the routine culture for detection of microorganisms from the types of sterile body fluids included in this study.

Bourgault A.M. et al. *Update on Pan-American activities in the field of anaerobes: Canada.* Clin Infect Dis. 1997; 25 Suppl 2 : S237-40.p Abstract: During the past 15 years, important contributions have been made to the field of anaerobes in Canada. Studies on the importance of the intestinal flora as a source of vitamin K for humans, investigations of the mechanisms of synergy in polymicrobial infections, and extensive research on the field of immunocompetence of surgical patients have provided interesting and valuable information. Several clinical and epidemiological studies of anaerobic infections have been carried out. Rapid methods have been developed for the identification and susceptibility testing of clinical isolates. National and regional surveys have been conducted on the susceptibility patterns of the Bacteroides fragilis group. Studies on the mechanism of action of metronidazole and on the mechanisms of resistance of Bacteroides species have also been carried out. The Canadian Infectious. Disease Society has published position papers on therapy with cefotetan, ceftizoxime, and imipenem and on antimicrobial prophylaxis in surgical patients.

Bourget P. et al. *Clinical pharmacokinetics of piperacillin-tazobactam combination in patients with major burns and signs of infection.* Antimicrob Agents Chemother. 1996; 40(1) : 139-45.p Abstract: The pathophysiology associated with major burns is complex and subject to a state of flux. The combination of beta-lactamase inhibitors with powerful penicillins is an interesting and an attractive potential solution to the emergence of bacterial resistance. The kinetics in serum and urine and the clinical safety of a fixed combination of 4 g of piperacillin (PPR) and 0.5 g of tazobactam (TZB) were studied in 10 patients (22 to 50 years old and weighing 45 to 105 kg) with major burns who were infected with Pseudomonas aeruginosa and various entero-bacteria. All of them received additional antimicrobial drugs. Treatment involved one dose every 6 h. The mean body surface area affected by third-degree burns was 30.0% +/- 4.0%. The study took place in accordance with current ethical guidelines. Two series of blood samples were drawn after the first (day 1) and ninth (day 3 at steady state) doses; urine was collected during the same periods. Levels of PPR and TZB in serum and urine were measured by high-pressure liquid chromatography. A noncompartmental method was used for kinetic and graphic analysis of concentration-time pairs. The safety of the treatment was excellent. There was no systemic accumulation of the beta-lactam combination. Residual concentrations measured on days 1 and 3 [mean (standard error of the mean)] were above the MIC for the organism responsible for infection; i.e., C(min)day1 = 26.3 (8.5) and C(min)day3 = 21.0 (9.1) for PPR and C(min)day1 = 1.9 (0.6) and C(min)day3 = 1.4 (0.3) for TZB. There was no statistically significant difference between pharmacokinetic parameters determined for day 1 and day 3. Evidence was found in burn patients, in contrast to healthy subjects, of a marked increase in apparent volumes of distribution, in such a way that the apparent elimination half-lives of the combination were notably prolonged, i.e., 1.8 (0.3) versus 1.5 (0.3) h for PPR in patients and healthy subjects, respectively, and 1.7 (0.3) versus 1.4 (0.3) h for TZB. These findings indicate the possibility of nonrenal translesional diffusion of PPR-TZB in burn patients. The polarity of the association would further support this hypothesis. It has been shown here that the recommended dosage regimen for administration of PPR-TZB must be high in major-burn patients, i.e., 4 g/0.5 g every 6 h. The data obtained provide valuable information, which is suitable for immediate application in everyday clinical practice.

Bower C.K. et al. *Protein antimicrobial barriers to bacterial adhesion.* J Dairy Sci. 1998; 81(10) : 2771-8.p Abstract: The ability of microorganisms to adhere to solid surfaces is a problem of high visibility and has been the focus of numerous investigations because these organisms can cause disease and food spoilage. During the last several years, considerable attention has been focused on the development of food-grade antimicrobial barriers to adhesion in order to inhibit the

initial adhesion of microbial contaminants by application of an antimicrobial agent to the surface rather than trying to remove these contaminants once they are adhered. The premise is that, if both the presence of the agent and its antimicrobial activity are maintained at the interface, sensitive bacterial cells or spores that attempt to attach would be killed. Nisin has been used in foods as a direct additive to inhibit the growth of Gram-positive cells and spores. Similarly, hen lysozyme is a commercially available antimicrobial protein that offers application in food processing systems, but the mode of action of this enzyme differs from that of nisin. We have shown that nisin can adsorb to surfaces, maintain activity, and kill cells that have adhered. In addition, we have addressed questions relating to the short- and long-term stability of adsorbed nisin, the degree to which immobilized nisin can resist exchange with dissolved solution components, and the surface concentrations that are necessary to inhibit biofilm formation. More recently, we have focused on basic questions relating to molecular influences on antimicrobial activity at interfaces using synthetic mutants of bacteriophage T4 lysozyme and hen lysozyme in addition to nisin.

Bowler P.G. et al. *The microbiology of infected and noninfected leg ulcers.* Int J Dermatol. 1999; 38(8) : 573-8.p Abstract: BACKGROUND: A clinical study was undertaken to investigate and compare specifically the aerobic and anaerobic microbiology of infected and noninfected leg ulcers. METHODS: Leg ulcers, defined as being infected on the basis of clinical signs, were swab sampled and investigated for aerobic and anaerobic microorganisms using stringent isolation and identification techniques. RESULTS: Two hundred and twenty isolates were cultured from 44 infected leg ulcers, in comparison with 110 isolates from 30 noninfected leg ulcers. Statistical analysis indicated a significantly greater mean number of anaerobic bacteria per infected ulcer (particularly Peptostreptococcus spp. and Prevotella spp.) in comparison with the noninfected ulcer group (2.5 vs. 1.3, respectively) ($P < 0.05$). Also, anaerobes represented 49% of the total microbial composition in infected leg ulcers compared with 36% in noninfected leg ulcers. The mean numbers of aerobes per wound in the two ulcer groups were not statistically different ($P > 0.05$). The study failed to demonstrate a clear correlation between commonly implicated facultative pathogens and wound infection. The isolation rate of Pseudomonas aeruginosa was generally low and, although Staphylococcus aureus was a frequent isolate in both wound types, it was more prevalent in noninfected leg ulcers. CONCLUSIONS: This study has demonstrated the complex aerobic-anaerobic microflora which exists in leg ulcers, the prevalence of anaerobes in infected wounds, and a poor correlation between the presence of specific aerobic pathogens and wound infection. In view of these findings, the role of microbial synergistic interactions in the pathogenesis of chronic wound infection may be of greater clinical importance than the isolated involvement of any specific potential pathogen.

Boyanova L. et al. *Primary and combined resistance to four antimicrobial agents in Helicobacter pylori in Sofia, Bulgaria*. J Med Microbiol. 2000; 49(5) : 415-8.p Abstract: The aim of this study was to evaluate the primary and combined resistance of Helicobacter pylori against four antimicrobial agents by a screening agar method (SAM) and a modified disk diffusion method (MDDM) alone and in combination. Pre-treatment H. pylori isolates from 192 consecutive H. pylori-positive patients at three hospitals in Sofia were investigated. MDDM was performed with disks containing metronidazole (5 microg), clarithromycin (15 microg) or erythromycin (15 microg), ciprofloxacin (5 microg) and tetracycline (30 microg). Resistance was determined by an inhibitory zone of <16 mm for metronidazole and < or =30 mm for other agents tested. The cut-off concentrations used to define resistance by SAM were: metronidazole >8 mg/L, clarithromycin >2 mg/L, tetracycline >4 mg/L and ciprofloxacin >1 mg/L. Primary resistance rates in H. pylori were: metronidazole 28.6%, clarithromycin 9.7%, metronidazole + clarithromycin 2.8%, ciprofloxacin 3.9%, metronidazole + ciprofloxacin 2.3%, tetracycline 1.9% and metronidazole + tetracycline 1.2%. Among metronidazole-resistant isolates, combined resistance to clarithromycin, ciprofloxacin and tetracycline was present in 11.4% (5 of 44 strains), 8.3% (3 of 36) and 4.9% (2 of 41), respectively. Two strains exhibited triple resistance to macrolides, metronidazole and either ciprofloxacin or tetracycline. Three tetracycline-resistant strains were detected in 1999; however, resistance rates to other agents were relatively stable during the 6 years. Primary H. pylori resistance to metronidazole is moderate and resistance to clarithromycin and to ciprofloxacin is considerable in comparison with results in most other countries. The alarming appearance of strains harbouring combined resistance or multiresistance provides the motivation for continued surveillance of H. pylori at global, national and regional levels.

Boyce S.T. et al. *Cytotoxicity testing of topical antimicrobial agents on human keratinocytes and fibroblasts for cultured skin grafts.* J Burn Care Rehabil. 1995; 16(2 Pt 1) : 97-103.p Abstract: Cultured epidermal skin has become an adjunctive therapy for treatment of major burn injuries, but its effectiveness is greatly limited because of destruction by microbial contamination. To evaluate candidate antimicrobial agents for use with cultured skin, a combined cytotoxicity-antimicrobial assay system was developed for determination of toxicity to cultured human keratinocytes and fibroblasts and for determination of susceptibility or resistance of common burn wound organisms. Candidate agents including chlorhexidine gluconate, polymyxin B, mupirocin, sparfloxacin, or nitrofurazone were tested separately for inhibition of growth of human cells and for inhibitory activity to microorganisms with the wet disk assay. The data showed that (1) chlorhexidine gluconate (0.05%) was uniformly toxic to both cultured human cells and microorganisms; (2) nitrofurazone (0.02%) had dose-dependent toxicity to human cells and limited effectiveness against gram-negative microorganisms; (3) sparfloxacin (30 micrograms/ml) had low toxicity to human cells and retained antimicrobial activity against both gram-positive and gram-negative bacteria; (4) polymyxin B (400 U/ml) was not toxic to human cells and had intermediate effectiveness on gram-negative bacteria; and (5) mupirocin (48 micrograms/ml) had no toxicity to skin cells and had uniform effectiveness against Staphylococcus aureus including methicillin-resistant Staphylococcus aureus. Selection of topical antimicrobial drugs by these assays may improve effectiveness of cultured skin for burns and may be used to control other surgical wound infections.

Bozdogan B. et al. *Effects of genes encoding resistance to streptogramins A and B on the activity of quinupristin-dalfopristin against Enterococcus faecium*. Antimicrob Agents Chemother. 1999; 43(11) : 2720-5.p Abstract: Quinupristin-dalfopristin is a streptogramin combination active against multiply resistant Enterococcus faecium. Among 45 E. faecium isolated from patients in various French hospitals, only two strains were intermediate (MIC = 2 microgram/ml) and one, E. faecium HM1032, was resistant (MIC = 16 microgram/ml) to quinupristin-dalfopristin, according to British Society for Antimicrobial Chemotherapy and National Committee for Clinical Laboratory Standards approved breakpoints. The latter strain contained the vgb and satA genes responsible for hydrolysis or acetylation of quinupristin and dalfopristin, respectively, and an ermB gene (also previously referred to as ermAM) encoding a ribosomal methylase. The two intermediate strains had an LS(A) phenotype characterized by resistance to lincomycin (L), increased MICs (>/=8 microgram/ml) of dalfopristin (streptogramin A [S(A)]), and susceptibility to erythromycin and quinupristin. This phenotype was also detected in eight other strains susceptible to quinupristin-dalfopristin. No genes already known and conferring resistance to dalfopristin by acetylation or active efflux were detected in these LS(A) strains. Nineteen other strains resistant to erythromycin but susceptible to the quinupristin-dalfopristin combination displayed elevated MICs of quinupristin after induction (from 16 to >128 microgram/ml) and contained ermB genes. The effects of ermB, vgb, and satA genes on the activity of the streptogramin combination were tested by cloning

these genes individually or in various combinations in recipient strains susceptible to quinupristin-dalfopristin, E. faecium HM1070 and Staphylococcus aureus RN4220. The presence of both the satA and vgb genes (regardless of the presence of an ermB gene) was necessary to confer full quinupristin-dalfopristin resistance to the host. The same genetic constructs were introduced into E. faecium BM4107 which displays a LS(A) phenotype. Addition of the satA or vgb gene to this LS(A) background conferred resistance to quinupristin-dalfopristin.

Bradley J.S. et al. *Carbapenems in clinical practice: a guide to their use in serious infection*. Int J Antimicrob Agents. 1999; 11(2) : 93-100.p Abstract: Meropenem and imipenem/cilastatin, currently the only available carbapenem agents in Europe and the United States, are characterised by a broad spectrum of antimicrobial activity and stability to beta-lactamase-mediated resistance mechanisms. A guide to the use of carbapenems in clinical practice is presented; the role of carbapenems in the treatment of several types of serious bacterial infection and an up-to-date account of their clinical efficacy and safety profiles are discussed. The good clinical efficacy and favourable safety profiles of the carbapenems make them valuable as initial empirical therapy in the treatment of ventilator-associated pneumonia, sepsis of unknown origin, post-operative peritonitis, paediatric meningitis, and febrile neutropenia. However, to maintain superior efficacy, the carbapenems should be used appropriately for definitive therapy.

Brady J.P. et al. *Vancomycin-resistant enterococcus in end-stage renal disease.* Am J Kidney Dis. 1998; 32(3) : 415-8.p Abstract: The percentage of nosocomial vancomycin-resistant enterococci (VRE) has been increasing rapidly in the United States. This has recently resulted in recommendations to reserve vancomycin use for cases with proven resistance to other antimicrobials. We prospectively investigated the incidence of VRE in our dialysis population and compared it with a control group of 40 clinic patients with chronic renal insufficiency (CRI) who had a serum creatinine level greater than 1.5 mg/dL, but were not undergoing dialysis. The incidence of VRE on our campus is almost 10%, which is similar to US data. We studied 50 chronic hemodialysis (HD) patients and 50 peritoneal dialysis (PD) patients. Each patient had a rectal swab test performed and cultured for the presence of enterococci. Antimicrobial exposures over the 6 months before the initial swab test were reviewed in each patient. At least one repeated swab test was performed in 30 CRI, 45 HD, and 37 PD patients. From the initial swab culture, vancomycin-sensitive enterococci (VSE) were isolated in 65% of CRI, 54% of HD, and 70% of PD patients. No CRI or HD patients had VRE isolated and 2% (1 of 50) of PD patients had VRE isolated. The remaining patients had no enterococci isolated. Review of antimicrobial exposures in the 6 months before the initial swab test showed 0% of CRI, 32% of HD, and 36% of PD patients received vancomycin. Other antimicrobials were administered to 40% of CRI, 46% of HD, and 78% of PD patients in the same time period. In the month immediately preceding the initial swab test, 0% of CRI, 12% of HD, and 22% of PD patients received vancomycin and 18% of CRI, 20% of HD, and 36% of PD patients received other antimicrobials. Results from repeated cultures showed that 57% of CRI, 40% of HD, and 38% of PD patients changed their culture status related to VSE, VRE, or no enterococci present. Cultures of 342 swabs from 140 patients yielded three VRE isolates in two patients. We conclude that despite the frequent use of vancomycin and other antimicrobials, the incidence of VRE in our renal population is less than the reported incidence. Given this lack of VRE isolates, we recommend the continued judicious use of vancomycin in treating renal patients and continued enterococcal sensitivity surveillance.

Brakstad O.G. et al. *Mechanisms of methicillin resistance in staphylococci*. APMIS. 1997; 105(4) : 264-76.p Abstract: The continuously high prevalence of methicillin-resistant staphylococci (MRS) throughout the world is a constant threat to public health, owing to the multiresistant characteristics of these bacteria. Methicillin resistance is phenotypically associated with the presence of the penicillin-binding protein 2a (PBP2a) not present in susceptible staphylococci. This protein has a low binding affinity for beta-lactam antibiotics. It is a transpeptidase which may take over cell wall synthesis during antibiotic treatment when normally occurring PBPs are inactivated by ligating beta-lactams. PBP2a is encoded by the mecA gene, which is located in mec, a foreign DNA region. Expression of PBP2a is regulated by proteins encoded by the plasmid-borne blaR1-bla1 inducer-repressor system and the corresponding genomic mecRl-mecl system. The blaRl-blal products are important both for the regulation of beta-lactamase and for mecA expression. Methicillin resistance is influenced by a number of additional factors, e.g. the products of the chromosomal fem genes which are important in the synthesis of normal peptidoglycan precursor molecules. Inactivation of fem-genes results in structurally deficient precursors which are not accepted as cell wall building blocks by the ligating PBP2a transpeptidase during antibiotic treatment. This may result in reduced resistance to beta-lactam antibiotics. Inactivation of genes affecting autolysis has shown that autolytic enzymes are also of importance in the expression of methicillin resistance. Methicillin resistance has evolved among earth microorganisms for protection against exogenous or endogenous antibiotics. Presumably the mec region was originally transferred from coagulase negative staphylococci (CNS) to Staphylococcus aureus (SA). A single or a few events of this kind with little subsequent interspecies transfer had been anticipated. However, recent data suggest a continuous horizontal acquisition by S. aureus of mec, being unidirectional from CNS to SA. Methicillin resistance may also be associated with mechanisms independent of mecA, resulting in borderline methicillin resistance. These mechanisms include beta-lactamase hyperproduction, production of methicillinases, acquisition of structurally modified normal PBPs, or the appearance of small colony variants of SA. Most MRS are multiresistant, and the mec region may harbour several resistance determinants, resulting in a clustering of resistance genes within this region.

Brandileone M.C. et al. *Prevalence of serotypes and antimicrobial resistance of streptococcus pneumoniae strains isolated from Brazilian children with invasive infections. Pneumococcal Study Group in Brazil for the SIREVA Project. Regional System for Vaccines in Latin America.* Microb Drug Resist. 1997; 3(2) : 141-6.p Abstract : A laboratory surveillance study was developed in Brazil in 1993 to determine capsular types and antimicrobial susceptibility of Streptococcus pneumoniae strains. By studying 360 strains isolated from children with invasive infections in three different cities, 8 out of 34 types were identified as being the most prevalent and considered as the reference group for further analyses. This group comprised 77.7% of all strains studied, and includes the types 1, 5, 6A/B, 9V, 14, 19F, 19A, and 23F. The prevalence of this reference group was significantly higher among strains isolated from children with pneumonia than meningitis. Similarly, this group was more prevalent among strains isolated from children 3 to 6 years of age than from children under 2 years of age. Most strains (78.6%) were found to be susceptible to penicillin and only 1.4% showed high resistance to this antibiotic. However, intermediate resistance to penicillin was detected in 20% of the strains. This laboratory surveillance will be maintained and extended to other cities of Brazil to better define and monitor the trends of pneumococcal infections for proper control and prevention.

Brandtzaeg P. et al. *The leucocyte protein L1 (calprotectin): a putative nonspecific defence factor at epithelial surfaces.* Adv Exp Med Biol. 1995; 371A : 201-6.p Abstract: The L1 protein occurs at high concentrations in neutrophils, monocytes, certain reactive tissue macrophages, squamous mucosal epithelia, and reactive epidermis. It constitutes in fact about 60% of the neutrophilic cytosol protein fraction. The two L1 chains (L1H and L1L) are referred to by a bewildering collection of names, various authors having different preferences (MRP-8 and MRP-14; CFA or calgranulin A and B).

The most recent proposal is calprotectin because of its calcium-binding properties and antimicrobial effect shown in vitro. L1 belongs to the S-100 protein family and may be involved in the regulation of keratinocyte proliferation and differentiation. It exists at high levels in blood and interstitial tissue fluid in several infectious, inflammatory, and malignant disorders, and it is released abundantly in foci of granulocytes and macrophages. The C-terminal sequence of the L1H chain has been shown to be identical to the N-terminus of peptides known as neutrophil immobilizing factors. Such an activity of L1 could be important for the accumulation of vital granulocytes, while L1 released from neutrophils, macrophages and epithelial cells might exert antimicrobial activity, perhaps by depriving microorganisms of zinc. The minimum inhibitory concentrations of L1 in vitro were found to be 4-32 mg/l for Candida albicans, 64 mg/l for Staphylococcus aureus, 64-256 mg/l for S. epidermidis, and 256 mg/ml for Escherichia coli and Klebsiella spp. Killing was observed at 2-4 times higher concentrations. In patients with HIV infection, those who developed oral candidiasis had significantly lower parotid L1 levels than those who did not (67 micrograms/l vs. 216 micrograms/l).

Brauner J.S. et al. *Circulating endothelin-1 and tumor necrosis factor-alpha: early predictors of mortality in patients with septic shock*. Intensive Care Med. 2000; 26(3) : 305-13.p Abstract: OBJECTIVES: To determine the predictive value of early determination of tumor necrosis factor (TNF)-alpha, TNF-alpha 1 and 2 soluble receptors (sTNFR1 and sTNFR2) and endothelin-1 (ET-1) for mortality in patients with septic shock. DESIGN: Prospective study. SETTING: Intensive care unit of a university hospital. PATIENTS: Twenty-one patients with septic shock. INTERVENTIONS: None. MEASUREMENTS AND RESULTS: Patients with septic shock had a pulmonary artery catheter inserted and blood samples drawn at time zero, 6, 12 and 24 h, simultaneously with hemodynamic assessments. Plasma levels of all markers were measured by ELISA. All patients were followed up to hospital discharge or death. Age and APACHE II scores were significantly higher in nonsurvivors (n = 11) than in survivors (n = 10). Hemodynamic assessments did not aid in the discrimination between the two groups of patients ($P > 0.05$). Levels of TNF-alpha were higher in nonsurvivors than in survivors at all time-points. sTNFR1 and sTNFR2 were also significantly elevated in nonsurvivors, but not in all measurements. Endothelin-1, however, was significantly higher in nonsurvivors than in survivors only at 6 h ($P = 0.02$). When both TNF-alpha and ET-1 were increased at early time-points, the best predictive values for mortality were obtained [positive and negative predictive values of 72 and 100% at 6 h, odds ratio 3.0, 95% CI (1.2-7.6)]. CONCLUSIONS: Increased levels of TNF-alpha were consistently higher at all time-points in nonsurvivors with septic shock. ET-1 levels, however, appeared also to be an early and sensitive predictor of mortality. Very early determination of TNF-alpha and ET-1 in septic shock may help to identify patients at higher risk for adverse outcome.

Breneman D.L. et al. *The effect of antibacterial soap with 1.5% triclocarban on Staphylococcus aureus in patients with atopic dermatitis.* Cutis. 2000; 66(4) : 296-300.p Abstract: This double-blind study determined whether daily bathing with an antibacterial soap would reduce the number of Staphylococcus aureus on the skin and result in clinical improvement of atopic dermatitis. For 9 weeks, 50 patients with moderately severe atopic dermatitis bathed daily with either an antimicrobial soap containing 1.5% triclocarban or the placebo soap. They also used a nonmedicated moisturizer and 0.025% triamcinolone acetonide cream as needed, but the availability of the corticosteroid cream was discontinued after 6 weeks. The antimicrobial soap regimen caused significantly greater improvement in the severity and extent of skin lesions than the placebo soap regimen, which correlated with reductions both in S aureus in patients with positive cultures at baseline and in total aerobic organisms. Outcome measures included reductions in S aureus, total aerobic organisms, and dermatologic assessments. Overall, daily bathing with an antibacterial soap was well tolerated, provided clinical improvement, and reduced levels of skin microorganisms.

Brennand G.L.P.B. et al. *Resistência a drogas e produção de bacteriocinas em linhagens de Escherichia coli e Enterobacter isoladas de indivíduos hospitalizados.* J. bras. patol. 1999; 35(2) : 86-9.p Abstract: Escherichia coli e Enterobacter foram isolados de grupos de indivíduos hospitalizados (H), recém-hospitalizados (P), sendo estudados quanto ao perfil de resistência às drogas ampicilina, cefalotina, cloranfenicol, estreptomicina, tetraciclina, gentamicina, canamicina e ao bicloreto de mercúrio, por meio da técnica de diluição em meio sólido, e quanto à produção de colicinas. A resistência aos antibióticos betalact*f*micos foi maior nas amostras isoladas dos grupos de portadores não-hospitalizados (P) (modelo ampicilina-cefalosporina), em especial para o gênero Enterobacter. Por outro lado, a freqüencia das amostras colicinogênicas descresceu no grupo H em comparação com amostras colicinogênicas decresceu no grupo H em comparação com as amostras do grupo P. provável que, em ambientes seletivos pela presença de elevadas concentraçöes de antibióticos, as linhagens portadoras de fenótipos sejam selecionadas e a colicinogênese, deslocada ou substituída, sendo mantida em ambientes não-seletivos, devido à competitividade as linhagens de uma mesma espécie (AU).

Brennen C. et al. *Vancomycin-resistant Enterococcus faecium in a long-term care facility.* J Am Geriatr Soc. 1998; 46(2) : 157-60.p Abstract: OBJECTIVE: To describe the epidemiology and natural history of colonization with vancomycin-resistant Enterococcus faecium (VREF) in a long-term care facility. DESIGN: All patients in whom VREF was isolated were followed prospectively, with rectal swab cultures at 2-week intervals, until discharge, death, or clearance of VREF. Clearance was defined as two consecutive negative cultures. In addition, three prevalence surveys were conducted of all patients in residence on one 34-bed intermediate care ward. SETTING: A 400-bed, long-term care Veterans Affairs facility. PARTICIPANTS: Thirty-six patients colonized with VREF. RESULTS: Vancomycin-resistant Enterococcus faecium was identified in 24 of the 36 patients at the time of transfer from an acute care facility. Seventeen patients had concomitant methicillin-resistant Staphylococcus aureus, and seven patients had a recent history of Clostridium difficile-associated diarrhea. VREF in these patients persisted for a median of 67 days after identification. Treatment of VREF colonization with antimicrobials was associated with prolongation of colonization. Serial surveillance of the 34-bed ward found stable rates of colonization, with only three documented instances of VREF acquisition. During 2.5 years of surveillance for infection, a single case of bacteremia occurred in a patient in whom colonization with VREF could not be demonstrated by rectal swab culture. No infections occurred in patients colonized with VREF. CONCLUSIONS: Long-term care patients have protracted carriage of VREF. Most will improve over time; however, receipt of antimicrobial therapy is associated with prolongation of VREF carriage. The risk of VREF infection is low in this population. When there are appropriate contact precautions, patient to patient transmission occurs at a low rate. These observations can be used to design a practical infection control strategy for long-term care facilities.

Breschan C. et al. *Anaesthetic management of liver haemorrhage during laparotomy in a premature infant with necrotizing enterocolitis.* Paediatr Anaesth. 2000; 10(4) : 425-8.p Abstract: The case of a 680 g premature baby who developed massive spontaneous liver haemorrhage during laparotomy for necrotizing enterocolitis is reported. The infant survived due to rapid and massive fluid administration, including transfusion of large volumes of blood and blood products, in combination with high dose inotropic support and the surgical use of packing with thrombostatic sponges. Good venous access, including two central venous lines, turned out to be very useful.

Brett M.S. *Antimicrobial resistances among Shigella in New Zealand*. N Z Med J. 1998; 111(1068) : 234-5.p Abstract: AIM: To determine the prevalence of antimicrobial resistances among recent isolates of Shigella in New Zealand. METHOD: A total of 107 Shigella isolates referred to the Institute of Environmental Science and Research from 20 hospital and community laboratories between January and June 1996 were tested by an agar dilution method. RESULTS: Shigella sonnei accounted for 70% of the isolates and S flexneri for 23%. Resistance to ampicillin and cotrimoxazole was detected in 42% and 57% of the isolates respectively, and combined ampicillin and co-trimoxazole resistance occurred in 30.8% of the isolates. The prevalence of cephalothin resistance was 5.6%. Resistance to cefotaxime, ciprofloxacid and gentamicin was not detected and 31.8% were sensitive to all agents tested. Ampicillin resistance was significantly more prevalent in S flexneri than S sonnei. CONCLUSIONS: The high prevalence of ampicillin and cotrimoxazole resistance indicates that ampicillin and cotrimoxazole are no longer useful for empirical treatment of shigellosis in New Zealand. The findings indicate a need to monitor the prevalence of antimicrobial resistances among Shigella and suggest that antimicrobial susceptibility testing might be needed to guide antimicrobial therapy.

Brett M.S. et al. *A significant increase in antimicrobial resistance among pneumococci causing invasive disease in New Zealand*. N Z Med J. 1999; 112(1085) : 113-5.p Abstract: AIMS: To review the prevalence of antibiotic resistance and the distribution of capsular types among pneumococci from invasive disease in New Zealand from 1995 through 1997. METHOD: Pneumococci isolated from sterile sites that were referred to the Institute of Environmental Science and Research (ESR) were tested for antimicrobial susceptibility and capsular type. RESULTS: A total of 994 pneumococci were referred by 27 hospital and community laboratories. Almost 74% of the isolates were from patients aged < 15 years or > or = 60 years. The majority (88.2%) of the isolates were from blood cultures. In 1997, cefotaxime-resistant pneumococci were confirmed for the first time from invasive disease in New Zealand. Over the three years, 6.0% of the pneumococci were penicillin-nonsusceptible (MIC > or = 0.12 mg/L) and 3.7% were cefotaxime-nonsusceptible (MIC > or = 1 mg/L). Penicillin nonsusceptibility increased significantly from 1.9% in 1995 to 6.2% in 1996 and 9.9% in 1997. Similarly, cefotaxime nonsusceptibility increased from 0.6% in 1995 to 3.5% in 1996 and 6.9% in 1997. In descending order of frequency, the ten most common capsular types were 14, 19, 6, 9, 1, 4, 18, 7, 23, and 3. Eighty-three percent of the penicillin-nonsusceptible pneumococci belonged to serotypes 9V, 19A, 19F, 23F, 14 and 6B and 90% belonged to serotypes included in the 23-valent vaccine. CONCLUSIONS: The increasing prevalence of antimicrobial resistance among pneumococci highlights the need for continued surveillance and for effective measures to prevent pneumococcal infections.

Breuer T. et al. *Costs of diagnosis and treatment of Helicobacter pylori infection: when does choosing the treatment regimen based on susceptibility testing become cost effective?* Am J Gastroenterol. 1999; 94(3) : 725-9.p Abstract: OBJECTIVE: Antibiotic-resistant Helicobacter pylori (H. pylori) strains are becoming increasingly prevalent. Currently, most physicians treat H. pylori infections without relying on antimicrobial susceptibility testing to choose the best regimen. This study was conducted to evaluate whether routine pretreatment susceptibility testing is cost effective from a third party payer point of view. METHODS: A decision model was devised to compare direct costs and outcome for diagnosis and treatment over 1 year for two different strategies. Strategy A: Endoscopy plus biopsy followed by an empirical antibiotic treatment of H. pylori-positive ulcer patients. Treatment failure was followed by reendoscopy with biopsy and antibiotic susceptibility testing and a second treatment. Strategy B: Endoscopy as in strategy A now followed by antibiotic susceptibility testing and tailored antibiotic treatment. Treatment failure was handled as in strategy A. RESULTS: Following through with strategy A or B, the overall cure rate for both strategies was virtually identical. Therefore, cost effectiveness is defined as money saved per patient by using strategy B, while achieving similar effectiveness (cure rates). As an example we compared therapies for a population with known parameters for antibiotic resistance as well as cure rates. Pretreatment susceptibility testing would save $37,000 per 1,000 patients treated. According to our model (equal therapy-price assumption in strategy A and B), pretreatment susceptibility testing for metronidazole is less costly for all the reported populations worldwide. CONCLUSIONS: Our decision analysis suggests that routine pretreatment susceptibility testing can be cost effective under various settings. The model presented is easily transferable to any population as long as the following variables are known: 1) the proportion of H. pylori strains in the population that are resistant to the antibiotics of the initial regimen; 2) the cure rate in sensitive H. pylori strains; 3) the cure rate in resistant H. pylori strains; and 4) the costs for diagnosis and treatment used.

Breuer T. et al. *Clarithromycin, amoxycillin and H2-receptor antagonist therapy for Helicobacter pylori peptic ulcer disease in Korea*. Aliment Pharmacol Ther. 1997; 11(5) : 939-42.p Abstract: BACKGROUND: Effective anti-Helicobacter pylori therapies with few side-effects are needed. We previously showed that the regimen of amoxycillin, clarithromycin and an H2-receptor antagonist was effective in the United States. The current study tested whether this therapy would also be successful in Korea. METHODS: Patients with gastric or duodenal ulcers received amoxycillin (750 mg t.d.s.) plus clarithromycin (500 mg t.d.s.) for 2 weeks and nizatidine 300 mg at bedtime for 6 weeks. Endoscopic examinations were performed before treatment and 4 or more weeks after ending antimicrobial therapy. H. pylori status was confirmed by rapid urease testing and histological examination of gastric antrum and corpus biopsies using the Genta stain. Antibiotic resistance was tested using the E-test method. Cure was defined as no evidence of H. pylori infection 4 or more weeks after ending therapy. RESULTS: Seventy-two patients (59 males and 13 females; mean age 46 years), including 35 with duodenal ulcers, 30 with gastric ulcers and seven with both, were studied. H. pylori infection was cured in 95.8% (69/72 patients; 95% CI = 88.3-99.1%). Two of the treatment failures had culture data and one had pre-treatment resistance to clarithromycin. Smoking did not have an adverse effect on therapy. Ten patients (15%) developed side-effects during treatment, but all were mild and did not require treatment interruption. No case of reinfection was noted during follow-up. CONCLUSION: The combination of amoxycillin, clarithromycin and an H2-receptor antagonist is effective in Korean patients with H. pylori infection.

Breuer T. et al. *Successful low-dose amoxycillin, metronidazole and omeprazole combination therapy in a population with a high frequency of metronidazole-resistant Helicobacter pylori*. Aliment Pharmacol Ther. 1997; 11(3) : 523-7.p Abstract: AIM: Effective anti-Helicobacter pylori therapies with few side-effects are needed. We studied the effectiveness of a low-dose combination of metronidazole, amoxycillin and omeprazole for treatment of ulcer patients in Seoul, Korea. METHODS: Patients with gastric or duodenal ulcer received metronidazole (125 mg b.d.), amoxycillin (500 mg b.d.) and omeprazole (20 mg at bedtime) for 2 weeks. Endoscopic examinations were performed before treatment and at least 6 weeks after completion of antimicrobial therapy. H. pylori status was confirmed by histological examination of two gastric biopsies using the Genta stain. RESULTS: Seventy-nine patients (64 men, 15 women, mean age 46 years) with peptic ulcer were enrolled. H. pylori infection was cured in 56 (71%) 95% CI: 60-81%). The cure rate in non-smokers was significantly higher than in smokers (88% vs. 65%, P = 0.035). Twelve pre-treatment isolates were available and metronidazole resistance was noted in all; H. pylori infection was cured in 10. Thirty-six patients cured of H. pylori have been followed for 1 year (mean of 361 days) and 2 cases became reinfected (5.5%, 95% CI: 1-18%). CONCLUSIONS: The low-dose combination of metronidazole, amoxycillin and omeprazole was effective even the in face of metronidazole resistance.

Recurrence of H. pylori infection is infrequent even in countries with a high prevalence of H. pylori infection.

Brewster J.D. et al. *Immunoelectrochemical assays for bacteria: use of epifluorescence microscopy and rapid-scan electrochemical techniques in development of an assay for Salmonella.* Anal Chem. 1996; 68(23) : 4153-9.p Abstract: Immunoelectrochemical sensors in which the sensor surface functions as both analyte capture phase and electrochemical detector have recently been developed for bacteria analysis. The speed and sensitivity of these devices make them very attractive for applications such as the detection of pathogenic microorganisms in food and water. However, the development and optimization of assays utilizing these sensors can be complicated by undesired interactions between the capture and detection functions. Modification of the sensor to achieve improvements in one function can have deleterious effects on the other function, and such effects can be difficult to diagnose and correct. In the course of investigations on immunoelectrochemical detection of Salmonella, we developed a rapid, nondestructive epifluorescence microscopy method to determine bacteria capture efficiency. This method enabled us to study capture and detection functions independently and efficiently identify performance-limiting factors. Rapid-scan electrochemical methods were used to optimize detection sensitivity and to provide diagnostic information on detection performance.

Bridger J.C. *A study of nurses' views about the prevention of nosocomial urinary tract infections.* J Clin Nurs. 1997; 6(5) : 379-87.p Abstract: This study sought to discover the contribution of nursing practice to the prevention of hospital-acquired or nosocomial urinary tract infections (NUTIs), the most commonly occurring nosocomial infection. Seventy-five per cent of such infections are associated with urethral catheters. The practices of nurses who are caring for patients on a 24 h basis would appear to be fundamental to achieving any reduction in the incidence of NUTIs. This qualitative study utilized unstructured interviews to explore the views of 12 registered nurses about three key issues: first, what care do nurses give with the aim of preventing catheter-associated NUTIs; secondly, what improvements in practice would further prevent catheter-associated NUTIs; thirdly, what do nurses see as constraints to the prevention of catheter-associated NUTIs? The nurses identified many of the measures that were cited in the literature as effective for preventing NUTIs; however in reality, they stated that their practice differed because of a lack of time to give care and to update themselves. The consequences of under-staffing were that junior and temporary staff (whose competence in preventing NUTIs was questioned) worked unsupervised. Those interviewed identified feelings of powerlessness in effecting preventative measures, and identified not only the role of medical staff in influencing NUTIs but also their inconsistent approach to care. All these forces effectively limited the nurses' ability to prevent NUTIs. The study is concluded with recommendations for changes in practice and further research.

Briedigkeit H. et al. *[Anaerobic bacteria as the cause of endogenous infections].* Z Arztl Fortbild Qualitatssich. 1997; 91(2) : 165-70.p Abstract: Most mucocutaneous surfaces of humans harbor a rich indigenous microbial flora with predominance of anaerobes. Anaerobic infections are usually endogenous indicating that they originate from the host's own flora. Important exceptions are botulism, tetanus, food poisoning by Clostridium perfringens, some cases of gas gangrene and cases of hospital-acquired C. difficile-induced diarrhea. Endogenous anaerobic infections often occur in adjacent to the mucosal surfaces. Other organs are infected by penetration or hematogenous spread. A predisposing condition to anaerobic infections is a low redox potential resulting from tissue destruction, foreign bodies, malignancy or vascular insufficiency. A mixed anaerobic-aerobic infection is often found in abscesses or tissue necrosis. Antimicrobial therapy must take into account that anaerobic infections are often associated with aerobic bacteria.

Brodie S.B. et al. *Occurrence of nosocomial bloodstream infections in six neonatal intensive care units.* Pediatr Infect Dis J. 2000; 19(1) : 56-65.p Abstract: BACKGROUND: Nosocomial bloodstream infections (NBSIs) occur frequently in neonatal intensive care units (NICUs) and are associated with substantial morbidity and mortality. Little has been published regarding variation in NBSI among institutions. OBJECTIVE: To determine NBSI incidence among six NICUs and to explore how much variation is explained by patient characteristics and NICU practice patterns. METHODS: From October, 1994, to June, 1996, six regional NICUs prospectively abstracted clinical records of all neonates weighing <1,500 g. Occurrence of NBSI, defined as first positive culture occurring >48 h after admission, was analyzed in relation to baseline patient characteristics and several common therapeutic interventions. Variables significant in univariate analyses were analyzed by Cox proportional hazards regression. RESULTS: There were 258 NBSIs (incidence, 19.1%) among 1,354 inborn first admissions. Incidence varied significantly by site, from 8.5 to 42%. Birth weight, Broviac catheter use and parenteral nutrition were significantly associated with NBSI ($P < 0.05$). When controlling for these variables interinstitutional variation in NBSI occurrence decreased but remained significant. CONCLUSIONS: Neonatal NBSI incidence varies substantially among institutions despite adjustment for length of stay and some known risk factors. The uses of Broviac catheters and especially intravenous nutrition supplements were significant determinants of NBSI risk.

Brook I. *Anaerobic infections in children.* Adv Pediatr. 2000; 47 : 395-437.p Abstract : Anaerobic bacteria commonly cause infection in children. Anaerobes are the most predominant components of the normal human skin and mucous membrane bacterial flora, and are therefore a common cause of bacterial infections of endogenous origin. Because of their fastidious nature, they are difficult to isolate from infectious sites and are often overlooked. Anaerobic infections can occur in all body sites, including the central nervous system, oral cavity, head and neck, chest, abdomen, pelvis, skin, and soft tissues. Anaerobic bacteria colonize the newborn after delivery and have been recovered from several types of neonatal infections. These include cellulitis of the site of fetal monitoring, neonatal aspiration pneumonia, bacteremia, conjunctivitis, omphalitis, and infant botulism. The lack of directing adequate therapy against these organisms may lead to clinical failures. Their isolation requires appropriate methods of collection, transportation, and cultivation of specimens. Treatment of anaerobic infection is complicated by the slow growth of these organisms, by their polymicrobial nature, and by the growing resistance of anaerobic bacteria to antimicrobials. Antimicrobial therapy is often the only form of therapy required, whereas in other cases it is an important adjunct to a surgical approach. Because anaerobic bacteria generally are recovered mixed with aerobic organisms, the choice of appropriate antimicrobial agents should provide for adequate coverage of both types of pathogens.

Brook I. *Bacterial flora of stethoscopes' earpieces and otitis externa.* Ann Otol Rhinol Laryngol. 1997; 106(9) : 751-2.p Abstract: External otitis caused by Staphylococcus aureus was observed in a nurse after extensive use of a stethoscope. The infection recurred and a similar organism was isolated from the stethoscope's earpiece. The infection did not recur after the earpiece was cleansed after each use. In a prospective study, the bacterial flora of 35 earpieces was evaluated. Fifty-three isolates, 36 aerobic or facultative and 17 anaerobic, were recovered. The number of organisms per earpiece ranged from 14 to 204 (average 92 +/- 17). The predominant isolates were Staphylococcus epidermidis (16 isolates), Propionibacterium acnes (12), and Saureus (7). The study demonstrates the colonization of the stethoscope's earpiece with microorganisms that possess the potential for causing nosocomial infection.

Brook I. et al. *Aerobic and anaerobic microbiology of chronic venous ulcers.* Int J Dermatol. 1998; 37(6) : 426-8.p Abstract: BACKGROUND: The role of bacteria in the pathogenesis of chronic venous leg ulcers

(CVLU) is unclear. The objective of the study was to establish the aerobic and anaerobic bacteriology of CVLU. METHODS: A retrospective review was carried out of the clinical and microbiological laboratory records obtained from patients with CVLU. Microorganisms were grown from 43 specimens obtained from 41 patients. RESULTS: Aerobic or facultative bacteria alone were present in 18 (42%) specimens, anaerobic bacteria only in three (7%), and mixed aerobic-anaerobic flora in 22 (51%). In total, there were 97 isolates, 64 aerobic or facultative and 33 anaerobic, an average of 2.3 isolates per specimen (1.5 aerobes and 0.8 anaerobes). The predominant aerobic organisms were Staphylococcus aureus (26 isolates), group D streptococci (5), and Escherichia coli(5). The predominant anaerobes were Peptostreptococcus spp. (15), Bacteroides fragilis group (6), Propionibacterium acnes (4), and Prevotella spp. (3). CONCLUSIONS: CVLU have a polymicrobial aerobic-anaerobic flora.

Brook I. et al. *Microbiology of cervical lymphadenitis in adults.* Acta Otolaryngol. 1998; 118(3) : 443-6.p Abstract: The microbiology of needle aspirates from 40 inflamed cervical lymph glands was studied for aerobic and anaerobic bacteria, fungi and mycobacteria. Forty-two bacterial, 11 mycobacterial and six fungal isolates were isolated. Aerobic bacteria only were recovered in 11 (27.5%), anaerobes alone in five (12.5%) and mixed aerobic and anaerobic bacteria in seven (17.5%). Mycobacterium sp. were recovered in 11 (27.5%) and fungi in six (15%). The recovery of anaerobes was associated with dental infection. Eighteen aerobic bacteria were isolated and the predominant ones were Staphylococcus aureus (eight isolates) and group A streptococci (four). Twenty-four anaerobic bacteria were recovered and the predominant ones were: Prevotella sp. (six), Peptostreptococcus sp. (five), Propionibacterium acnes (four) and Fusobacterium sp. (three). These findings demonstrate the role of anaerobic organisms in cervical lymphadenitis and the need to culture aspirated material from the glands for both aerobic and anaerobic microorganisms.

Brook I. et al. *Microbiology of the transition from acute to chronic maxillary sinusitis.* J Med Microbiol. 1996; 45(5) : 372-5.p Abstract: Repeated aspirations of sinus secretions by endoscopy was performed in five patients over a period of 34-50 days and, ultimately, surgical drainage was done in three who presented with acute maxillary sinusitis that did not respond to antimicrobial therapy and became chronic. The aspirates were cultured for aerobic and anaerobic bacteria. Most of the bacteria isolated from the first culture were aerobic or facultative bacteria: Streptococcus pneumoniae (three isolates), Haemophilus influenzae non-type-b (two) and Moraxella catarrhalis (one). Three of these cultures yielded bacteria that were resistant to the antimicrobial agents prescribed for treatment. Failure to respond to therapy was associated with the emergence of resistant aerobic and anaerobic bacteria in subsequent aspirates. These organisms included Fusobacterium nucleatum, pigmented Prevotella and Porphyromonas spp. and Peptostreptococcus spp. Eradication of the infection was achieved in all instances following the administration of antimicrobial agents effective against these bacteria, and in three instances by surgical drainage. This study illustrates the microbial dynamics of maxillary sinusitis that did not respond to antimicrobial therapy.

Brook I. et al. *Bacterial colonization of pacifiers of infants with acute otitis media.* J Laryngol Otol. 1997; 111(7) : 614-5.p Abstract: The presence of aerobic and facultative anaerobic bacteria on the surface of pacifiers used by children with acute otitis media was investigated. The surface of 40 recently used pacifiers was swabbed after they were allowed to dry for five to six minutes. The swabs were processed quantitatively for the presence of aerobic bacteria. The antibacterial activity of the pacifier material was tested in vitro. Microorganisms were isolated from 21 (52.5 per cent) pacifiers. The number of colonies per pacifier varied between one and 35 (average six). The isolates included eight alpha-haemolytic streptococci, six Staphylococcus epidermis, five Candida albicans, five alpha-haemolytic streptococci, three Neisseria spp. and two Staphylococcus aureus. The pacifier material was shown to be inhibitory against S. aureus. This study illustrated that pacifiers do not contain high numbers of organisms and therefore are not likely to serve as a source of persistence of transfer of organisms.

Brook I. et al. *Microbiologic characteristics of persistent otitis media.* Arch Otolaryngol Head Neck Surg. 1998; 124(12) : 1350-2.p Abstract: OBJECTIVE: To identify the pathogens isolated from children with acute otitis media who did not respond to antimicrobial drug therapy. METHODS: Retrospective analysis of cultures obtained by tympanocentesis from 46 children. RESULTS: Organisms were recovered from 34 children (74%), and 43 isolates were recovered from these individuals. The organisms were Streptococcus pneumoniae (16 isolates), Haemophilus influenzae non-type b (12 isolates), Moraxella catarrhalis (5 isolates), Streptococcus pyogenes (5 isolates), Staphylococcus aureus (3 isolates), and Peptostreptococcus species (2 isolates). Resistance to the antimicrobial agent used was found in 27 (63%) of 43 isolates found in 22 patients (48%). Of patients who did not respond to amoxicillin therapy, H influenzae predominated. Streptococcus pneumoniae was recovered from 5 (56%) of 9 of those who did not respond to trimethoprim and sulfamethoxazole therapy, 4 (44%) of 9 patients after azithromycin therapy, 3 (25%) of 12 patients after amoxicillin therapy, and 2 (40%) of 5 patients after cefixime therapy. Streptococcus pyogenes was recovered from 2 (40%) of 5 patients after trimethoprim and sulfamethoxazole therapy and from 2 (40%) of 5 patients after cefixime therapy. CONCLUSIONS: The data illustrate the relation between resistance to antimicrobial drug therapy and failure of patients with otitis media to improve. They also highlight the importance of diagnostic tympanocentesis in establishing the presence of resistant microorganisms.

Brook I. et al. *Resistance to antimicrobials used for therapy of otitis media and sinusitis: effect of previous antimicrobial therapy and smoking.* Ann Otol Rhinol Laryngol. 1999; 108(7 Pt 1) : 645-7.p Abstract: We undertook to identify the antimicrobial susceptibility of the pathogens isolated from patients with otitis media or maxillary sinusitis who failed to respond to antimicrobial therapy, and correlate it with previous antimicrobial therapy and smoking. We analyzed isolates recovered from 2 consecutive cultures obtained from middle ear aspirate obtained through an open perforation in 22 children with otitis, and maxillary sinus aspirate collected by endoscopy from 20 patients. Forty-seven isolates were repeatedly recovered from 42 culture-positive individuals. The organisms isolated were Streptococcus pneumoniae (15 isolates), Haemophilus influenzae (14), Staphylococcus aureus (7), Moraxella catarrhalis (6), and Streptococcus pyogenes (5). Resistance of at least 2 tube dilutions to the antimicrobial agents used was found in 23 of the 47 (49%) isolates that were found in 20 (48%) of the patients. These included 10 of 15 (67%) isolates of S pneumoniae, 4 of 14 (29%) H influenzae (all were beta-lactamase producers), 4 of 7 (57%) S aureus (all beta-lactamase producers), 5 of 6 (83%) M catarrhalis (all beta-lactamase producers), and none of 5 S pyogenes. In the 21 patients who failed to respond to amoxicillin, H influenzae and S pneumoniae predominated. Streptococcus pneumoniae was recovered from 4 of the 11 (36%) after trimethoprim-sulfamethoxazole, 4 of 21 (19%) after amoxicillin, 2 of 3 (67%) after azithromycin dihydrate, and 1 of 4 (25%) after cefixime. A statistically significant higher recovery of resistant organisms was noted in those treated 2 to 6 months previously, and in those with sinusitis who smoked. The data illustrate the relationship between resistance to antimicrobials and failure of patients with otitis media and sinusitis to improve.

Brook I. et al. *Antimicrobial management of chronic sinusitis in children.* J Laryngol Otol. 1995; 109(12) : 1159-62.p Abstract: This study retrospectively investigated the microbiology and management of 40 children who suffered from chronic sinusitis. The sinuses infected were the maxillary (15 cases), ethmoid (13), and frontal (seven).

Pansinusitis was present in five patients. All aspirates were cultured for aerobic and anaerobic bacteria. A total of 121 isolates (97 anaerobic and 24 aerobic) were recovered. Anaerobes were recovered from all 37 culture-positive specimens, and in 14 cases (38 per cent) they were mixed with aerobes. Twenty-three beta-lactamase-producing bacteria were isolated from 16 (43 per cent) patients. The 15 patients who received clindamycin had the most rapid response to therapy and a change of therapy and surgical drainage was required in one case. Of the 16 patients who received amoxycillin or ampicillin, 16 responded to therapy, six needed a change of therapy, including four who also had surgical drainage. Of the six who were treated with erythromycin, three needed antibiotic change, two with surgical drainage. Of the three that received cefaclor, two were cured, and one had an antibiotic change. Resistant organisms were recovered in all the cases that required therapeutic change. These findings support the important role of anaerobic bacteria in the polymicrobial cause of chronic sinusitis in children, and the superiority of therapy effective against these organisms.

Broskey J. et al. *Efflux and target mutations as quinolone resistance mechanisms in clinical isolates of Streptococcus pneumoniae.* J Antimicrob Chemother. 2000; 45 Suppl 1 : 95-9.p Abstract: The aim of this study was to characterize quinolone resistance mechanisms in strains of Streptococcus pneumoniae with increased MICs of ofloxacin. These strains were also tested for their susceptibility to a battery of quinolone antimicrobial agents, including gemifloxacin. Of the S. pneumoniae isolates used, 27 were susceptible to ofloxacin, 18 intermediate and 48 resistant (ofloxacin MIC <4, 4 and >4 mg/L, respectively). In general, the ofloxacin-susceptible strains had no amino acid substitutions in GyrA, GyrB, ParC or ParE. Moderate increases in MIC were associated with substitutions in the quinolone resistance-determining region (QRDR) of ParC, while the highest MICs were found for strains that also had substitutions in the QRDR of GyrA. The most common substitutions were Ser79—>Phe in ParC and Ser81—>Phe in GyrA. Other substitutions were identified within the QRDR of ParC and outside the QRDR of ParC and ParE; these did not appear to affect susceptibility. The effects of antimicrobial efflux pumps were studied by determining MICs of a range of quinolones in the presence and absence of reserpine, an inhibitor of Gram-positive efflux pumps. Our results indicated that high-level resistance, caused entirely by efflux, was seen in a minority of ofloxacin-resistant S. pneumoniae strains. Testing the susceptibility of quinolone-resistant strains to gemifloxacin, ciprofloxacin, norfloxacin, ofloxacin and trovafloxacin revealed that gemifloxacin was least affected by this large variety of resistance mechanisms and was the only quinolone with MICs of < or =0.5 mg/L for all strains in this study. These results suggest that gemifloxacin is highly potent against S. pneumoniae and may also be effective against strains resistant to other quinolones.

Brown P.D. et al. *Community-acquired pneumonia.* Lancet. 1998; 352(9136) : 1295-302.p Abstract: This seminar reviews the aetiology, clinical presentation, approach to diagnosis, and management of immunocompetent adults with community-acquired pneumonia (CAP). Pneumonia is a common clinical entity, particularly among the elderly. A thorough understanding of the epidemiology and microbiology of CAP is essential for appropriate diagnosis and management. Although the microbiology of CAP has remained relatively stable over the last decade, there is new information on the incidence of atypical pathogens, particularly in patients not admitted to hospital, and new information on the incidence of pathogens in cases of severe CAP and in CAP in the elderly. Recent studies have provided new data on risk factors for mortality in CAP, which can assist the clinician in decisions about the need for hospital admission. The emergence of antimicrobial resistance in Streptococcus pneumoniae, the organism responsible for most cases of CAP, has greatly affected the approach to therapy, especially in those patients who are treated empirically. Guidelines for the therapy of CAP have been published by the American Thoracic Society, the British Thoracic Society, and, most recently, the Infectious Diseases Society of America. These guidelines differ in their emphasis on empirical versus pathogenic-specific management.

Bruchhaus J.D. et al. *Hospital-acquired pneumonia: recent advances in diagnosis, microbiology and treatment.* Curr Opin Pulm Med. 1998; 4(3) : 180-4.p Abstract: Nosocomial or hospital-acquired pneumonia occurs frequently, despite preventative measures and advances in diagnostic procedures and treatment of this severe infection. This article will highlight the recent literature with emphasis on significant publications and advances in the area of pneumonia pathogenesis, microbiology, diagnosis, and response to antimicrobial therapy.

Brulez H.F. et al. *The efficacy of intraperitoneally administered gentamicin and rifampin as initial treatment of peritoneal dialysis-related peritonitis.* Adv Perit Dial. 1995; 11 : 182-6.p Abstract: For the initial treatment of peritonitis complicating peritoneal dialysis (PD), we use intraperitoneally administered gentamicin (broad spectrum and low costs) and rifampin (intracellular bactericidal activity). In order to assess the efficacy of this treatment, the outcome of 248 suspected episodes of peritonitis (abdominal pain, cloudy effluent, and a leukocyte count over 100/mm3) was evaluated. Of 227 cases with a positive culture of the PD effluent, one bacterial species was cultured in 188 cases (75.8%), more than one in 32 cases (12.9%), and in 7 cases (2.8%) yeasts. In 87.2% of the culture-positive cases, a good clinical response to the initialized antibiotic therapy was found. In 20 cases (8.1%) antibiotic treatment was discontinued within one week because no micro-organisms were cultured. In one case no effluent was cultured. Although in vitro resistance or indifference to both antibiotics was found in 45 cases (19.8%), in only 29 culture-positive cases (12.8%) the clinical condition did not improve on initial therapy. Of the peritonitis episodes in which micro-organisms resistant to both antibiotics were cultured, 23 were Staphylococcus epidermidis, 5 were E. coli, 7 were yeasts, and there were miscellaneous (mostly enteral) bacteria in 10 cases. In the studied period no significant changes were found in the susceptibility of the cultured microorganisms to gentamicin and rifampin. Susceptibility profile per episode, however, showed an increasing resistance against both antibiotics. It is concluded that the combination of gentamicin and rifampin as initial treatment of peritonitis is effective in most (87%) cases. (ABSTRACT TRUNCATED AT 250 WORDS).

Brumfield C.G. et al. *Puerperal infection after cesarean delivery: evaluation of a standardized protocol.* Am J Obstet Gynecol. 2000; 182(5) : 1147-51.p Abstract: OBJECTIVE: Our goal was to evaluate an antibiotic protocol for treatment of postcesarean endometritis. STUDY DESIGN: Endometritis was diagnosed as a persistent fever > or =100.4 degrees F beyond 24 hours after cesarean delivery and one or more of the following: uterine tenderness, tachycardia, foul lochia, or leukocytosis. Antibiotic therapy included gentamicin plus clindamycin and ampicillin (or vancomycin) as a triple antimicrobial in 148 women. Antibiotic failure was defined as persistent fever after 5 days of antibiotics and 72 hours of triple antibiotics. RESULTS: Between 1993 and 1996, 322 of 1643 (20%) women were diagnosed with postcesarean endometritis. One hundred seventy-four patients (54%) were cured with clindamycin-gentamicin, and 129 who additionally received ampicillin or vancomycin (40%) were cured. Nineteen of the 322 (6%) women had persistent fever despite triple antibiotics. Of these, 6 had a wound complication, 12 were suspected to have antimicrobial resistance, and 1 had an infected hematoma. CONCLUSION: A prospective protocol consisting of clindamycin-gentamicin plus the selective addition of ampicillin or vancomycin cured 303 of 322 (94%) women with postcesarean endometritis.

Brunello F. et al. *Reliability of the MB/BacT system for testing susceptibility of Mycobacterium tuberculosis complex isolates to antituberculous drugs.* J Clin Microbiol. 2000; 38(2) : 872-3.p Abstract: The susceptibility of 115 Mycobacterium tuberculosis complex clinical isolates to isoniazid, streptomycin, ethambutol, and rifampin was assessed by the

MB/BacT and BACTEC 460TB systems. The correlation between the two tests was 98.3% for isoniazid, 100% for streptomycin and rifampin, and 95.8% for ethambutol. Turnaround times for antimicrobial susceptibility testing ranged from 5 to 11 days (median, 8.5 days) for MB/BacT and from 4 to 8 days (median, 6 days) for BACTEC 460TB.

Bryce E.A. et al. *Focused microbiological surveillance and gram-negative beta-lactamase—mediated resistance in an intensive care unit.* Infect Control Hosp Epidemiol. 1995; 16(6) : 331-4.p Abstract: OBJECTIVE: To evaluate the use of focused surveillance in following resistance patterns within an intensive care unit (ICU). DESIGN: Antibiograms of 167 gram-negative isolates from ICU patients were compared to the hospitalwide antibiograms. ICU isolates were examined for the newer forms of beta-lactamase resistance. An outbreak of multiresistant Pseudomonas aeruginosa during the survey illustrated the usefulness of focused surveillance in early intervention and containment. SETTING: A 700-bed adult tertiary care hospital with a 16-bed medical and surgical ICU. RESULTS: Hospitalwide and ICU antibiograms of the Enterobacteriaceae were similar. However, resistance of P aeruginosa in the ICU was underestimated by hospitalwide rates. Susceptibility of ICU isolates to ceftazidime, ciprofloxacin, and piperacillin was 54%, 54%, and 42%, compared with 81%, 77%, and 85%, respectively, in the hospital at large. Thirty-five percent of isolates exhibited one of the newer forms of beta-lactamase-mediated resistance, with 17% of isolates exhibiting Class I cephalosporinase production. CONCLUSION: Targeted survey of high antibiotic-use hospital units should be used to study bacterial epidemiology, rather than relying on general hospital data to evaluate patterns of antimicrobial resistance. Monitoring of potential problem areas leads to prompt identification of changes in resistance and allows early intervention.

Bryl M. et al. *[Carrier status of Staphylococcus aureus among students of different courses].* Przegl Epidemiol. 1995; 49(1-2) : 17-21.p Abstract: Staphylococcus aureus is a frequent pathogen of nosocomial infections. The main part in the spread of these microorganisms take symptomless carriers. The aim the research was defining the carrierstate of S. aureus among students of Medical Academy and University. The investigation showed a greater carrierstate in the group of Medical students (33%) than in the group of University students. Strains isolated from the Medical students were more differentiated in biochemical tests and they were more drug-resistant mainly to Augmentin (51.5% resistant strains) and doxycycline (24% resistant strains). A great percentage of ampicillin-resistant strains (94%) was found among the strains isolated from both groups. Results of the research showed greater carrierstate among people who had direct contact with patients and infectious materials and proved a wide range of drug-resistance among hospital strains. Carriers of S. aureus among medical personnel could influence the spreading of nosocomial infections mainly on ICU and Newborn Wards.

Buchholz S. et al. *[Tubercular psoas abscess].* Dtsch Med Wochenschr. 2000; 125(28-29) : 866-8.p Abstract: HISTORY AND ADMISSION FINDINGS: A 43-year-old patient suffered from fatigue, nocturnal sweating, rigor and a weight loss of 5 kg over the last 4 weeks. A year before he had been anaemic and he was treated with omeprazole and iron. On admission physical examination was unremarkable, except for the known swelling in the right flank. His general condition was good. INVESTIGATIONS: Computed tomography showed an extensive abscess of the right psoas muscle with deplacement of the right ureter, causing hydronephrosis, and infiltration of the abdominal wall. Cytological and bacteriological tests of the abscess aspirate indicated tuberculosis. TREATMENT AND COURSE: The abscess markedly shrank within 2 months of starting antituberculosis treatment, which was continued for another 4 months. A catheter, which had been inserted into the right ureter to relieve hydronephrosis, was removed without further complications. CONCLUSION: Because of an increase in the number of immigrants from countries with a high incidence of tuberculosis or HIV infection, extrapulmonary tuberculosis should be included in the differential diagnosis, such as in this case of a psoas muscle abscess. Despite the size of the abscess surgical intervention is rarely required because it will heal under appropriate antituberculosis treatment.

Buckley M.J. et al. *Metronidazole resistance reduces efficacy of triple therapy and leads to secondary clarithromycin resistance.* Dig Dis Sci. 1997; 42(10) : 2111-5.p Abstract: There has been a significant increase in the prevalence of H. pylori resistance to metronidazole in recent years, while clarithromycin resistance is still relatively rare. In this study we assessed: (1) the effect of primary H. pylori resistance to metronidazole and clarithromycin on the clinical efficacy of a one-week regimen consisting of omeprazole, metronidazole, and clarithromycin; and (2) the rate of acquisition of secondary antimicrobial resistance after treatment failure. Eighty-seven patients with duodenal ulceration or nonulcer dyspepsia were included in the study. The primary metronidazole and clarithromycin resistance rates were 35.6% and 3.4%, respectively (all three pretreatment clarithromycin resistant strains had concurrent metronidazole resistance). H. pylori was eradicated in 81.6% of patients. The eradication rate for fully sensitive isolates was 98.2% (55/56) but was significantly reduced to 57.1% (16/28) for isolates that were resistant to metronidazole alone and 0% (0/3) in cases of dual resistance ($P < 0.001$). Secondary resistance to clarithromycin was acquired in 58.3% of cases of treatment failure. In areas of high prevalence of primary metronidazole resistance, this is a significant cause of treatment failure with this triple therapy regimen. This leads to the selection of strains with dual resistance that are difficult to eradicate and may contribute to an increase in the prevalence of clarithromycin resistance. In such areas an alternative first-line treatment should be prescribed.

Bujdakova H. et al. *Study of beta-lactam resistance in ceftazidime-resistant clinical isolates of Enterobacteriaceae.* Int J Antimicrob Agents. 1998; 10(2) : 135-41.p Abstract: Mechanisms and transferability of beta-lactam resistance in 50 ceftazidime resistant strains of Enterobacteriaceae was studied. These strains were selected from 1991 E. coli, 1035 Enterobacter spp., 168 Citrobacter spp. and 1371 Klebsiella spp., isolated from patients hospitalized in ICUs and in the pediatric and urology departments of six hospitals in Bratislava during the years 1994-1996. The selected strains expressed the resistance not only to ceftazidime (50/50) but also to ampicillin (50/50), ceftriaxone (50/50), cefotaxime (49/50) and cefoxitin (45/50). The mechanism of resistance in all 50 strains was the production of beta-lactamases by conjugation, using either ceftazidime or cefotaxime for the selection of transconjugants and by isolation of R-plasmids ranging from to 55-87 kb from donor strains and from transconjugants. A total of 21 isolates possessed chromosomally encoded resistance and 25 clinical isolates and their transconjugants expressed ESBL sensitive to clavulanate. Selected E. coli and Klebsiella pneumoniae isolates expressed the presence of TEM and SHV enzymes determined by isoelectric focusing. The possible trends in the development of antimicrobial resistance in Slovakia in the future are indicated.

Bukharin O.V. et al. *[The photometric determination of the antilysozyme activity of microorganisms].* Zh Mikrobiol Epidemiol Immunobiol. 1997; (4) : 117-20.p Abstract: The method for the determination of the antilysozyme activity (ALA) of microorganisms, based on the photometric determination of the residual activity of enzyme with the use of Micrococcus lysodeikticus test culture after the incubation of the strain under test and lysozyme, is proposed. The new method enhances the reliability of the determination of the ALA of microorganisms due to an increase in the accuracy of the quantitative determination of ALA. The elimination of the stage of interaction between the growing bacterial culture and lysozyme and the presence of the antilysozyme factor in the supernatant fluid confirm the constructive and secretory character of antilysozyme activity.

Bukhrin O.V. et al. *[Role of intraspecific phenotypic diversity in the ecology of escherichia coli and staphylococcus aureus].* Vestn Ross Akad Med Nauk. 1997; (3) : 34-40.p Abstract: Investigating a complex of biological characteristics, including the inactivating ability of some antiinfectious resistance agents (lysozyme, complement, immunoglobulins, the bactericide component of interferon) in 229 and 257 E. coli and S. aureus strains, respectively, isolated from various sources has revealed the phenotypical polymorphism in the populations of these microorganisms, whose degree and specific features may be characterized by the indices of biological diversity and by the spectra of dominant biological profiles. Interpopulational variability in the bacteria was found to be determined by the specific features of their colonized ecotopes and to reflect the level of their adaptation to their inhabitance. There is a view of the organizational structure of the bacterial species as a whole complex of discrete populations of microorganisms, which include representatives of phenotypically different clone lines that occupy the optimum and some marginal econiches whose relation is supported by migration processes.

Burgos Sanchez A. et al. *[Descriptive study of infectious ear disease in relation to summer].* Acta Otorrinolaringol Esp. 2000; 51(1) : 19-24.p Abstract: A descriptive study was made of infectious ear disease (including diffuse otitis externa, otomycosis, acute-on-chronic otitis media, and superinfection of a radical mastoidectomy cavity) in relation to changes of weather and habits in summer. During the months of June, July, and August 1996, 179 patients were evaluated in the emergency room of the Alicante General University Hospital, Spain. Average patient age at presentation was 30.52 (+/- 20.08) years and 56% were men. The most frequent disease was diffuse otitis externa (78%) followed by acute-on-chronic otitis media (12%), otomycosis (8%), and superinfection of a radical mastoidectomy cavity (2%). The most frequently involved microorganisms were Pseudomonas aeruginosa in diffuse otitis externa, Aspergillus niger and Candida in otomycosis, Escherichia coli, Haemophilus influenzae, Proteus mirabilis, and Staphylococcus aureus in acute-on-chronic otitis media. Patients were treated by cleaning detritus and secretions, usually followed by topical antibiotics for a maximum period of one week.

Burke J.P. et al. *Antibiotic use and microbial resistance in intensive care units: impact of computer-assisted decision support.* J Chemother. 1999; 11(6) : 530-5.p Abstract: As part of our integrated hospital information system (the HELP system), we developed computer-assisted decision support programs for antimicrobial prescribing that are available at bedside terminals throughout our 520-bed community hospital. Recently, options have been added to allow direct physician order entry of anti-infective agents in the shock-trauma intensive care unit (STRICU). Physicians prescribed the computer-suggested regimens for 46% but followed the suggested dose and interval for 93% of the orders during a 1-year study period. In comparison to a 2-year preintervention period, improved drug selection and reductions in adverse drug events and costs were seen. Antimicrobial resistance patterns for nosocomial gram-negative isolates remained stable or improved in the STRICU over an 11-year period of computer-assisted antibiotic management. We conclude that strategies for optimizing antimicrobial prescribing have the potential to stabilize resistance and reduce costs by encouraging heterogeneous prescribing patterns, use of local antimicrobial susceptibility patterns to inform empiric drug selection, and reduced "tonnage" of antibiotic use.

Burne R.A. et al. *Physiologic homeostasis and stress responses in oral biofilms.* Methods Enzymol. 1999; 310 : 441-60.p Abstract: Studies performed since the early, 1970s have yielded tremendous amounts of information about the physiology, genetics, and interactions of oral bacteria. This pioneering work has provided a solid foundation to begin to apply the knowledge and technologies developed using suspended populations for studying oral bacteria under conditions that more closely mimic conditions in the oral cavity, in biofilms. Our current understanding of phenotypic capabilities of individual and complex mixtures of adherent oral bacteria is in its infancy. There is ample evidence that oral streptococci have different patterns of gene expression than planktonic cells, but we have little understanding of the basis for these observations. Even in biofilmforming bacteria with very well-developed genetic systems it is only very recently that genetic loci involved in biofilm formation and responses to surface growth have been identified. A comprehensive study of the physiology and gene expression characteristics of adherent oral bacteria not only will enhance our abilities to control oral diseases, but it will provide critical information that can be applied to a variety of other pathogenic microorganisms.

Burnett R.J. et al. *Definition of the role of enterococcus in intraabdominal infection: analysis of a prospective randomized trial.* Surgery. 1995; 118(4) : 716-21; discussion 721-3.p Abstract: BACKGROUND. The role of enterococcus in intraabdominal infection is controversial. This study examines the contribution of enterococcus to adverse outcome in a large intraabdominal infection trial. METHODS. A randomized prospective double-blind trial was performed to compare two different antimicrobial regimens in combination with surgical or percutaneous drainage in the treatment of complicated intraabdominal infections. A total of 330 valid patients was enrolled from 22 centers in North America. RESULTS. In 330 valid patients, 71 had enterococcus isolated from the initial drainage of an intraabdominal focus of infection. This finding was associated with a significantly higher treatment failure rate than that of patients without enterococcus (28% versus 14%, $p < 0.01$). In addition, only Acute Physiology and Chronic Health Evaluation II score and presence of enterococcus were significant independent predictors of treatment failure when stepwise logistic regression was performed ($p < 0.01$ and < 0.03). Risk factors for the presence of enterococcus include age, Acute Physiology and Chronic Health Evaluation II, preinfection hospital length of stay, postoperative infections, and anatomic source of infection. There was no difference between the clinical trial treatment regimens with regard to overall failure, failure associated with enterococcus, or frequency of enterococcal isolation. CONCLUSIONS. This study is the first to report enterococcus as a predictor of treatment failure in complicated intraabdominal infections. This trial also identifies several significant risk factors for the presence of enterococcus in such infections.

Burnie J.P. et al. *An epidemiological study of blood culture isolates of coagulase-negative staphylococci demonstrating hospital-acquired infection.* J Clin Microbiol. 1997; 35(7) : 1746-50.p Abstract: We applied pulsed-field gel electrophoresis (PFGE) after SmaI digestion and random amplification of polymorphic DNA (RAPD) analysis with nine oligonucleotide primers to 146 blood culture isolates of Staphylococcus epidermidis and 25 blood culture isolates of Staphylococcus haemolyticus. These were obtained over a 12-month period from patients on the neonatal and hematology units of the Central Manchester Health Care Trust. PFGE demonstrated two clusters of isolates of S. epidermidis (type A and type B) on the neonatal ward and a single cluster (type C) on the hematology unit. Type A was represented by 10 indistinguishable isolates from nine patients, type B was represented by 20 isolates from 14 patients, and type C was represented by 26 isolates from 10 patients. Type A isolates were resistant to chloramphenicol and type C isolates were resistant to ciprofloxacin, mirroring current antibiotic usage. There was no evidence of cross infection due to S. haemolyticus. RAPD analysis, on the basis of a single band difference, produced 58 types of S. epidermidis and 12 types of S. haemolyticus with primer 8 (ATG TAA GCT CCT GGG GAT TCA C; 5' to 3') and 54 types of S. epidermidis and 10 types of S. haemolyticus with primer 9 (AAG TAA GTG ACT GGG GTG AGC G; 5' to 3'). Combining the results confirmed cross infection. Types A, B, and C were concurrently isolated from the hands of the staff of the appropriate unit. Partial control was achieved by withdrawing ciprofloxacin use in the case of the hematology unit and improving hand hygiene in both units.

Burns J.L. et al. *Comparison of agar diffusion methodologies for antimicrobial susceptibility testing of Pseudomonas aeruginosa isolates from cystic fibrosis patients.* J Clin Microbiol. 2000; 38(5) : 1818-22.p Abstract: Pseudomonas aeruginosa is the most common pathogen infecting the lungs of patients with cystic fibrosis (CF). Improved antimicrobial chemotherapy has significantly increased the life expectancy of these patients. However, accurate susceptibility testing of P. aeruginosa isolates from CF sputum may be difficult because the organisms are often mucoid and slow growing. This study of 597 CF isolates of P. aeruginosa examined the correlation of disk diffusion and Etest (AB BIODISK, Solna, Sweden) results with a reference broth microdilution method. The rates of interpretive errors for 12 commonly used antipseudomonal antimicrobials were determined. The disk diffusion method correlated well (zone diameter versus MIC) for all of the agents tested. However, for mucoid isolates, correlation coefficients (r values) for piperacillin, piperacillin-tazobactam, and meropenem were <0.80. The Etest correlation with reference broth microdilution results (MIC versus MIC) was acceptable for all of the agents tested, for both mucoid and nonmucoid isolates. Category interpretation errors were similar for the disk diffusion and Etest methods with 0.4 and 0.1%, respectively, very major errors (false susceptibility) and 1.1 and 2.2% major errors (false resistance). Overall, both agar diffusion methods appear to be broadly acceptable for routine clinical use in susceptibility testing of CF isolates of P. aeruginosa.

Burtnick M.N. et al. *Isolation of polymyxin B-susceptible mutants of Burkholderia pseudomallei and molecular characterization of genetic loci involved in polymyxin B resistance.* Antimicrob Agents Chemother. 1999; 43(11) : 2648-56.p Abstract: Burkholderia pseudomallei is a gram-negative bacterium that causes the disease known as melioidosis. This pathogen is endemic to Southeast Asia and northern Australia and is particularly problematic in northeastern Thailand. It has been previously reported that B. pseudomallei is resistant to the killing action of cationic antimicrobial peptides, including human neutrophil peptide, protamine sulfate, poly-L-lysine, magainins, and polymyxins. Recently, we have also found that the virulent clinical isolate B. pseudomallei 1026b is capable of replicating in media containing polymyxin B at concentrations of >100 mg/ml. In order to identify genetic loci that are associated with this particular resistance phenotype, we employed a Tn5-OT182 mutagenesis system in coordination with a replica plating screen to isolate polymyxin B-susceptible mutants. Of the 17,000 Tn5-OT182 mutants screened via this approach, five polymyxin B-susceptible mutants were obtained. Three of these mutants harbored Tn5-OT182 insertions within a genetic locus demonstrating strong homology to the lytB gene present in other gram-negative bacteria. Of the remaining two mutants, one contained a transposon insertion in a locus involved in lipopolysaccharide core biosynthesis (waaF), while the other contained an insertion in an open reading frame homologous to UDP-glucose dehydrogenase genes. Isogenic mutants were also constructed via allelic exchange and used in complementation analysis studies to further characterize the relative importance of each of the various genetic loci with respect to the polymyxin B resistance phenotype exhibited by B. pseudomallei 1026b.

Bush K. *beta-Lactamases of increasing clinical importance.* Curr Pharm Des. 1999; 5(11) : 839-45.p Abstract: Resistance to b-lactam-containing antimicrobial agents continues to increase, frequently due to the presence of b-lactamases in Gram-negative bacteria. Over the past twenty-five years broad-spectrum enzymes such as TEM- and SHV-variants and the metallo-b-lactamases have become more prolific. As a result of the ability of plasmids to continue to acquire additional resistance determinants, many of the b-lactamase-producing Gram-negative pathogens have become multi-drug resistant. In combination with decreased permeability, the organisms can become virtually untreatable with current therapies. The major groups of b-lactamases that pose the most serious therapeutic problems include the extended-spectrum b-lactamases, the plasmid-mediated cephalosporinases, the inhibitor-resistant TEM- or SHV-derived b-lactamases and the carbapenem-hydrolyzing b-lactamases. Those enzymes that can be transferred on mobile elements are the most serious of the newer b-lactamases, and include enzymes in each of the four groups outlined above.

Busscher H.J. et al. *Lateral and perpendicular interaction forces involved in mobile and immobile adhesion of microorganisms on model solid surfaces.* Curr Microbiol. 1998; 37(5) : 319-23.p Abstract: Gliding and near-surface swimming of microorganisms are described as a mobile form of microbial adhesion that need not necessarily be reversible. It is argued that the reversibility of microbial adhesion depends on the depth of the secondary interaction minimum, calculated from the forces between an organism and a substratum acting in a direction perpendicular to the substratum surface. The mobility of adhering microorganisms depends on lateral interactions between the organisms. On ideally homogeneous and smooth model surfaces, only mobile adhesion occurs because the multibody, lateral interactions are weak compared with the thermal or Brownian motion energy of the organisms. Minor chemical or structural heterogeneities, which exist on all real-life surfaces, yield a lateral interaction on adhering microorganisms. This causes their immobilization, which helps to explain the physicochemical nature of microbial gliding or near-surface swimming. Moreover, these lateral interaction energies are one order of magnitude smaller than the Lifshitz-Van der Waals, electrostatic, and acid-base forces acting perpendicular to substratum surfaces that are responsible for adhesion.

Busscher H.J. et al. *Streptococcus thermophilus and its biosurfactants inhibit adhesion by Candida spp. on silicone rubber.* Appl Environ Microbiol. 1997; 63(10) : 3810-7.p Abstract: The adhesion of yeasts, two Candida albicans and two Candida tropicalis strains isolated from naturally colonized voice prostheses, to silicone rubber with and without a salivary conditioning film in the absence and presence of adhering Streptococcus thermophilus B, a biosurfactant-releasing dairy isolate, was studied. Coverage of 1 to 4% of the surface of silicone rubber substrata with adhering S. thermophilus B gave significant reductions in the initial yeast adhesion regardless of the presence of a conditioning film. Mechanistically, this interference in yeast adhesion by S. thermophilus B was not due to direct physical effects but to biosurfactant release by the adhering bacteria, because experiments with S. thermophilus B cells that had released their biosurfactants prior to adhesion to silicone rubber and competition with yeasts did not show interference with initial yeast adhesion. The amounts of biosurfactants released were highest for mid-exponential- and early-stationary-phase bacteria (37 mg.g of cells-1 [dry weight]), but biosurfactants released by stationary-phase bacteria (14 mg.g of cells-1 [dry weight]) were the most surface active. The crude biosurfactants released were mixtures of various components, with a glycolipid-like component being the most surface active. A lipid-enriched biosurfactant fraction reduced the surface tension of an aqueous solution to about 35 mJ.m-2 at a concentration of only 0.5 mg.ml-1. The amount of biosurfactant released per S. thermophilus B cell was estimated to be sufficient to cover approximately 12 times the area of the cross section of the bacterium, making biosurfactant release a powerful defense weapon in the postadhesion competition of the bacterium with microorganisms such as yeasts. Preadsorption of biosurfactants to the silicone rubber prior to allowing yeasts to adhere was as effective against C. albicans GB 1/2 adhesion as covering 1 to 2% of the silicone rubber surface with adhering S. thermophilus B, but a preadsorbed biosurfactant layer was less effective against C. tropicalis GB 9/9.

Butler J.C. et al. *Pneumococcal drug resistance: the new "special enemy of old age".* Clin Infect Dis. 1999; 28(4) : 730-5.p Abstract: Streptococcus pneumoniae is a leading cause of illness and death among the elderly. The recent emergence of drug-resistant strains has complicated selection of antimicrobial therapy for suspected pneumococcal infections. In some areas of North America, nearly 40% of

pneumococcal isolates from the blood or cerebrospinal fluid of persons > or = 65 years old had reduced susceptibility to penicillin. Of all penicillin-resistant infections, >30% occur in persons > or = 65 years old. The increasing prevalence of drug-resistant pneumococci and recent outbreaks of pneumococcal disease in chronic-care facilities emphasize the importance of efforts to prevent these infections in the elderly. Limiting selection for drug-resistant strains through judicious use of antimicrobial drugs and preventing invasive pneumococcal infections through increased use of pneumococcal vaccine form the foundation of these efforts.

Butler J.C. et al. *The continued emergence of drug-resistant Streptococcus pneumoniae in the United States: an update from the Centers for Disease Control and Prevention's Pneumococcal Sentinel Surveillance System.* J Infect Dis. 1996; 174(5) : 986-93.p Abstract: As part of ongoing national surveillance, serotyping and antimicrobial susceptibility testing were done on all pneumococcal isolates recovered from normally sterile body sites of patients at 12 hospitals in 11 states during 1993-1994. Of 740 isolates, 14.1% were penicillin-nonsusceptible Streptococcus pneumoniae (PNSP; MIC > or = 0.1 microgram/mL), 3.2% were penicillin-resistant (MIC > or = 2.0 micrograms/mL), and 25.5% were nonsusceptible to more than one antimicrobial agent. PNSP were more prevalent among children < 6 years old (18.4%) than patients > or = 18 years old (11.7%) and among white persons (16.2%) than black persons (12.1%). PNSP represented 15 serotypes, but 89% of PNSP were serotypes in the 23-valent pneumococcal vaccine. The proportion of isolates with reduced susceptibility and the number of serotypes of nonsusceptible strains are increasing in the United States. Improved local surveillance for PNSP infections, judicious use of antibiotics, and development and use of effective pneumococcal vaccines will be required to treat and prevent disease caused by these strains.

Butt H.L. et al. *In vitro susceptibility patterns of nonserotypable Haemophilus influenzae from patients with chronic bronchitis.* Pathology. 1997; 29(1) : 72-5.p Abstract: The antimicrobial susceptibility patterns of 76 nonserotypable Haemophilus influenzae (biotypes I-IV) from patients with chronic bronchitis were compared against ten orally administered antimicrobial agents. In addition the sputum ampicillin concentrations one hour after standard therapy were determined in five patients with chronic bronchitis. Ampicillin resistance was demonstrated in one strain (biotype IV) which produced beta-lactamase and two strains (biotype II) with innate resistance (MIC = 4 mg/l). Resistance to trimethoprim, chloramphenicol, ciprofloxacin and cefaclor was not detected. The incidence of resistance to tetracycline was 0.5% and cephalexin 13.2%. A high incidence of resistance to erythromycin (95%) was noted. There was no association between resistance and biotype of nonserotypable H. influenzae. The sputum ampicillin concentrations from four out of five patients given standard antibiotic doses were shown to be sufficient to inhibit the growth of the majority of nonserotypable H. influenzae strains one hour after treatment. This study shows that the incidence of nonserotypable H. influenzae resistant to ampicillin is low in this community but that resistance levels to erythromycin, commonly prescribed for the management of acute bronchitis, are high. Regular sensitivity screens are important in monitoring the value of various antibiotic regimens in the management of acute bronchitis.

Buxbaum A. et al. *Postantibiotic effect of ceftriaxone and gentamicin alone and in combination on Klebsiella pneumoniae, Pseudomonas aeruginosa and Streptococcus viridans.* Infection. 1996; 24(6) : 459-64.p Abstract: A persistent suppression of bacterial growth following limited exposure to an antimicrobial agent, the postantibiotic effect (PAE), has been described for a variety of antibiotics and microorganisms. In this study the PAE of ceftriaxone and gentamicin was determined in vitro on three strains each of Klebsiella pneumoniae, Pseudomonas aeruginosa and Streptococcus viridans. The strains were exposed to the substances for 2 h at varying concentrations. Ceftriaxone was used at the minimal inhibitory concentration (MIC) and 1/2 MIC and gentamicin at 1/2 MIC, 1/4 MIC, and 1/8 MIC, each alone and in combination. Antibiotic concentrations were reduced by 1,000-fold dilution, bacterial regrowth was consequently monitored by viable count. The PAE of ceftriaxone alone reached up to 145 min (MIC) and 50 min (1/2 MIC), that of gentamicin alone up to 170 min (1/2 MIC), 135 min (1/4 MIC) and 70 min (1/8 MIC), depending on the bacterial species. Combinations of the antibiotics produced longer PAEs than one substance alone; the longest PAE was produced by the combination of ceftriaxone (MIC) and gentamicin (1/2 MIC) lasting up to 320 min (S. viridans). It may be important to take the PAE into account when evaluating dosing intervals.

Buzoleva L.S. et al. *[The gas trophicity of pathogenic bacteria].* Zh Mikrobiol Epidemiol Immunobiol. 1997; (5) : 63-7.p Abstract: Yersinia pseudotuberculosis and Listeria have been shown to be capable of assimilating carbon dioxide from the air and using its carbon for the synthesis of biopolymers of the bacterial cell. These microorganisms, the causative agents of saprozoonotic infections, have also been found to be capable of assimilating molecular nitrogen from the air in small amounts. The data on the influence of the growth conditions of the cultures (hydrogen concentration, the presence of carbon dioxide and oxygen, temperature) on the activity of acetylene reduction by microbial cells. At low temperature molecular nitrogen is fixed by Listeria twice as actively as by Y.pseudotuberculosis. Not all bacterial strains under study have been found to be capable of acetylene reduction. The presence of fixed nitrogen in the medium suppresses the process of the reduction of acetylene into ethylene.

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Caballero-Granado F.J. et al. *Comparative study of bacteremias caused by Enterococcus spp. with and without high-level resistance to gentamicin. The Grupo Andaluz para el estudio de las Enfermedades Infecciosas.* J Clin Microbiol. 1998; 36(2) : 520-5.p Abstract: A prospective, multicenter study was carried out over a period of 10 months. All patients with clinically significant bacteremia caused by Enterococcus spp. were included. The epidemiological, microbiological, clinical, and prognostic features and the relationship of these features to the presence of high-level resistance to gentamicin (HLRG) were studied. Ninety-three patients with enterococcal bacteremia were included, and 31 of these cases were caused by HLRG (33%). The multivariate analysis selected chronic renal failure, intensive care unit stay, previous use of antimicrobial agents, and Enterococcus faecalis species as the independent risk factors that influenced the development of HLRG. The strains with HLRG showed lower levels of susceptibility to penicillin and ciprofloxacin. Clinical features (except for chronic renal failure) were similar in both groups of patients. HLRG did not influence the prognosis for patients with enterococcal bacteremia in terms of either the crude mortality rate (29% for patients with bacteremia caused by enterococci with HLRG and 28% for patients not infected with strains with HLRG) or the hospital stay after the acquisition of enterococcal bacteremia. Hemodynamic compromise, inappropriate antimicrobial therapy, and mechanical ventilation were revealed in the multivariate analysis to be the independent risk factors for mortality. Prolonged hospitalization was associated with the nosocomial acquisition of bacteremia and polymicrobial infections.

Cabellos C. et al. *Streptococcal meningitis in adult patients: current epidemiology and clinical spectrum.* Clin Infect Dis. 1999; 28(5) : 1104-8.p Abstract: Streptococci other than Streptococcus pneumoniae are a rare cause of bacterial meningitis in adults. We report 29 cases of streptococcal meningitis (1977-1997). The patients comprised 19 men and 10 women, with a mean age +/- standard deviation of 47 +/- 18 years. Nine cases were secondary to neurosurgical procedures, seven to brain abscess, five to cerebrospinal fluid pericranial fistula, and three to endocarditis. Causative microorganisms included

the following: viridans group streptococci, 20 cases; anaerobic streptococci, 3; Streptococcus agalactiae, 3; Streptococcus bovis, 2; and Streptococcus pyogenes, 1. Four Streptococcus mitis strains showed decreased susceptibility to penicillin (MIC, 0.5-2 microg/mL). Five patients (17%) died. The infection is increasing in the hospital setting. Streptococci resistant to penicillin should be considered in the empirical treatment of nosocomial meningitis. In cases of community-acquired infection, anaerobic streptococci or streptococci of the Streptococcus milleri group should alert the clinician to the presence of an undiagnosed brain abscess, whereas oral streptococci of the viridans group suggest the diagnosis of bacterial endocarditis.

Cabrera S. et al. *Patrón de sensibilidad a tres aminoglucósidos in vitro de bacterias gram negativas aisladas en urocultivos.* Pediatr. edicion int. 1999; 2(1) : 18-20.p Abstract: OBJETIVO. Comparar la sensibilidad entre la Tobramicina,Gentamicina y Amikacina en urocultivos positivos para bacterias gram negativas. DISEÑO. Estudio descriptivo, comparativo. Población. Cincuenta urocultivos. METODOLOGIA. A cada urocultivo se colocó un disco de sensibilidad de los tres aminoglucósidos midiendo en cada uno un halo de sensibilidad formado, para clasificarlo como sensible o resistente. Realizando luego cuadros comparativos y aplicándoles el método estadístico de Test exacto de Fisher's. RESULTADOS. Se encontraron 34 uroculticos positivos para E. coli y el resto para gram negativos menos frecuentes como Proteus mirabilis, Klebsiella oxytoca, Citrobacter, Enterobacter y Pseudomona. El aminoglucósido más sensible fue la Tobramicina cuando se trata de bacteria E. coli y se determinó que la diferecia es insignificante cuando se trata de gram negativos en general. CONCLUSIONES. La sensibilidad de Tobramicina, Amikacina y Gentamicina por medio de discos fue similar (AU).

Caceres M. et al. *Antimicrobial susceptibility of anaerobic and aerobic bacteria isolated from patients with mixed infections in Nicaragua.* Rev Esp Quimioter. 1999; 12(4) : 332-9.p Abstract: The agar dilution method was used to test the activity of ampicillin, benzylpenicillin, cefoxitin, imipenem, clindamycin, metronidazole, chloramphenicol, gentamicin, methicillin and vancomycin against 241 anaerobic and 227 aerobic bacteria isolated from 136 patients with intraabdominal infections and 49 with nonintraabdominal infections. Beta-lactamase production was tested in all strains. Overall, imipenem, metronidazole and chloramphenicol were the most active antimicrobial agents against anaerobic bacteria followed by clindamycin. Only the Bacteroides fragilis group was shown to be less susceptible to clindamycin (MIC90 8 mg/l). Ampicillin and cefoxitin were the least active beta-lactam antibiotics against the most common isolated B. fragilis group strains (MIC(90) >1024 and 64 mg/l, respectively) and against Escherichia coli strains (MIC(90) >1024 and >1024 mg/l, respectively). Chloramphenicol showed low activity against the Gram-negative aerobic bacteria, while gentamicin had good activity against the aerobic bacteria tested, except for E. coli and Pseudomonas. Among the Gram-positive aerobic and anaerobic bacteria tested, Staphylococcus aureus was shown to be less susceptible to beta-lactam antibiotics (29% were methicillin resistant). No vancomycin-resistant S. aureus strains were found. A good correlation between beta-lactamase production and beta-lactam resistance was observed.

Cade A. et al. *Acute bronchopulmonary infection due to Streptococcus milleri in a child with cystic fibrosis.* Arch Dis Child. 1999; 80(3) : 278-9.p Abstract: An 8 year old girl with cystic fibrosis had severe respiratory disease associated with chronic Pseudomonas aeruginosa bronchopulmonary infection. Despite regular courses of intravenous antipseudomonal antibiotics, she continued to deteriorate over 18 months with persistent productive cough, worsening respiratory function, and increasing oxygen dependence. During her 11th admission Streptococcus milleri was isolated from sputum cultures in addition to P aeruginosa. She failed to respond to antipseudomonal antibiotics but improved dramatically with the addition of intravenous benzylpenicillin. Although S milleri is considered a normal mouth commensal and its isolation from sputum of cystic fibrosis patients is of uncertain significance, it was associated with clinically significant infection in this child. S milleri was eradicated with antibiotic treatment and clinical improvement has been maintained.

Cahen P. et al. *[Nitrofurans: a modern treatment for uncomplicated urinary infections?].* Pathol Biol (Paris). 2000; 48(5) : 470-1.p Abstract: From January 1995 to December 1998, 2,912 strains of enteric bacilli were isolated from the urinary tract. Increasing antibiotic resistance in Enterobacteriaceae as a cause of urinary tract infection (UTI) led us to reevaluate first- and second-line therapies. We studied antimicrobial susceptibilities of these strains to norfloxacin (NOR), nalidixic acid (NAL), trimethoprim sulfamethoxazole (TS) and nitrofurantoin (FT) using the disk diffusion method. These results show no significant superiority of the activity of nitrofurantoin against Enterobacteriaceae compared with the other antibiotics with sustained concentration in urine. However, if we consider only multiresistant Enterobacteriaceae (cefotaxime resistant), this molecule appears to be very active. These results show a significant superiority of nitrofurantoin in vitro against these multiresistant Enterobacteriaceae. Thus, this molecule could once again become a good choice for the treatment of uncomplicated UTI.

Caines C. et al. *Non-Clostridium difficile nosocomial diarrhea in the intensive care unit.* Heart Lung. 1997; 26(1) : 83-4.p Abstract: It is assumed that most cases of nosocomial diarrhea are due to Clostridium difficile because of the widespread use of broad-spectrum antibiotic agents. Enteral tube feedings are another important cause of hospital-acquired diarrhea, especially in intensive care units (ICUs). We report the results of a recent survey of patients in the ICU with nosocomial diarrhea and describe an illustrative case. We conclude on the basis of this and a previous larger study that C. difficile diarrhea is very uncommon in enterally fed patients in the ICU; nosocomial diarrhea in the ICU is most commonly caused by enteral tube feedings.

Calkins E.R. *Nosocomial infections in hand surgery.* Hand Clin. 1998; 14(4) : 531-45, vii.p Abstract: The active and experienced hand surgeon should have enough knowledge to recognize both common and uncommon hand infections. Control of hospital-acquired infections, including surgical site infections, requires a knowledge of potential personal risk factors and ongoing surveillance systems to aid in prevention and early detection. Current national trends may soon require that surgical-site infections be diagnosed by specific criteria that will allow comparisons of data from various locations. Although most hand surgery procedures are now performed on an ambulatory basis, it is important for the hand surgeon to be aware of current methodologies for the prevention, control, surveillance, and treatment of hospital-acquired infections. These intriguing aspects of hospital-acquired infections are reviewed in this article.

Calore E.E. et al. *Esophageal ulcers in AIDS.* Pathologica. 1997; 89(2) : 155-8.p Abstract: Thirty five esophageal biopsies from AIDS patients with clinical symptoms of esophagitis sent to "Emilio Ribas Institute", Pathology Laboratory, in a 2 year period were revised for possible infectious agents. Microorganisms were seen in 17 cases (48.6%). In 6 cases (17.1%), Acid-Fast bacilli were observed. One of these cases also had characteristic cytomegalic inclusions in endothelial cells. Inflammatory responses were composed of lymphocytes, some plasma cells and many histiocytes, with absence of giant cells in 4 cases of mycobacteriosis; in the other 2 cases, acid-fast bacilli were seen over the epithelium. Exclusive infection by cytomegalovirus was detected in 5 cases (14.3%), and candidiasis in 5 cases (14.3%). In one case there was association of cytomegalovirus and candidiasis. Esophageal ulcers in AIDS patients caused by Mycobacterium sp, may be more common than previously reported, and certainly an overlooked diagnosis. Once esophageal biopsy is an easy diagnostic procedure, this method may be used in routine screening for tuberculosis in patients with AIDS.

Calva J.J. et al. *Antimicrobial resistance in fecal flora: longitudinal community-based surveillance of children from urban Mexico.* Antimicrob Agents Chemother. 1996; 40(7) : 1699-702.p Abstract: We assessed the colonization patterns, over time, of three sentinel drug-resistant enteric bacterial genera in samples from a cohort of 20 healthy small children in a periurban community in Mexico. The children were monitored during a 13-week period by means of weekly home visits and examinations of stool collections. These specimens were tested for the presence of Escherichia coli, Klebsiella species, and Shigella species resistant to one or more of seven antimicrobial agents. Ninety, 77, and 62% of the stool specimens had E. coli isolates resistant to ampicillin, trimethoprim, and tetracycline, respectively. Simultaneous resistance to more than one antibiotic by an E. coli isolate was observed in 88.5% of stool samples. Persistent fecal shedding of ampicillin-, trimethoprim-, and tetracycline-resistant E. coli occurred during the study period in the majority of children. We detected colonization by E. coli resistant to chloramphenicol, gentamicin, nitrofurantoin, or norfloxacin, as well as by Klebsiella species and Shigella species resistant to one of these antibiotics, in fewer children and for shorter periods. These data suggest the common and persistent intestinal shedding of multidrug-resistant E. coli strains by small healthy children.

Campbell G.D. Jr. *Commentary on the 1993 American Thoracic Society guidelines for the treatment of community-acquired pneumonia.* Chest. 1999; 115(3 Suppl) : 14S-18S.p Abstract: Early treatment of community-acquired pneumonia (CAP) is associated with improved outcome. Since extensive diagnostic testing identifies an etiologic agent in only half of the cases and usually requires several hours or even days for results, CAP is most often initially treated empirically. In 1993, the American Thoracic Society (ATS) established guidelines to assist primary care physicians in antibiotic selection for the initial empiric treatment of CAP in immunocompetent adults. Since publication of the guidelines, the incidence of certain bacteria has been redefined, antimicrobial resistance patterns have changed, risk factors for stratifying need for hospitalization have been further defined, and newer antibiotics have been introduced. These changes necessitate a reevaluation of the 1993 ATS guidelines. This article proposes a modification of the ATS guidelines. This modification continues to classify patients into groups, based on specific risk factors, to which a limited number of likely pathogens are identified and for which antibiotic treatment regimens are developed. The modification differs from the original ATS guidelines because of the changes in risk factors. Patient groups are still broadly divided into outpatient and inpatient care, but earlier risk factors of age and coexisting illness have been refined. Risk factors suggested herein as considerations to guide treatment include the presence of cardiopulmonary disease, history of smoking, severity of illness, risk of drug-resistant Streptococcus pneumoniae and Pseudomonas aeruginosa, and need for ICU admission.

Campbell G.D. Jr et al. *Drug-resistant Streptococcus pneumoniae.* Clin Infect Dis. 1998; 26(5) : 1188-95.p Abstract: Streptococcus pneumoniae remains a major cause of infection in both children and adults, annually resulting in significant morbidity and mortality. The past two decades have seen an alarming worldwide increase in the incidence of drug-resistant S. pneumoniae (DRSP). DRSP is now common throughout the United States, and physicians are questioning how best to approach this epidemic. With the introduction of a number of newer antimicrobial agents, the potential for improved preventive measures, and a better understanding of DRSP, the approach to the management of DRSP infections may change greatly in the next few years. In this article we will review the development of DRSP, identify populations at increased risk of exposure to DRSP, address what approaches might be used to limit its spread, and suggest initial empirical therapy when treating patients with pneumonia due to DRSP.

Campillo B. et al. *Epidemiology of severe hospital-acquired infections in patients with liver cirrhosis: effect of long-term administration of norfloxacin.* Clin Infect Dis. 1998; 26(5) : 1066-70.p Abstract: We performed a 5-year retrospective study to evaluate the effect of long-term administration of norfloxacin on the epidemiology of severe hospital-acquired infections in patients with advanced cirrhosis. Sixty-seven episodes of spontaneous bacterial peritonitis and 60 episodes of bacteremia occurred in, respectively, 46 patients (group 1a) and 52 patients (group 1b) who did not receive norfloxacin, while 23 and 17 episodes occurred in 21 patients (group 2a) and 17 patients (group 2b) during or within 10 days after long-term administration of norfloxacin. Enterobacteriaceae were more prevalent in groups 1a and 1b than in the other two groups ($P < .001$ and $P < .01$, respectively); conversely, staphylococci were more prevalent in groups 2a and 2b ($P < .001$ and $P < .05$, respectively). The rate of staphylococcal resistance to methicillin was 53.6% in groups 1a and 1b and 77.3% in groups 2a and 2b. We conclude that long-term norfloxacin administration to cirrhotic patients reduces the risk of gram-negative infections but increases the risk of severe hospital-acquired staphylococcal infections and of high-level resistance to antibiotics.

Campo P. et al. *Evolution of susceptibility of non-typhi Salmonella in a Spanish hospital (1992-1994) and report of a Salmonella ser. Typhimurium isolate resistant to quinolones.* Eur J Epidemiol. 1997; 13(2) : 239-41.p Abstract: We report the evolution of the antimicrobial resistance of non-typhi Salmonella (1992-1994) in a Spanish hospital in relation with a case of infection due to a fluoroquinolone-resistant strain of Salmonella ser. Typhimurium. None of the isolates were resistant to ciprofloxacin. The resistance to ampicillin has increased from 20.6% (1992) to 29.5% (1994) whereas no significative differences in chloramphenicol and cotrimoxazole susceptibility were noted.

Campos A. et al. *Study of common aerobic flora of human cerumen.* J Laryngol Otol. 1998; 112(7) : 613-6.p Abstract: Cerumen is the product of the secretion of the sebaceous, ceruminous or apocrine glands together with cells exfoliated from the cornified stratum of the epithelium of the external auditory canal (EAC). In the present study we identified and quantified common flora of human cerumen. The mean count obtained was 10(6) microorganisms per ml of cerumen suspension. In 24 pools of cerumen (33.3 per cent) the isolates were monomicrobial, Staphylococcus epidermidis (12), Corynebacterium spp (10), Staphylococcus aureus (1) and Streptococcus saprophyticum (1). In 48 pools (66.6 per cent) we found polymicrobial isolates. The most commonly isolated bacteria in these polymicrobial isolates were S. epidermidis (35) and Corynebacterium spp. (43). It is noteworthy that there were isolates of Candida albicans in three cases; in one case of Pseudomonas stutzeri, in one case of Pseudomonas aeruginosa, and, on seven occasions, of S. aureus. The organisms isolated as common bacterial components of human cerumen in our experience were similar to those found by other authors. However, the mean count was much higher. This could be related to climatic conditions and to the length of time the cerumen had remained in the external auditory canal.

Campos G.M. et al. *[Bacteremia after endoscopic retrograde cholangiopancreatography with and without therapeutic procedure: frequency, associated factors and clinical significance].* Rev Assoc Med Bras. 1997; 43(4) : 326-34.p Abstract: PURPOSE: To determine the frequency, associate factors and clinical features of bacteremia in patients undergoing endoscopic retrograde cholangiopancreatography (ERCP), with or without therapeutic procedures. METHODS: Prospectively, 42 consecutives patients undergoing 46 endoscopic retrograde cholangiopancreatographies (ERCPs) from August to December 1994 were analyzed. The search for bacteremia was done by drawing 6 blood samples for cultures from peripheral blood. Two blood samples were collected before the ERCP and 4 of them after. The bottles used for cultures were Bactec bottles. The bottles were incubated in the Bactec 9240 system, and eventual bacteria detect were identificated by the manual routine of the laboratory and also with the autoScan/Microscan system. RESULTS: All blood cultures obtained

before the ERCPs were negatives. Bacteremia were detected after 7 endoscopic procedures. In two episodes of bacteremia, the microorganism identified (Staphylococcus epidermidis) was considered to be a contaminant. The other 5 episodes of bacteremia were considered true bacteremia (frequency- 10.9%), and the microorganisms identified were: Streptococcus viridans, Corynebacterium sp., Enterobacter cloacae, Klebsiello oxytoca and Enterobacter aerogenes. This episodes were more frequent in the blood cultures obtained immediately after the ERCPs ($p < 0.05$), and occurred exclusively in the patients who were not receiving antibiotics ($p = 0.0192$). Clinical manifestation of the episodes of bacteremia were not detected. CONCLUSION: The episodes of bacteremia occurred exclusively in the patients who were not receiving antibiotics, were transient and completely no symptomatic.

Campos M.A. et al. *Etiology and therapy of chronic suppurative otitis.* J Chemother. 1995; 7(5) : 427-31.p Abstract: Infectious diseases of the ear are important in adults due to their incidence and relapses. We carried out a study of aerobic microorganisms on 251 otic exudates from patients diagnosed as having chronic suppurative otitis media without cholesteatoma (119), chronic suppurative otitis media with cholesteatoma (85) and chronic external otitis (47). The microorganisms predominantly isolated were, Pseudomonas aeruginosa, Staphylococcus aureus and other Enterobacteriaceae. 86% of isolates were monomicrobial and 14% of isolates were polymicrobial. In these latter the predominantly isolated microorganisms were also P. aeruginosa, S. aureus, Corynebacterium spp. and Proteus mirabilis. P. aeruginosa was the most commonly isolated and showed the highest percentages of resistance against antimicrobial agents tested. P. aeruginosa was most susceptible to ciprofloxacin and imipenem, but much less susceptible to cefotaxime, moxalactam and trimethoprim-sulfamethoxazole. S. aureus was highly sensitive to amoxicillin/clavulanate, trimethoprim-sulfamethoxazole, rifampin and teichoplanin. 100% of the isolates were resistant to penicillin G and ampicillin.

Canganella F. et al. *A microbiology investigation on probiotic pharmaceutical products used for human health.* Microbiol Res. 1997; 152(2) : 171-9.p Abstract: Many and different probiotic pharmaceutical products are presently commercialised in the world. On this regard, a microbiological investigation was carried out to screen the microorganisms incorporated into these products, commonly used for human health. After determination of the cell number and viability of bacteria, several experiments were performed in vitro in order to characterise the microorganisms and to evaluate their probiotic value. Among all the strains identified, best results were obtained with Lactobacillus rhamnosus, Enterococcus faecium and Saccharomyces cerevisiae as far as regards growth rates, pH and bile salts tolerance. Moreover, the identification profiles of microorganisms showed a better reliability for the products containing a single species whereas the ones composed of different strains were usually not satisfactory. In some cases, the presence of Lactobacillus and Saccharomyces species was in disagreement with the claimed composition of the product and some species of lactobacilli, bifidobacteria and streptococci were found not viable. In defined mixed cultures experiments, the antagonism of Lactobacillus acidophilus and Enterococcus faecium versus Yersinia enterocolitica was demonstrated and explained as acid and/or antimicrobials production.

Canton R. et al. *Evaluation of the Wider system, a new computer-assisted image-processing device for bacterial identification and susceptibility testing.* J Clin Microbiol. 2000; 38(4) : 1339-46.p Abstract: The Wider system is a newly developed computer-assisted image-processing device for both bacterial identification and antimicrobial susceptibility testing. It has been adapted to be able to read and interpret commercial MicroScan panels. Two hundred forty-four fresh consecutive clinical isolates (138 isolates of the family Enterobacteriaceae, 25 nonfermentative gram-negative rods [NFGNRs], and 81 gram-positive cocci) were tested. In addition, 100 enterobacterial strains with known beta-lactam resistance mechanisms (22 strains with chromosomal AmpC beta-lactamase, 8 strains with chromosomal class A beta-lactamase, 21 broad-spectrum and IRT beta-lactamase-producing strains, 41 extended-spectrum beta-lactamase-producing strains, and 8 permeability mutants) were tested. API galleries and National Committee for Clinical Laboratory Standards (NCCLS) microdilution methods were used as reference methods. The Wider system correctly identified 97.5% of the clinical isolates at the species level. Overall essential agreement (+/-1 log(2) dilution for 3,719 organism-antimicrobial drug combinations) was 95.6% (isolates of the family Enterobacteriaceae, 96.6%; NFGNRs, 88.0%; gram-positive cocci, 95.6%). The lowest essential agreement was observed with Enterobacteriaceae versus imipenem (84.0%), NFGNR versus piperacillin (88.0%) and cefepime (88.0%), and gram-positive isolates versus penicillin (80.4%). The category error rate (NCCLS criteria) was 4.2% (2.0% very major errors, 0.6% major errors, and 1. 5% minor errors). Essential agreement and interpretive error rates for eight beta-lactam antibiotics against isolates of the family Enterobacteriaceae with known beta-lactam resistance mechanisms were 94.8 and 5.4%, respectively. Interestingly, the very major error rate was only 0.8%. Minor errors (3.6%) were mainly observed with amoxicillin-clavulanate and cefepime against extended-spectrum beta-lactamase-producing isolates. The Wider system is a new reliable tool which applies the image-processing technology to the reading of commercial trays for both bacterial identification and susceptibility testing.

Capaccioli L. et al. *[Insertion and management of long-term central venous devices: role of radiologic imaging techniques].* Radiol Med (Torino). 1998; 96(4) : 369-74.p Abstract: INTRODUCTION: Anticancer chemotherapy causes irreversible damage to the endothelial wall of small vessels. This is the reason why long-term (more than 3 months) central venous devices are essential to administer chemotherapy drugs to cancer patients and antibiotics for chronic or severe infections and in patients requiring long-term parenteral nutrition. We report our experience with the percutaneous implantation of central venous devices in a radiology department. MATERIAL AND METHODS: March, 1993, to August, 1997, eighty-seven consecutive patients (26 men and 61 women, mean age: 55 years) were examined. The indications for central venous catheter placement included anticancer chemotherapy in 82 cancer patients, repeated blood transfusion in one patient with bone marrow aplasia and nutritional support in four cancer patients. Eighty-four central venous devices (75 totally subcutaneous systems—Port-a-cath Dome—, and 9 partially tunneled catheters—Groshong) were inserted. The average follow-up was 6.5 months (range: 1-18). All procedures were performed in the radiology department and venous access was achieved with fluoroscopy using the Seldinger technique. Chest radiography with the patient standing was routinely performed after the procedure and repeated the day after to assess the catheter position and the presence of pneumothorax. The venous catheters were placed in the subclavian vein in 68 cases (12 in the right side and 56 in the left side), internal jugular vein in 12 cases (9 in the right side and 3 in the left side) and right femoral vein in 4 cases. We prefer the subclavian vein (80.9%) for better cosmetic results, wider catheter angulation and easier fixation to the deep plane. RESULTS: The first access failed in 6 cases (6.8%). A pneumothorax occurred in 4 patients (4.7%) and late complications were seen in 15 patients (17.8%) after a mean of 15.7 weeks (range: 2-48). Catheter-related infections developed in 6 patients (7.1%) after a mean of 20 weeks (range: 5-48). The microorganisms cultured from these catheters was the Staphylococcus epidermidis. After two weeks' specific antibiotic therapy, all the devices were removed. Deep venous thrombosis occurred only in one patient after 10 months and was successfully treated with direct thrombolytic infusion. The catheter was displaced in the right atrium in two patients after 11 and 12 weeks, respectively: both catheters were removed by transfemoral catheterization. CONCLUSIONS: The percutaneous implantation of—long-term central venous devices is a safe and tol-

erable procedure. In our experience, the radiology-assisted placement of these devices offers many advantages over surgical implantation. In particular, fluoroscopy allows direct visualization of the catheter position while insertion and positioning are essentially "blind" at surgery, which complicates venous access and increases the risk of catheter malpositioning. Radiologic follow-up is also useful to depict and correct complications.

Capdevila J.A. et al. *[Enterobacter amnigenus. An unusual human pathogen].* Enferm Infecc Microbiol Clin. 1998; 16(8) : 364-6.p Abstract: BACKGROUND: Enterobacter amnigenus is a bacteria with doubtful pathogenicity. The observation of a patient with a well-documented E. amnigenus infection has prompted us to review the pathology caused by this microorganism. METHODS: Retrospective evaluation of the clinical charts of patients with any isolate positive for E. amnigenus over a period of 46 months. Based on the clinical data, presence or absence of other causal microorganisms and/or alternative diagnosis, E. amnigenus was classified as definitive, probable, or improbable cause of infection. RESULTS: We analyzed 15 E. amnigenus isolates, representing 0.97 of 10,000, the total bacterial isolates in our laboratory for this period, and 0.52% of those corresponding to Enterobacter sp. We were able to clinically evaluate E. amnigenus in 7 patients, in whom infection by this microorganism was classified as definitive in 4, probable in 1, and improbable in 2. Antibiotic susceptibility studies showed a resistance level of 83% to ampicillin, 75% to cefazoline and cefoxitine, and 33% to amoxicillin-clavulanic acid. All isolates were susceptible to third-generation cephalosporins, aztreonam, ciprofloxacin, cotrimoxazole and aminoglycosides. CONCLUSIONS: E. amnigenus cause well-documented bacterial infection in man. Thus, isolation of this microorganism should not be considered as a contaminant or simple colonizer. The clinical behavior and antimicrobial susceptibility of E. amnigenus is similar to that of E. cloacae, a taxonomically-related species.

Capoluongo E. et al. *DNA heterogeneity of Staphylococcus aureus strains evaluated by SmaI and SgrAI pulsed-field gel electrophoresis in patients with impetigo.* Res Microbiol. 2000; 151(1) : 53-61.p Abstract: To our knowledge, no studies have previously been carried out on the heterogeneity and intrafamily colonization of impetigo Staphylococcus aureus strains obtained by powerful discriminating methods such as pulsed-field gel electrophoresis (PFGE). To explore this topic, macrorestriction patterns of S. aureus strains were analyzed after SmaI and SgrAI digestion. The two enzymes provided superimposable results. A total of ninety-seven S. aureus strains was found in the 26 families whose lesions and nasal and pharyngeal samples were examined. There were 39 strains which were different by PFGE, and of these, 24 were found in the lesions. Although 85% of impetigo patients showed nasal colonization and 58% showed pharyngeal colonization, only 54% of the patients had the same PFGE strain in the lesion and in the nose, and 35% in the lesion and the pharynx. In half of the 26 families, at least one member (mother, father, or relative) presented a S. aureus strain identical, by PFGE, to strains isolated in patients' lesions. Nineteen percent of mothers, 15% of fathers, and 19% of the other relatives presented nasal colonization with strains identical to those isolated in the children's lesions. Lesional strains showed higher antimicrobial resistance than nonlesional isolates.

Cappelletty D. *Microbiology of bacterial respiratory infections.* Pediatr Infect Dis J. 1998; 17(8 Suppl) : S55-61.p Abstract: The upper respiratory tract may become susceptible to bacterial infection as a result of health conditions such as allergies and viral infections, as well as the effects of smoking and airborne environmental pollutants. Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis are the most common bacterial pathogens in upper and lower respiratory tract infections. Streptococcus pyogenes is the predominant bacterial pathogen in pharyngitis and tonsillitis. Bacterial pathogens adhere to mucous membranes and colonization ensues. In an otherwise healthy individual the host immune system responds to the invading bacteria resulting in edema and swelling. If antimicrobial treatment does not eradicate the invading organisms and successfully interrupt the progress of the infection, the patient may develop recurrent or chronic disease. S. pneumoniae and other pathogens once susceptible to penicillin and other antibiotics are now becoming resistant. Bacterial resistance has developed and disseminated because of the widespread use of antibiotics. Major mechanisms of bacterial resistance to antimicrobials in upper respiratory tract infections include enzymatic inhibition, membrane impermeability, alteration of target enzymes, active pumping out of antibiotic and alteration of the ribosomal target.

Carbon C. *Costs of treating infections caused by methicillin-resistant staphylococci and vancomycin-resistant enterococci.* J Antimicrob Chemother. 1999; 44 Suppl A : 31-6.p Abstract: Infection with methicillin-resistant Staphylococcus aureus (MRSA) or vancomycin-resistant Enterococcus faecium (VREF) increases the risk of mortality and results in prolonged hospitalization and high utilization of costly treatment modalities. Measures to prevent the spread of MRSA (and possibly VREF) include patient isolation and decontamination, hygiene measures, ward closure, and screening of patients and staff for carriage. In seriously ill patients, the increased use of vancomycin for the treatment of MRSA can lead to the emergence of VREF colonization/infection. Quinupristin/dalfopristin is effective in the treatment of MRSA infections, including nosocomial pneumonia, skin and soft tissue infection, and septicaemia. In the treatment of nosocomial pneumonia, clinical success rates were equivalent between quinupristin/dalfopristin and vancomycin. In the context of a hospital policy which emphasizes effective hygiene measures and the prudent use of antibacterials, quinupristin/dalfopristin is an effective antimicrobial that can help to control the high costs associated with multiresistant MRSA and VREF infections.

Cardenas M.E. et al. *Antifungal activities of antineoplastic agents: Saccharomyces cerevisiae as a model system to study drug action.* Clin Microbiol Rev. 1999; 12(4) : 583-611.p Abstract: Recent evolutionary studies reveal that microorganisms including yeasts and fungi are more closely related to mammals than was previously appreciated. Possibly as a consequence, many natural-product toxins that have antimicrobial activity are also toxic to mammalian cells. While this makes it difficult to discover antifungal agents without toxic side effects, it also has enabled detailed studies of drug action in simple genetic model systems. We review here studies on the antifungal actions of antineoplasmic agents. Topics covered include the mechanisms of action of inhibitors of topoisomerases I and II; the immunosuppressants rapamycin, cyclosporin A, and FK506; the phosphatidylinositol 3-kinase inhibitor wortmannin; the angiogenesis inhibitors fumagillin and ovalicin; the HSP90 inhibitor geldanamycin; and agents that inhibit sphingolipid metabolism. In general, these natural products inhibit target proteins conserved from microorganisms to humans. These studies highlight the potential of microorganisms as screening tools to elucidate the mechanisms of action of novel pharmacological agents with unique effects against specific mammalian cell types, including neoplastic cells. In addition, this analysis suggests that antineoplastic agents and derivatives might find novel indications in the treatment of fungal infections, for which few agents are presently available, toxicity remains a serious concern, and drug resistance is emerging.

Caridi J.G. et al. *Internal jugular and upper extremity central venous access in interventional radiology: is a postprocedure chest radiograph necessary?* AJR Am J Roentgenol. 2000; 174(2) : 363-6.p Abstract: OBJECTIVE: The necessity of obtaining a postprocedure chest radiograph after central venous access using the upper extremity or internal jugular veins and interventional radiologic techniques was evaluated. SUBJECTS AND METHODS: A prospective study of 937 consecutive central venous access procedures in interventional radiology using the internal jugular veins or upper extremities was performed from June 1995 through September 1997. Established interventional radiologic techniques were used to place various ports (n = 34) and tun-

neled (n = 670) and nontunneled (n = 233) catheters. All catheters were positioned using fluoroscopy and readjusted if necessary before termination of the procedure. Afterward, a chest radiograph was obtained with the patient upright to evaluate catheter position and possible procedural complications. Procedural complications and manipulations or interventions that resulted from the radiographic findings were noted. In addition, nursing time for acquisition of the chest radiograph was recorded. RESULTS: We found seven procedural complications (four air emboli, two pneumothoraces, one innominate vein laceration) significant enough to alter the patient's treatment. These complications were apparent during the examination. Postprocedure chest radiography failed to reveal any unknown complications and revealed only one catheter sufficiently malpositioned to require manipulation. The amount of nursing time to acquire postprocedure chest radiographs ranged from 8 to 40 min (mean, 23 min) per patient. CONCLUSION: When imaging guidance and interventional radiologic techniques are used for upper extremity and internal jugular central venous access, performing postprocedure chest radiography yields little benefit.

Carlson P. et al. *Antimicrobial susceptibilities and biotypes of Arcanobacterium haemolyticum blood isolates.* Eur J Clin Microbiol Infect Dis. 1999; 18(12) : 915-7.p Abstract: Isolates obtained from the blood of ten patients with Arcanobacterium haemolyticum septicaemia were biotyped as smooth or rough using morphological and biochemical criteria, and their susceptibilities to 18 antibacterial agents were determined. Nine of the clinical cases included here have not been reported previously and are discussed in brief. One of the strains was highly resistant to macrolides and clindamycin. With one exception, the strains belonged to the smooth biotype. The data presented here indicates that the treatment of systemic Arcanobacterium haemolyticum infections should be based on the antibacterial susceptibility profiles of individual strains and on the site of the infection.

Carlsson J. et al. *Prior cytomegalovirus, Chlamydia pneumoniae or Helicobacter pylori infection and the risk of restenosis after percutaneous transluminal coronary angioplasty.* Int J Cardiol. 2000; 73(2) : 165-71.p Abstract: We investigated a possible correlation between the serologic status concerning Cytomegalovirus (CMV), Chlamydia pneumoniae (CP) and Helicobacter pylori (HP) and the occurrence of restenosis in patients undergoing percutaneous transluminal coronary angioplasty for symptomatic coronary artery disease. Tests for anti-CMV IgG, anti-Chlamydia pneumoniae IgG and IgA and HP IgG and IgA were performed with an enzyme-linked immunosorbent assay (ELISA). Restenosis was defined as >/=50% stenosis at follow-up angiography in a vessel with less than 50% stenosis immediately after PTCA. Of 148 patients, 112 (75.7%) were seropositive for CMV, 75 (50.7%) were seropositive for CP and 78 (52.7%) were seropositive for HP. Restenosis occured in 31.8% of patients. CMV seropositivity was established in 74.5% of patients with restenosis versus 76.2% without restenosis (P=0.82), CP seropositivity was established in 44. 7% of patients with restenosis versus 53.5% without restenosis (P=0. 32), HP seropositivity was established in 53.2% of patients with restenosis versus 52.5% without restenosis (P=0.94). In contrast to some earlier studies CMV or HP seropositivity could not be found to be associated with the risk of restenosis after coronary intervention. An association between the serological status of CP and restenosis could also not be established.

Carmeli Y. et al. *The association between antecedent vancomycin treatment and hospital-acquired vancomycin-resistant enterococci: a meta-analysis.* Arch Intern Med. 1999; 159(20) : 2461-8.p Abstract: BACKGROUND: The association between vancomycin hydrochloride treatment and vancomycin-resistant enterococci (VRE) has been investigated in numerous studies with variable results. OBJECTIVES: To conduct a meta-analysis to estimate the magnitude of the association between vancomycin treatment and individual risk of VRE and to identify study characteristics that accounted for heterogeneity in study results. METHODS: Studies were identified using MEDLINE with index terms "Enterococcus," "Enterococcus faecalis," or "Enterococcus faecium" and "vancomycin," "drug resistance," "drug resistance, microbial," or "drug resistance, multiple or risk factors." Reports from conferences and reference lists of recent reviews were used. A total of 420 published reports and 98 conference reports were reviewed; 20 studies described in 15 published reports were included in the analysis. We recorded study period, hospital setting, case and control definitions, length of hospital stay, method of adjustment for differences in length of stay, and data on treatment with vancomycin. The odds ratio (OR) of vancomycin treatment provided the measure of association analyzed. A random-effects model was used to estimate the pooled OR. RESULTS: When results from all 20 studies were combined, the pooled OR was 4.5 (95% confidence interval, 3.0-6.9), but the test for heterogeneity was highly significant (P<.001). The 5 studies that used patients with vancomycin-susceptible enterococci as controls found a stronger association (pooled OR, 10.7; 95% confidence interval, 4.8-23.8) than the 15 studies that used controls who had no VRE isolated (pooled OR, 2.7; 95% confidence interval, 2.0-3.8). After restricting the analysis to the latter studies only, no heterogeneity was evident in the unadjusted study results. Patients with VRE had stayed in the hospital much longer than control patients. Studies that adjusted for this difference found only a small and nonsignificant association between vancomycin treatment and VRE (pooled OR, 1.4; 95% confidence interval, 0.74-2.60). We also detected publication bias, favoring report of studies that found a large measure of association. CONCLUSIONS: The reported strong association between vancomycin treatment and hospital-acquired VRE results from the selection of the reference group, confounding by duration of hospitalization, and publication bias. Studies that accounted for these factors found only a small and nonsignificant association.

Carmona O. et al. *Vigilancia de la resistencia bacteriana a los antibioticos en Venezuela.* Rev. Fac. Med. 1995; 18(1) : 74-80.p Abstract: Se presentan los datos de resistencia bacteriana de quince hospitales venezolanos. Se hacen consideraciones sobre la resistencia a los agentes antibacterianos clínicamente relevantes. Se analizan los resultados de las siguientes bacterias: Staphyiciccus aureus, taphylococcus epidermis, enterococcus sp Escherichia coli, Klebsiella pneumoniae, Enterobacter aerogenes, Enterobacter cloacae, Proteus mirabilis, Proteus vulgaris, Salmonella sp., Shigella sp Pseudomas aeruginosa, Streptococcus pneumoniae, Neisseria gonorrhoeae y Neisseria meningitidis(AU).

Carpenter H.A. *Bacterial and parasitic cholangitis.* Mayo Clin Proc. 1998; 73(5) : 473-8.p Abstract: Bacterial cholangitis is a clinically defined syndrome caused by the regurgitation of infected bile into the circulation. The pathogenic mechanism is unclear, and systemic sepsis may not occur. Prerequisite conditions are the presence of microorganisms in the bile and increased biliary pressure. Bacteria that commonly cause cholangitis are Escherichia coli, Klebsiella, Enterococcus, Enterobacter, Pseudomonas, and anaerobes. Although most infections are polymicrobial, this situation may not always prevail. Successful treatment depends on relieving biliary obstruction and administering antibiotics effective against bacteria in the circulation and the bile. The causes of biliary obstruction that predispose to bacterial cholangitis are myriad. Common conditions include biliary stones and benign strictures. In many parts of the world, biliary parasites are an important factor. Biliary parasites cause necrosis, inflammation, fibrosis, strictures, and cholangiectasis of the bile ducts by several mechanisms: (1) as a direct result of the irritating chemical composition of the parasite, parasitic secretions, or eggs; (2) physical obstruction of the bile ducts; (3) induction of formation of biliary stones; and (4) introduction of bacteria into the biliary system during migration from the duodenum. Therefore, bacterial cholangitis has an important and frequently dominant role in the pathogenesis and clinical course of biliary disease due to these parasitic infestations. Common biliary parasites include the nematode Ascaris lumbricoides, the trematodes Opisthorchis viverrini and felineus,

Clonorchis sinensis, and Fasciola hepatica, and the cestodes Echinococcus granulosus and multilocularis. The epidemiologic, pathologic, and clinical manifestations of these parasitic infestations are reviewed.

Carr H.A. *A short history of the Foley catheter: from handmade instrument to infection-prevention device.* J Endourol. 2000; 14(1) : 5-8.p Abstract: Although it is one of the most frequently utilized devices in the hospitalized patient, the Foley catheter has often been taken for granted. This lack of attention is unfortunate, as the Foley catheter remains one of the primary sources of hospital-acquired infections, which increase morbidity, mortality, and the financial burden on the healthcare system. Although education on the appropriate techniques, proper use, and early removal of Foley catheters is important, such measures unfortunately result in transient benefits. Current technologic advancements have moved the coating technology to a state where bacterial adhesion and migration can be limited and the frequency of catheter-associated urinary tract infections can be reduced. Future technological advances in the Foley catheter will help provide better care and comfort for the catheterized patient.

Carricajo A. et al. *Comparative evaluation of five chromogenic media for detection, enumeration and identification of urinary tract pathogens.* Eur J Clin Microbiol Infect Dis. 1999; 18(11) : 796-803.p Abstract: Five chromogenic agar plates—CPS ID2 medium (bioMerieux, France), CHROMagar Orientation medium (Becton Dickinson, France), UriSelect3 medium (Sanofi Diagnostics Pasteur, France), Rainbow Agar UTI medium (Biolog, USA) and Chromogenic UTI medium (Oxoid, Germany)—for the detection, enumeration and direct identification of urinary tract pathogens were compared using 443 urine specimens at two hospital laboratories. The enumeration of microorganisms was consistent on the five media for 403 of the 477 (84.5%) microorganisms. Chromogenic UTI, CPS ID2, UriSelect3, CHROMagar Orientation and Rainbow UTI gave detection rates of 98.3%, 97.9%, 97.3%, 96.9% and 94.1%, respectively, with some problems in yeast growth occurring on Rainbow UTI agar and problems in Staphylococcus spp. growth occurring on UriSelect3. For the direct identification of Escherichia coli, sensitivities were 93.8%, 88.5%, 86.1% and 82.2% for CHROMagar Orientation, CPS ID2, UriSelect3 and Rainbow UTI, respectively. Chromogenic UTI medium did not allow the accurate identification of Escherichia coli, since the indole reaction cannot be applied to this medium. Depending on the media, Enterococcus spp. could be identified at the genus or the species level. Slight differences were detected in the presumptive identification of the Proteus-Morganella-Providencia group and the Klebsiella-Enterobacter-Serratia group. Additionally, on Rainbow UTI agar, 12 of 20 Klebsiella pneumoniae strains and two of nine Pseudomonas aeruginosa strains were correctly identified. In conclusion, CPS ID2 medium and CHROMagar Orientation medium showed similar performance overall, while the UriSelect3, Rainbow UTI and Chromogenic UTI media require some improvement.

Carrion M.I. et al. *Accidental removal of endotracheal and nasogastric tubes and intravascular catheters.* Crit Care Med. 2000; 28(1) : 63-6.p Abstract: OBJECTIVES: To characterize the rates of accidental removal of endotracheal tubes, nasogastric tubes, central venous catheters, and arterial catheters. To assess the efficacy of corrective measures aimed at reducing the accidental removal of these devices. DESIGN: Prospective, observational, and interventional study. SETTING: Eighteen-bed medical-surgical intensive care unit of a 650-bed tertiary care hospital. PATIENTS: Patients admitted to the intensive care unit who had any of the following devices in place for more than 24 hrs: endotracheal tube, nasogastric tube, central venous catheter, arterial catheter. MEASUREMENTS AND INTERVENTIONS: Data were collected on the date of placement of tubes and catheters, position of vascular catheters, date of removal, and reason for removal. The study involved three consecutive 6-month periods. At the end of the first and the second periods, information about rates of accidental removal was provided to the physicians and nurses. In addition, the personnel were instructed to be more vigilant and specific measures aimed at reducing the accidental removal were introduced. MAIN RESULTS: In the first period, 289 endotracheal tubes were placed and 13.1% (24.7 per 1000 days) were removed accidentally. In the second and third periods, 17.1% (25.5 per 1000 days) and 11.4% (15.1 per 1000 days) were removed accidentally, respectively. In the first period, 368 nasogastric tubes were placed and 41% (73.9 per 1000 days) were removed accidentally. In both the second and the third period, a significant reduction in the rate of accidental removal was observed (32.4% or 41.2 per 1000 days and 25.8% or 29.8 per 1000 days, respectively). A significant decrease was observed in the rates of accidental removal of central venous catheters from 7.5% (12.4 per 1000 days) in the first period to 3.6% (5.4 per 1000 days) in the second period. The rate of arterial catheters accidentally removed expressed according to the time at risk significantly decreased from 46.5 per 1000 days in the first period to 19.1 per 1000 days in the second period and 25.3 per 1000 days in the third period. CONCLUSIONS: The information provided by the rates of accidental removal expressed by patient-days is helpful to compare results obtained in populations with different times of follow-up. Education of medical personnel and limiting upper-extremity access to within 20 cm from any catheter or tube resulted in a significant reduction of patient-related removal of tubes and catheters.

Carroll K.C. et al. *Susceptibility of beta-hemolytic streptococci to nine antimicrobial agents among four medical centers in Salt Lake City, Utah, USA.* Diagn Microbiol Infect Dis. 1997; 27(4) : 123-8.p Abstract: A multicenter study was performed to evaluate the susceptibility of beta-hemolytic streptococci to nine antimicrobial agents. MICs were performed in cation-supplemented Mueller-Hinton broth with 3.5% lysed sheep red blood cells according to NCCLS guidelines. A total of 646 isolates were tested: 300 (46%) group A; 170 (26%) group B; 38 (6%) group C, 35 (5%) group F; 83 (17%) group G; and 20 (3%) nongroupable. Six percent of the total isolates were resistant to one or more of the antibiotics tested. Approximately 7% of 387 strains from the University of Utah Hospital and Clinics were resistant to erythromycin. Four isolates were resistant to clindamycin. Six strains (3%) from Primary Children's Medical Center (207 tested) were resistant to one or more of the macrolides. Resistance was rare at the LDS Hospital and the Salt Lake Veteran's Affairs Hospital. Overall, resistance among beta-hemolytic streptococci in this geographic location does not seem to be a significant problem, except at the tertiary care university hospital.

Carsenti-Etesse H. et al. *Epidemiology of bacterial infection during management of open leg fractures.* Eur J Clin Microbiol Infect Dis. 1999; 18(5) : 315-23.p Abstract: In a randomised double-blind trial conducted between 1990 and 1994, 616 patients from 43 centres, pefloxacin (group P, 316 patients) and a cefazolin-oxacillin combination (group C, 300 patients) were compared in the prophylaxis of bone infection after grade 1 and 2 open leg fractures. Samples were obtained at emergency, before and during surgery, and from drain aspirates. Antimicrobial susceptibility, slime production and adherence properties of the bacteria were tested. Cultures at emergency and before surgery showed similar distributions of gram-positive and gram-negative bacteria in both groups, while wound closure and infecting isolates showed prevailing gram-positive bacteria in group P and gram-negative bacteria in group C. Positive cultures at each stage were correlated with the occurrence of infection but were not predictive of the infecting species, which were nosocomial bacteria in most cases. Positive cultures at wound closure warn of a higher infection risk. Twenty-one of 316 (6.6%) patients in group P and 24 of 300 (8%) in group C were considered infected within 3 months. The difference is not significant (chi-square test = 0.42; P = 0.51). Infecting strains were isolated from 38 patients (group P, 18; group C, 20). Infecting species, although not predictable, appear to be those escaping the spectrum of the prescribed antimicrobial prophylaxis.

Carvalho C.B.M. et al. *Transfer of clindamicyn resistance between Bacteroides fragilis group strains isolated from clinical specimens.* Rev. microbiol. 1998; 29. (3. 3) : 183-6.p Abstract: Clindamycin resistance was trasferred by a conjugation-like from Bacteroides thetaiotaomicron 52, a multiple antibiotic-resistant strain isolated from clinical specimens, to other Bacteroides species. A possible association between a plasmid detected in the donor strain and clindamycin resistance in discussed (AU).

Carvalho C.B.M.d. et al. *Epidemiology and antimicrobial resistance of B. fragilis group organisms isolated from clinical specimen and human intestinal microbiota.* Rev. Inst. Med. Trop. Sao Paulo. 1996; 38(5) : 329-35.p Abstract: Alguns aspectos epidemiologicos e o perfil de sensibilidade a antimicrobianos de amostras do grupo B. fragilis isoladas de especime clinico e microbiota intestinal humana foram delineados neste estudo. As especies do grupo B. fragilis foram isoladas de 46 (37 por cento) de 124 especimes clinicos, como segue: hemocultura (3), infeccao intra-abdominal (27), abscesso cerebral (2), infeccao de tecido mole (17), seios da face (3), aspirado pleural (9), abscesso pulmonar (3), ferida cirurgica (22), doenca inflamatoria pelvica (22), otite media cronica (9) e diversos (7). Mais da metade destes microorganismos foram isolados de infeccao intra-abdominal e infeccao de tecido mole...(AU)_.

Casado J.L. et al. *Zidovudine therapy protects against Salmonella bacteremia recurrence in human immunodeficiency virus-infected patients.* J Infect Dis. 1999; 179(6) : 1553-6.p Abstract: Fifty-five human immunodeficiency virus-infected patients with Salmonella bacteremia were studied to assess the rate of and causes for recurrence and to determine the influence on relapse of zidovudine, cotrimoxazole, and antimicrobial suppressive therapy according to the susceptibility of the isolates. Overall, 22% of patients relapsed in a median time of 87 days, independent of CD4 cell count, Salmonella serotype, or duration of antibiotic therapy. The use of zidovudine was associated with the lowest rate of recurrences compared with cotrimoxazole or amoxicillin as suppressive therapy. In the microbiologic assay, zidovudine showed bactericidal effect on Salmonella species at current dosages, and resistance to zidovudine was uncommon (2 cases, 4%). Due to its direct effect on Salmonella species, a zidovudine-containing regimen may protect against the recurrence of the disease.

Casagrande S.T. et al. *Antimicrobial resistance patterns of Haemophilus influenzae isolated from patients with meningitis in São Paulo, Brazil.* Braz. j. med. biol. res. 2000; 33(3) : 295-300.p Abstract: From 1989 to 1995, a total of 391 Haemophilus influenzae isolates were recovered from the cerebrospinal fluid (CSF) of hospitalized patients in São Paulo, Brazil. The majority of strains were isolated from infants aged less than 5 years. Strains belonging to biotype I (64.7 per cent), biotype II (34.5 per cent) and biotype IV (0.76 per cent) were detected. Ninety-nine percent of these strains were serotype b. Minimal inhibitory concentration (MIC) was determined for ampicillin, chloramphenicol and ceftriaxone. The á-lactamase assay was performed for all strains. The rate of á-lactamase producer strains ranged from 10 to 21.4 per cent during a period of 7 years, with an overall rate of 13.8 per cent. Of the 391 strains analyzed, none was -lactamase negative ampicillin resistant (BLNAR). A total of 9.7 per cent of strains showed resistance to both ampicillin and chloramphenicol; however, 4 per cent of them were resistant to ampicillin only and 2 per cent to chloramphenicol. All strains were susceptible to ceftriaxone and the MIC90 was 0.007 mg/ml, suggesting that ceftriaxone could be an option for the treatment of bacterial meningitis in pediatric patients who have not been screened for drug sensitivity. (Au).

Casal M. et al. *Preliminary study of the in vitro activity of irloxacin against mycobacteria.* Chemotherapy. 1995; 41(3) : 204-7.p Abstract: Today Mycobacterium avium and Mycobacterium tuberculosis multidrug resistance are responsible for frequent and severe infections in humans and especially in AIDS patients. Irloxacin is a new quinolone derivative, and shows greater activity with an acid pH. It has a good in vitro antimicrobial spectrum against both gram-positive and gram-negative bacteria. We have compared the in vitro activity of irloxacin against mycobacteria (20 M. tuberculosis, 17 M. avium, 5 Mycobacterium bovis, 5 Mycobacterium chelonae, 5 Mycobacterium fortuitum and 1 Mycobacterium gadium) using the Bactec at pH 6.8 and 5.0, with other quinolones (ofloxacin, ciprofloxacin, pefloxacin and 27753 RP). All quinolones tested showed good activity against mycobacteria at pH 6.8 and 5.0. Irloxacin at pH 5.0 had a greater activity against M. avium.

Casal M. et al. *Study of the in vitro susceptibility of M. tuberculosis to ofloxacin in Spain. Spanish Study Group of M. tuberculosis resistance.* Int J Tuberc Lung Dis. 2000; 4(6) : 588-91.p Abstract: The aim of this study was to determine the proportion of antituberculosis ofloxacin resistance among Mycobacterium tuberculosis strain isolates in Spain. Over a period of one month, 213 M. tuberculosis strains collected from 14 different hospitals were studied, including strains both susceptible and resistant to primary antituberculosis drugs. In 28.1% of the strains, a minimum inhibitory concentration (MIC) for ofloxacin of 0.25 microg/ml was obtained; in 43.6% the MIC was 0.5 microg/ml; in 22.06% it was 1 microg/ml; and in 6.1% it was > or =2 microg/ml. Ofloxacin currently seems to be an effective antimicrobial in vitro against susceptible or multiresistant strains of M. tuberculosis in human immunodeficiency virus (HIV)-negative or HIV-positive patients in Spain.

Casewell M.W. *New threats to the control of methicillin-resistant Staphylococcus aureus.* J Hosp Infect. 1995; 30 Suppl : 465-71.p Abstract: Several countries have achieved considerable success in the control of epidemic methicillin-resistant Staphylococcus aureus (MRSA). However, in several hospitals in the UK, MRSA strains of enhanced epidemicity, notably EMRSA-16, are becoming endemic. Our inability to eliminate the cause of a single-strain outbreak is unfamiliar and unnerving. Factors in 'market-led' health care delivery that hinder control of MRSA include a shortage of inpatient beds, patients moving from ward to ward, and more mixed-specialty wards. Increasing use of day treatments leaves an inpatient hospital population with more risk factors for infection. Early discharge of infected patients to convalescent homes, or to homes for the elderly, has created a new reservoir of infected and colonized patients. The emergence of high-level mupirocin resistance may soon also contribute to failure of control. The transfer of vancomycin resistance from Enterococcus faecium to a laboratory strain of S. aureus suggests that, especially in hospitals with both vancomycin-resistant enterococci and MRSA, there is the opportunity for the emergence of vancomycin-resistant MRSA for which there may be no effective antimicrobial prophylaxis or treatment. It is increasingly important to persuade hospital managers that even partial control of MRSA, whilst expensive, is still cost-effective and is a quality issue for individual hospitals. The control of EMRSA-16 in one hospital has recently been estimated to have saved more than 629,000 pounds extra costs. MRSA continues to be at the forefront of those organisms that seriously challenge modern technological medicine and surgery.

Cassiere H.A. et al. *Community-acquired pneumonia.* Dis Mon. 1998; 44(11) : 613-75.p Abstract: Community-acquired pneumonia (CAP) is a significant cause of morbidity and mortality in all age groups, especially the elderly, which is a patient population that continues to grow. Recently the spectrum and clinical picture of pneumonia has been changing as a reflection of this aging population; this requires a reassessment of and a new approach to the patient with pneumonia. Currently, pneumonia patients are classified as having either community-acquired or hospital-acquired infection rather than typical versus atypical. Patients who have CAP are categorized by age, presence of a coexisting medical illness, and the severity of the pneumonia. The rationale behind categorizing patients is to stratify them in terms of mortality risk to help determine the loca-

tion of therapy (e.g., outpatient, inpatient, intensive care unit) and focus the choice of initial antimicrobial therapy. Once the decision to hospitalize a patient with pneumonia is made, the next step is to decide on an appropriate diagnostic evaluation and antibiotic therapy. Both decisions have evolved over the last several years since the publication of the American Thoracic Society's CAP guidelines. The current approach to the diagnostic work-up of pneumonia stresses a limited role of diagnostic tests and procedures. The antimicrobial regimen has now evolved into one that is empiric in nature and based on the age of the patient, the presence of coexisting medical disease, and the overall severity of the pneumonia. This process is a dynamic once because bacterial resistance to commonly used antibiotics can further complicate the course of pneumonia therapy, but the impact of resistance on outcome is less clear. Resistance of Streptococcus pneumoniae to penicillin is a prime example of this growing problem, and adjustment to pneumonia therapy may be required. A difficult but not uncommon problem in pneumonia patients is slow recovery and delayed resolution of radiographic infiltrates. Factors that impact negatively on pneumonia resolution include advanced age and the presence of serious comorbid illnesses such as diabetes mellitus, renal disease, or chronic obstructive pulmonary disease. In addition, certain organism factors (e.g., intrinsic virulence) may interact with host factors and advanced age to delay pneumonia resolution. For example, 50% of patients with pneumococcal pneumonia have radiographic clearing at 5 weeks, and the majority clear within 2 to 3 months. Recent data demonstrate that radiographic resolution of CAP is most influenced by the number of lobes involved and the age of the patient. Radiographic clearance of CAP decreases by 20% per decade after age 20, and patients with multilobar infiltrates take longer to clear than those with unilobar disease. In general, when approaching slowly resolving infiltrates after pneumonia, bronchoscopic evaluation and lung biopsy are more likely to yield a specific diagnosis if the patient is a nonsmoker younger than 55 years old with multilobar disease. If the patients has either no identifiable factors associated with prolonged pneumonia resolution or the repeat chest radiograph at 1 month shows no appreciable change, further diagnostic testing is indicated. The route and duration of antibiotic therapy, another detail of the management of CAP patients that has changed recently, is complicated by the fact that the majority of patients with CAP have no pathogen identified. Therefore, in most instances the physician initiates empiric antibiotics on the basis of epidemiologic data. If an etiologic pathogen is identified (either initially or at a later time), then the antibiotic spectrum can be narrowed. When no pathogen is discovered, broad-spectrum empiric antibiotics are continued. (ABSTRACT TRUNCATED).

Castaneda E. et al. *Distribution of capsular types and antimicrobial susceptibility of invasive isolates of Streptococcus pneumoniae in Colombian children. Pneumococcal Study Group in Colombia.* Microb Drug Resist. 1997; 3(2) : 147-52.p Abstract: Streptococcus pneumoniae is the leading bacterial cause of childhood pneumonia in the developing world. This study describes the type distribution and antimicrobial susceptibility of invasive pneumococcal isolates from Colombian children and is part of the Sistema Regional de Vacunas (SIREVA), a PAHO regional initiative designed to determine the ideal serotype composition of a protein polysaccharide pneumococcal conjugate vaccine for use in children less than 5 years old in Latin America. In Colombia, during the study period, centres in Bogota, Medellin, and Cali collected 324 S. pneumoniae isolates from invasive diseases, 238 (73.5%) from children under the age of 2. Pneumonia was the clinical diagnosis in 41.3% cases, meningitis in 41%, and sepsis in 11.2%. The seven most frequent types included 14(21.9%), 5(10.5%), 23F(9.6%), 1(9%), 6B(9%), 19F(7.1%), and 6A(6.2%). The frequency of diminished susceptibility to penicillin (DSP) was 12%, with 8.9% of isolates showing intermediate level resistance and 3.1% showing high level resistance. Among DSP isolates, 23% were also resistant to cefotaxime, 33.3% to erythromycin, 48.7% to chloramphenicol, and 74.3% to trimethoprim/sulfamethoxazole. Multiple resistance was detected in 59% of the isolates that have DSP. Penicillin resistance was associated with types 23F (53.8%) and 14 (25.6%). These data provides information on capsular types prevalent in Colombia that will not only allow the formulation of an ideal vaccine for the region but also reinforce the need for ongoing regional surveillance.

Castaneda E. et al. *Penicillin-resistant Streptococcus pneumoniae in Colombia: presence of international epidemic clones. Colombian pneumococcal study group.* Microb Drug Resist. 1998; 4(3) : 233-9.p Abstract: The global spread of multidrug-resistant Streptococcus pneumoniae clones is well documented in the literature. A study to determine type distribution and antimicrobial susceptibility of invasive pneumococcal isolates from Colombian children under the age of 5 was conducted from 1994 to 1996. Health centers in Santa Fe de Bogota, Medellin, Cali, and other cities collected 409 Streptococcus pneumoniae isolates. Diminished susceptibility to penicillin (DSP) was 15.6%; from these, 11.5% showed intermediate-level resistance (ILR) and 4.1% showed high-level resistance (HLR). Fifty-nine of the DSP isolates were examined by pulse field gel electrophoresis (PFGE). Capsular isolate types were 23F (54%), 14 (24%), 19F (10%), 6B (7%), 9V (3%), and 34 (2%). PFGE analysis revealed that 8 isolates shared the Spanish/USA international clone's characteristic features: PFGE pattern type A, serotype 23F; 87.5% exhibited HLR for penicillin, and all were resistant to trimethoprim/sulfamethoxazole (TMP-SMX), tetracycline, and chloramphenicol. Another 7 isolates showed the French/Spanish international clone's features: PFGE pattern type B, 2 of them being serotype 9V; and 5 type 14; HLR to penicillin was 71%, and all proved resistant to TMP-SMX. A large cluster of 24 isolates (41% of all isolates examined) shared a common PFGE type C, with 14 subtypes; all but one, serotype 34, were serotype 23F and had ILR to penicillin; 58% were resistant to TMP-SMX and 50% to tetracycline, but none presented erythromycin or chloramphenicol resistance. The remaining 20 isolates could be grouped into 12 different PFGE types; ILR was shown in 75% of isolates, 70% were resistant to TMP-SMX and to tetracycline, 15% were resistant to erythromycin, and none were resistant to chloramphenicol. These data suggest that some Colombian isolates are clonally related to two of the well-known international epidemic S. pneumoniae clones.

Castellano de Santana A. et al. *Resistencia bacteriana a los antimicrobianos en el Hospital de Niños "J. M de los Ríos" 1991-1993.* Bol. Hosp. Niños J. M. de los Ríos. 1996; 32(3) : 43-58.p Abstract: Se presentan los primeros datos publicados de Resistencia Bacteriana a los antimicrobianos en el Hospital "J.M. de los Ríos" en los años 1991 a 1993 y las cartillas bacteriológicas clínicas. Se analizan los resultados de las siguientes bacterias: Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus sp, Eschericha coli, Klebsiella pneumoniae, Enterobacter cloacae, Enterobacter aerogenes, Proteus vulgaris, Acinetobacter sp, Pseudomona aeruginosa (AU).

Castelli M. et al. *Role of chemotherapeutic antagonism in opportunistic infections.* Anticancer Res. 1997; 17(6D) : 4339-44.p Abstract: The most widely-known anti-tumor drugs often induce marked immunosuppression which can give rise to one or more sepses. Anti-infection measures immediately applied can sometimes prove largely ineffective or even useless, the patient dying not as a result of the spread of the tumour but as a direct consequence of opportunistic infection. We postulate that antagonism between anti-tumour and antimicrobial drugs may also play an important part in this. By way of illustration of this hypothesis, we have studied the action of a number of known inhibitors of peptidoglycan synthesis and of DNA-gyrases on certain strains of Gram-positive and Gram-negative microorganisms cultured in medium containing various concentrations of some of the best-known anti-tumour antimetabolites. The experimental data show that antimicrobial and anti-tumour drugs can sometimes induce synergic or indifferent chemotherapeutic interactions with many bacteria, while in others the effect is antagonistic. In practice, the action of the drugs could lead to bacte-

rial selectivity, which, in conjunction with immunosuppression and the presence of resistant strains, could favour the evolution of opportunistic infection.

Castiglia M. et al. *The global problem of antimicrobial resistance.* J Am Pharm Assoc (Wash). 1997; NS37(4) : 383-7.p Abstract: Along with other multidrug-resistant pathogens previously identified, Streptococcus pneumoniae is becoming a serious concern in hospital and ambulatory care settings. The AIDS pandemic has increased the threat of resistance in Mycobacterium tuberculosis. Antimicrobial drug resistance involves three molecular mechanisms drug inactivation, altered cell permeability, and alteration of target sites. Surveillance and multidisciplinary approaches will be key to containing the threat of global antimicrobial resistance.

Catalano O.A. et al. *Efficacy of percutaneous abscess drainage in patients with vancomycin-resistant enterococci.* AJR Am J Roentgenol. 2000; 175(2) : 533-6.p Abstract: OBJECTIVE: We reviewed a 4-year experience draining fluid collections infected with vancomycin-resistant enterococci to determine the outcome of percutaneous intervention in patients with this highly resistant and increasingly common organism. MATERIALS AND METHODS: Charts of patients from whom vancomycin-resistant enterococci had been isolated during percutaneous drainage were reviewed to determine patient response to drainage, catheter management, and outcome of treatment. RESULTS: Twenty-one patients underwent percutaneous drainage of 28 fluid collections from which vancomycin-resistant enterococci were isolated, including 16 intraabdominal abscesses, seven biliary or urinary obstructions, and five empyemas. The drainage of 27 (96%) of 28 collections were technically successful. In seven patients, drainage provided the first isolation of vancomycin-resistant enterococci from the patient. Five patients also had blood cultures with positive findings for vancomycin-resistant enterococci, and 14 collections were coinfected with other bacteria or with fungi. Twenty collections (71%) or obstructions were successfully treated with percutaneous drainage. Drainage was unsuccessful in treating eight collections in seven patients. CONCLUSION: Despite high-level antibiotic resistance, fluid collections infected with vancomycin-resistant enterococci can be successfully drained percutaneously, resulting in a favorable likelihood of recovery for patients.

Catalao Dionisio L.P. et al. *Occurrence of Salmonella spp in estuarine and coastal waters of Portugal.* Antonie Van Leeuwenhoek. 2000; 78(1) : 99-106.p Abstract: The presence of Salmonella and its relationship with indicator organisms of fecal pollution, such as total coliforms, fecal coliforms and fecal streptococci, was studied at two marine zones in Portugal. Seventeen different Salmonella serotypes were isolated and identified, S. virchow was the most frequently isolated (21.6%). In addition, a high percentage (35.1%) was recorded for some Salmonella serotypes of clinical significance, namely S. enteritidis, S. infantis, S. typhimurium and S. virchow. In any of the samples from the two zones Salmonella was not detected in the absence of any of the indicator organisms. However, the incidence of Salmonella as a function of indicator concentration intervals established by the EEC standards was 0, 10 and 19.3% at guide values of total coliforms, fecal coliforms and fecal streptococci, respectively in the Faro samples (south of Portugal). In contrast, Salmonella incidence rates of 37.5, 36.4 and 33.3% were recorded at the corresponding guide values the Caminha samples (north of Portugal). No significant correlations ($p>0.005$) were obtained between Salmonella and the indicators at the sampling stations; however, total coliforms and fecal streptococci were the indicators most closely related to Salmonella in Caminha and Faro samples, respectively. Survival experiments in Escherichia coli, Enterococcus faecalis and S. typhimurium, using diffusion chambers, were performed to verify whether the lack of correlation between indicators and Salmonella was due to different inactivation rates in seawater. The results indicate that survival percentages of the three microorganisms tested were similar after 48 h of exposure to seawater.

Catchpole C. et al. *Multidrug-resistant Streptococcus pneumoniae.* Microb Drug Resist. 1996; 2(4) : 431-2.p Abstract: Antimicrobial resistance in pneumococci is well established. Of major concern is the development of resistance to penicillin; however, reduced susceptibility to other commonly used agents such as chloramphenicol, erythromycin, and tetracycline has also been observed with increasing frequency. We wish to report the isolation of a clinical strain of Streptococcus pneumoniae with intermediate susceptibility to penicillin (minimum inhibitory concentration, 1 mg/L), which was also resistant to numerous other antimicrobial agents.

Caudry S.D. et al. *Contaminated toothbrushes and their disinfection.* J Can Dent Assoc. 1995; 61(6) : 511-6.p Abstract: Twenty toothbrushes used by healthy subjects were screened for the presence of microorganisms. Microbes were dislodged from the brushes by vortexing, and an average of 4 x 10(3) CFU/mL were recovered from the suspending fluid. Bristles removed from the vortexed brushes still yielded confluent bacterial growth on brain-heart infusion agar medium. Virkon (one per cent), Listerine, Cepacol, Scope, and Plax were tested for their bactericidal effects on microorganisms sedimented from the suspending fluid, on toothbrush bristles and proxabrushes, and on various test species including Candida albicans, Mycobacterium smegmatis, M. bovis, and Streptococcus mitis. Virkon and Listerine killed all the test species and virtually all the microorganisms on the toothbrush bristles and proxabrushes. Six volunteers tested the efficacy of a Listerine soaking regime to prevent the bacterial contamination of toothbrushes. Soaking the toothbrush head (bristles) in Listerine for 20 minutes after brushing was sufficient to eliminate bacterial contamination.

Cauet D. et al. *Surveillance of hospital acquired infections: presentation of a computerised system.* Eur J Epidemiol. 1999; 15(2) : 149-53.p Abstract: Day by day surveillance of hospital acquired infections is a time-consuming activity. Healthcare professionals need powerful computer tools to manage and analyse these data. Such a program must include all the functions needed to manage communication with other programs in order to minimise data entry. Coherence checks are then used to validate data. Automatic production of reports, graphics or tables enables users to quickly obtain timely and representative documents regarding the evolution of specific indicators. The local person in charge for the system must be able to easily modify many parts of the program (data entry screens, calculations, checks, etc.) without any direct intervention from a computer specialist. Using this description, we have created a specific software for the management of this information named NosoCom. The program has been used for four years in France and Belgium. An English release is now available.

Cazzadori A. et al. *Aetiology of pneumonia following isolated closed head injury.* Respir Med. 1997; 91(4) : 193-9.p Abstract: Patients undergoing mechanical ventilation (MV) after an isolated closed head injury (ICHI) have often been found to develop hospital-acquired pneumonia (HAP) well before subjects who require MV for different reasons. In a prospective study of patients receiving MV after an ICHI. 38 subjects (out of 65 with clinically suspected HAP) had a bacteriological diagnosis established on the basis of correspondence between cultures made from bronchoalveolar lavage and protected specimen brush (with quantitative thresholds of 10(4) and 10(3) cfu ml-1, respectively). Patients were separated according to the time of onset of HAP, with 20 subjects who developed HAP within 4 days of the start of MV (early onset pneumonia, EOP) and 18 subjects who developed HAP after the fourth day (late onset pneumonia, LOP). In those who had LOP, an expected spectrum of organisms was found, with Gram-negatives (especially Pseudomonas sp.) accounting for the majority of isolates. However, in EOP cases, Gram-positive bacteria (especially Staphylococcus sp. and Streptococcus pneumoniae) were found to largely predominate ($P = 0.0000026$). This confirms the high incidence of staphylococcal pneumonia in neurosurgery patients, and also provides evidence that

the vast majority of such staphylococcal pneumonia are EOP. Unlike most previous reports, the microbiological findings from the present study suggest that a cut-off point of 4 days successfully distinguishes between EOP and LOP. Since these two clinical entities differ significantly in terms of pathogenesis and aetiology, preventive measures and therapeutical protocols have to be tailored accordingly.

Celenligil H. et al. *Periodontal status and serum antibody responses to oral microorganisms in Sjogren's syndrome.* J Periodontol. 1998; 69(5) : 571-7.p Abstract: Sjogren's syndrome is an autoimmune disease characterized by keratoconjunctivitis sicca and xerostomia. Rapid bacterial plaque accumulation occurs in Sjogren's syndrome patients due to decreases in salivary flow rate. The purpose of this study was to evaluate the periodontal status of patients with Sjogren's syndrome and evaluate serum antibody responses to selected oral microorganisms, including major periodontopathogens, compared to healthy controls. Seventeen Sjogren's syndrome patients and 14 healthy subjects were included in the study. Plaque (PL), sulcular bleeding (SBI), periodontal index scores (PI), probing depths (PD), and total number of teeth were recorded. An ELISA was used to determine the serum IgG antibody level to a panel of 13 oral microorganisms. Significantly higher PL, SBI, PD, and PI scores, as well as an increased number of lost teeth were observed in patients with Sjogren's syndrome compared to healthy subjects (P <0.0001). Antibody levels to Streptococcus oralis were significantly lower in Sjogren's syndrome patients than controls (P <0.0002). These patients exhibited significantly elevated antibody levels to Actinobacillus actinomycetemcomitans and Porphyromonas gingivalis compared to controls (P <0.006 to 0.0004). Our findings indicate that Sjogren's syndrome patients have established periodontal disease and serum antibody responses to oral microorganisms previously identified as periodontopathogens in systemically healthy subjects. These results suggest that Sjogren's syndrome may affect bacterial colonization in plaque and contribute to increased periodontal disease in this compromised population.

Celenligil-Nazliel H. et al. *Periodontal findings and systemic antibody responses to oral microorganisms in Behcet's disease.* J Periodontol. 1999; 70(12) : 1449-56.p Abstract: BACKGROUND: Behcet's disease is a multisystem disorder of unknown etiology, affecting predominantly the oral mucosa, skin, and eyes. Recurrent and painful episodes of oral ulcerations interfere with regular oral hygiene leading to rapid bacterial plaque accumulation. The aims of this study were to evaluate the periodontal status of patients with Behcet's disease and determine serum antibody responses to selected oral microorganisms, including major periodontopathogens in these patients. METHODS: Thirty-three patients with Behcet's disease and 15 healthy subjects were included in the study. Plaque, sulcular bleeding, periodontal index scores, probing depths, and total number of teeth were recorded. Serum IgG antibody levels to a panel of 13 oral microorganisms were determined. RESULTS: Significantly higher values for each of the clinical measures were observed in patients with Behcet's disease compared to healthy subjects (P <0.0001). Antibody levels to selected members of plaque, including Actinomyces viscosus, Streptococcus mutans, Streptococcus sanguis, Streptococcus oralis, Eikenella corrodens, Campylobacter rectus, and Prevotella intermedia were significantly lower in patients with Behcet's disease than in controls (P <0.001-0.05). In contrast, these patients exhibited significantly elevated antibody levels to Actinobacillus actinomycetemcomitans Y4 compared to controls (P <0.01). CONCLUSIONS: Our data indicate that the patients with Behcet's disease generally exhibit clinical findings of established periodontal disease. Decreased antibody responses to early colonizers of both supra- and subgingival plaque were observed along with the elevation in antibody levels to A. actinomycetemcomitans. These results suggest that the bacterial plaque ecology and/or immune responses to these microorganisms may be affected in Behcet's disease which could lead to changes in the expression of periodontal disease.

Cellesi C. et al. *Susceptibility of macrolide and beta-lactam antibiotics of Streptococcus pyogenes strains isolated over a four-year period in central Italy.* J Chemother. 1996; 8(3) : 188-92.p Abstract: In vitro susceptibility to erythromycin, azithromycin, penicillin G, ceftriaxone and ceftibuten was investigated in 190 Streptococcus pyogenes strains isolated over a 4-year period (1991-1994) from patients attending a university hospital located in central Italy. The rate of susceptibility to macrolide antibiotics of the S. pyogenes strains showed a progressive decrease (from 90.3% in 1991 to 79.5% in 1994), while all strains were susceptible to the three beta-lactam antibiotics. Owing to the reduced prevalence of macrolide-susceptible S. pyogenes strains, in vitro susceptibility testing of streptococcal isolates appears to be always necessary before starting a macrolide-based chemotherapy. Concerning beta-lactams, ceftriaxone presented minimum inhibitory concentrations (MIC) always equal to or lower than those of penicillin G, while the oral long-acting cephalosporin, ceftibuten, had MICs higher than those of the other beta-lactams, although in the susceptible range. Results of in vitro susceptibility testing are discussed in relation to their implications for antimicrobial chemotherapy of S. pyogenes infections.

Centeno J.A. et al. *Main microbial flora present as natural starters in Cebreiro raw cow's-milk cheese (northwest Spain).* Int J Food Microbiol. 1996; 33(2-3) : 307-13.p Abstract: Thirty samples of Cebreiro, a fresh or short-time-ripened raw cow's-milk cheese produced in Northwest Spain, were analyzed for the presence of aerobic mesophilic bacteria, (AMC) lactic acid bacteria (LAB), enterococci and Micrococcaceae. Mean AMC and LAB counts exceeding 10(9)/g were higher than those reported for other fresh or short-time-ripened cheeses, although Micrococcaceae occurred in lower numbers (< 10(5)/g) than reported for other raw-milk cheeses. Out of a total of 126 LAB representation isolates, 59 were identified as enterococci (38 as Enterococcus faecalis) 30 as lactococci (24 as Lactococcus lactis subsp. lactis), 25 as leuconostocs (14 as Leuconostoc mesenteroides) and 6 were identified as mesophylic lactobacilli. The enterocci in general were more proteolytic and produced more diacetyl/acetoin than the other LAB groups lactic acid bacteria isolated. It seems that a starter for making Cebreiro cheese should contain these microorganisms so as to reproduce the typical characteristics of traditional raw milk Cebreiro cheeses.

Cercenado E. et al. *Enhanced activity of the combination of penicillin G and gentamicin against penicillin-resistant viridans group streptococci.* Antimicrob Agents Chemother. 1995; 39(12) : 2816-8.p Abstract: We evaluated the effects of the combination of penicillin G and gentamicin against 10 penicillin-resistant bacteremic isolates of viridans group streptococci for which the MICs of penicillin were 4 to 64 micrograms/ml. In time-kill studies, the combination resulted in more killing of eight isolates for which the MICs of penicillin were from 8 to 64 micrograms/ml than any of the antimicrobial agents tested alone. In general, clearly enhanced antimicrobial activity was observed with the combination.

Cercenado E. et al. *Emergence of teicoplanin-resistant coagulase-negative staphylococci.* J Clin Microbiol. 1996; 34(7) : 1765-8.p Abstract: Over a period of 5 years we have recovered 32 clinical isolates of coagulase-negative staphylococci (CoNS) exhibiting either decreased levels of susceptibility or true resistance to teicoplanin (MICs, 16 to 128 micrograms/ml); these isolates make up 0.55% of the total CoNS isolated by us. Twenty-nine of the strains were also methicillin resistant, and all were susceptible to vancomycin. Fourteen of the strains were Staphylococcus epidermidis, fourteen were Staphylococcus haemolyticus, and four were Staphylococcus hominis. In one case, a strain of S. haemolyticus was isolated with a vancomycin-resistant, teicoplanin-resistant Enterococcus faecalis strain. All strains were nosocomially acquired and were isolated from 17 different wards. Teicoplanin resistance occurred as a sporadic phenomenon, and none of the isolates were epidemiologically related. The isolates were from 30 patients, 13 of whom presented with true

infections (43%). Five (38%) of the 13 patients with true infections had been previously treated with vancomycin. None of the infected patients were previously treated with teicoplanin. The in vivo development of resistance to teicoplanin among CoNS strains limits the therapy of infections by these microorganisms. There is a need for surveillance of nosocomial isolates of CoNS to determine resistance to glycopeptides.

Cereda R.F. et al. *[In vitro susceptibility testing of 446 clinical isolates of gram-positive bacteria to new quinolones, carbapenems and cephalosporins].* Rev Assoc Med Bras. 1996; 42(3) : 130-4.p Abstract: OBJECTIVE: To assess the in vitro susceptibility of gram-positive bacteria isolated in the Sao Paulo Hospital against five fluoroquinolones, three carbapenems and three cephalosporins. MATERIALS AND METHOD: Susceptibility was tested in 77 isolates of streptococci, 38 enterococci, 25 S. aureus and 91 S. epidermidis. The strains were isolated in the Sao Paulo Hospital in June and July of 1992. The susceptibility testing was performed by broth microdilution according to the procedure described by the national committee for Clinical Laboratory Standards (NCCLS). The antimicrobial agents tested were: ciprofloxacin, ofloxacin, levofloxacin, grepafloxacin (formerly OPC 17116), DU-6859, imipenem, meropenem, biapenem, ceftazidime, cefepime and FK-037. RESULTS: The best in vitro activity was demonstrated by the new fluoroquinolones, especially DU 6859. Among the commercially available compounds, the fluoroquinolones ciprofloxacin and ofloxacin (81% susceptibility) and the carbapenem imipenem (74% susceptible) were the most active compounds. The highest resistance rates were shown by enterococci and oxacillin-resistant staphylococci. CONCLUSIONS: The results of the present study showed that the in vitro activities of the new carbapenems are similar to that of imipenem and the fourth generation cephalosporins are more active than ceftazidime against gram-positive bacteria. In addition, the newer fluoroquinolones were four to sixteen-fold more active than that showed by the commercially available compounds of this class, especially against enterococci and oxacillin-resistant staphylococci. These results indicate that these newer fluoroquinolones should be further evaluated in clinical trials.

Cereda R. et al. *In vitro antimicrobial activity against enterococci isolated in a university hospital in São Paulo, Brazil.* Braz. j. infect. dis. 1997; 1(2) : 83-90.p Abstract: The prevalence of multiresistant enterococci (MRE) is rapidly increasing and becoming an important problem in several countries. Säo Paulo Hospital is a 600-bed tertiary hospital located in Säo Paulo, Brazil. The use of vancomycin is very high in the hospital due to the high prevalence of multi-resistant S. aureus (around 70 percent). We susceptibillity tested 250 isolates were of Enterococci consecutively collected between March, 1994 and june, 1995. Isolates were susceptibility tested using agar dilution disc diffusion BHI screen plating, and E. test. In addition to vancomycin and teicoplanin, the isolates were tested against amplicillin, gentamicin, streptomycin and RP 59-500. Methods used for susceptibility testing were compared. None of the isolates showed high-level resistence to vancomycin or teicoplanin. The MIC9Os for teicoplanin were menor igual que 1æg/mL for E. faecalis (EF,n-216), E. faecium (EFM,n=23) and for the non-faecalis-non-faecium (NFNF,n=11) species. The MIC90s for vancomycin were 2æg/mL, 4æg/mL and 4æg/mL for EF, EFM and NFNF respectively. Eight isolates (3.2 percent), 5 E. faecalis, 2 E. caseliflavus and 1 E. gallinarum presented intermediate MICs for vancomycin (6 - 12æg/mL), but they were highly susceptible to teicoplanin (MIC0.19 - 1æg/mL). The percentage of resistence to amplicillin and high-level resistence to gentamicin and streptomycin were, respectively: 4.8 percent, 26.4 percent, and 24.8 percent. In spite of the high usage of vancomycin in our hospital, the prevalence of glycopeptide resistence among enterococci seems to be low. Teicoplanin appears to be more potent than vancomycin, RP59-500, gentamicin, streptomycin and amplicillin against this genus, especially EFM and NFNF species. (AU);.

Cervantes-Sanchez C.R. et al. *Syringe pressure irrigation of subdermic tissue after appendectomy to decrease the incidence of postoperative wound infection.* World J Surg. 2000; 24(1) : 38-41; discussion 41-2.p Abstract: To evaluate syringe pressure irrigation of the surgical wound to decrease its infection after appendectomy, we designed a randomized control trial at the Emergency Department of Mexico City General Hospital, including 350 patients with acute abdomen suggestive of appendicitis, without any other infection clinically evident. The trial was randomized into 2 groups. Group I patients received prophylactic systemic antibiotics before surgery. Group II patients received the same prophylactic systemic antibiotics plus syringe pressure irrigation of the surgical wound with 300 ml of saline solution using a 20-ml syringe with 19-gauge intravenous (IV) catheter to measure the incidence of postoperative wound infection. In our results, 283 patients had appendicitis. Of these, 188 were uncomplicated (66.4%) and 95 (33.6%) were complicated. Of the complicated cases, 40 were assigned to group I, and of these, 29 (72. 5%) developed wound infection. In group II there were 55 patients and only 9 (16.3%) developed wound infection after syringe pressure irrigation [p = 0.000001; 95% confidence interval (CI) = 0.02-0.22]. We conclude that syringe pressure irrigation of the surgical wound after appendectomy contributes significantly to decrease the incidence of postoperative wound infection in complicated cases. It is a cheap, safe, and accessible method in any surgical room.

Cestari V. et al. *[Surgical wound infection. Review of the guidelines and results of a prevalence study by the Presidio Ospedaliero de Voghera].* Minerva Chir. 1999; 54(5) : 319-23.p Abstract: BACKGROUND: A prevalence study regarding hospital acquired infections and particularly surgical wound infections was performed from 17-4-1995 to 17-7-1995 in the Voghera hospital, a large one in Northern Italy. METHODS: The records of all subjects who have operated since at least 24 hours have been checked and the surgical wounds have been classified according to the guidelines of CDC (Atlanta). RESULTS: The prevalence rate of surgical wound infections was 13.73% of operated patients, confirming the seriousness of the problem of nosocomial infections surveillance. Pseudonomas aeruginosa (31.27%) and Staphylococcus aureus (21.92%) were the most frequently isolated organisms. CONCLUSIONS: Finally, behaviour guideline have been reproposed to try to reduce surgical wound infections for a best Quality of care in the light of a Regional credit.

Cetinkaya Y. et al. *Vancomycin-resistant enterococci.* Clin Microbiol Rev. 2000; 13(4) : 686-707.p Abstract: After they were first identified in the mid-1980s, vancomycin-resistant enterococci (VRE) spread rapidly and became a major problem in many institutions both in Europe and the United States. Since VRE have intrinsic resistance to most of the commonly used antibiotics and the ability to acquire resistance to most of the current available antibiotics, either by mutation or by receipt of foreign genetic material, they have a selective advantage over other microorganisms in the intestinal flora and pose a major therapeutic challenge. The possibility of transfer of vancomycin resistance genes to other gram-positive organisms raises significant concerns about the emergence of vancomycin-resistant Staphylococcus aureus. We review VRE, including their history, mechanisms of resistance, epidemiology, control measures, and treatment.

Chachaty E. et al. *Shedding of antibiotic-resistant members of the family Enterobacteriaceae in healthy residents of France and Jordan.* Res Microbiol. 1995; 146(2) : 175-82.p Abstract: We compared the frequency of shedding of members of the family Enterobacteriaceae resistant to ampicillin, tetracycline, chloramphenicol, kanamycin, gentamicin and ceftazidime in 83 French residents of the Paris urban area and in 101 subjects in Jordan, 64 of whom resided in the urban area of Irbid, 15 in rural areas, and 22 of whom had a nomadic lifestyle. There was no significant difference between these populations regarding (i) the percentages of subjects with strains resistant to any of the antimicrobial agents tested and (ii) the proportions of total counts of organisms of the Enterobacteriaceae resistant to these

agents. The simultaneous shedding of strains resistant to ampicillin, chloramphenicol, tetracycline and kanamycin was significantly associated with (i) exposure to antibiotic treatment during the six months preceding the study and (ii) the presence of many children at home.

Chai F.C. et al. *Malignant otitis externa caused by Malassezia sympodialis.* Head Neck. 2000; 22(1) : 87-9.p Abstract: BACKGROUND: Malignant otitis externa caused by fungal infections is rare. A review of the literature showed only 9 cases, and the causative fungus in all cases was Aspergillus. This article reports an unusual case caused by Malassezia sympodialis. METHODS: A 53-year-old man with non-insulin dependent diabetes presented with malignant otitis externa. He deteriorated despite treatment with intravenous antipseudomonal therapy and surgical debridement. Microbiologic tests revealed M. sympodialis. He responded rapidly to intravenous amphotericin. RESULTS: Systemic human infections caused by M. sympodialis have not been reported. M. furfur systemic infection is rare and has been associated lipid hyperalimentation by means of a central catheter. Only 1 other case of M. fungemia without these associated risk factors has been reported. CONCLUSIONS: The first case of malignant otitis externa caused by M. sympodialis is presented. It highlights the difficulty of initial biologic diagnosis and the need for lipid-enriched media to grow this fastidious organism. Copyright 2000 John Wiley & Sons, Inc. Head Neck 22: 87-89, 2000.

Chaieb J.A. *Mecanismos infecciosos na patogenia da asma.* Rev. bras. alergia imunopatol. 1995; 18(1) : 27-32.p Abstract: There has been general acceptance that upper and lower respiratory infections are implicated in the pathogenesis of asthma. Identification of different virus infections associated with recurrent wheezing or asthmatic attacks opened a wide field for research that provided many conflicting results. This review analyses the more relevant, prospective and retrospective trials and discuss the mechanism of infection induced asthma (AU).

Chaisson R.E. et al. *Prevention of opportunistic infections in the era of improved antiretroviral therapy.* J Acquir Immune Defic Syndr Hum Retrovirol. 1997; 16 Suppl 1 : S14-22.p Abstract: Patients with advanced human immunodeficiency virus (HIV) infection who are severely immunosuppressed develop a variety of opportunistic infections that have a significant impact on their well-being, quality of life, health-care costs, and survival. The risk for development of opportunistic infections depends on exposure to potential pathogens, the virulence of the pathogens, the degree of host immunity, and the use of antimicrobial prophylaxis. Many studies have confirmed the benefits of prophylaxis in severely immunosuppressed patients. Factors that affect the use of prophylaxis for prevention of opportunistic infections in HIV-infected patients include the prevalence and potential severity of the disease, ease of treatment if infection occurs, the cost-effectiveness of the prophylactic regimen, and the potential for increased survival, drug toxicity, drug interactions, and emergence of resistance with the regimen. The United States Public Health Service and the Infectious Diseases Society of America (USPHS/IDSA) have established disease-specific recommendations for use of prophylaxis for opportunistic infections in HIV-infected patients. These guidelines identify regimens that are strongly recommended as standards of care, regimens that should be seriously considered in selected patients, and regimens that are not routinely indicated but may be considered in selected patients. Although further study is needed, advances in antiretroviral therapy may have an important impact on the recommendations for prophylaxis and may eventually allow discontinuation of these regimens in patients who regain functional immunity.

Chalandon Y. et al. *Agrobacterium yellow group: bacteremia and possible septic arthritis following peripheral blood stem cell transplantation.* Bone Marrow Transplant. 2000; 26(1) : 101-4.p Abstract: A 47-year-old male patient developed sepsis and monoarticular arthritis following autologous stem cell transplantation for recurrent Hodgkin's disease. Blood cultures were positive for Agrobacterium yellow group. The knee pain and swelling responded promptly to the institution of empirical broad-spectrum antibiotics. Recurrent bacteremia developed necessitating Hickman line removal for eventual resolution of the infection. Transplant physicians should be aware of this unusual pathogen and the potential for both persistent line-related sepsis and possible septic arthritis.

Chalkley L.J. et al. *Plasmid analysis of Neisseria gonorrhoeae isolates and dissemination of tetM genes in southern Africa 1993-1995.* J Antimicrob Chemother. 1997; 40(6) : 817-22.p Abstract: One group (145 isolates) of Neisseria gonorrhoeae was collected from municipal clinics in Bloemfontein in 1994 and a second group (65 isolates) in 1995. Penicillin and tetracycline MICs were determined and plasmid analysis performed to monitor antimicrobial susceptibilities in conjunction with the occurrence of plasmids in these isolates. The prevalence of penicillin resistance caused by beta-lactamase plasmids remained constant at 9% during the study period. Three high-level tetracycline-resistant strains (MICs 16 mg/L), the first to be detected in South Africa, were isolated in 1994. Although there was a reduction in the percentage of isolates harbouring 24.5 MDa conjugative plasmids (from 79% in 1994 to 46% in 1995), this was partially counteracted by an increase in TetM-encoding conjugative plasmids (25.2 MDa) from 2% to 18.5%. The tetM genes of 13 isolates shown to exhibit high-level tetracycline resistance were characterized as the American type. The American-type tetracycline resistance plasmid was demonstrated in 11 isolates. Digestion with Bg/l showed that two isolates harboured tetM-encoding plasmids that differed from the American- and Dutch-type plasmids described previously: one isolate contained a plasmid that produced two fragments of different sizes from those of the American-type plasmid and the second isolate possessed an American/Dutch hybrid plasmid. Auxotyping/serotyping and random amplified polymorphic DNA analysis revealed a predominant tetracycline-resistant family (NR/IA-6, genomic group I) in Bloemfontein. As there is a high incidence of chlamydial infections in southern Africa requiring tetracycline therapy, selective pressures exist in the environment for the maintenance and rapid spread of high-level tetracycline-resistant N. gonorrhoeae. It is possible that tetM genes may have emanated from Botswana and/or Namibia to Bloemfontein. The establishment of high-level tetracycline-resistant N. gonorrhoeae in Bloemfontein was seen to be complex as a related group of strains was identified, plasmid dissemination was evident and two new TetM-encoding plasmids were demonstrated. The appearance of these TetM-encoding plasmids indicates either that the American- and Dutch-type plasmids are continuing to evolve or that tetM genes are being introduced into different families of 24.5 MDa conjugative plasmids.

Chan R.K. *Antimicrobial therapy of non-viral sexually transmitted diseases—an update.* Ann Acad Med Singapore. 1995; 24(4) : 579-83.p Abstract: Azithromycin is an azalide antibiotic with important properties which allow it to be used as a single-dose treatment for genital Chlamydia trachomatic infections. A single 1 g dose is as effective as a standard seven-day course of doxycycline. Ofloxacin 400 mg bid for seven days is also effective against Chlamydia trachomatis. Both azithromycin 2 g and ofloxacin are also effective against uncomplicated gonorrhoea. Neisseria gonorrhoeae continues to be sensitive to third generation cephalosporins, e.g. ceftriaxone 125 mg. Oral single dose cephalosporins offer ease of administration and safety, e.g. cefixime (400 mg), cefuroxime axetil (1 g) and cefpodoxime proxetil (200 mg). The fluoroquinolones, e.g. ciprofloxacin (500 mg) and ofloxacin (400 mg), are being increasingly used as first-line medications, however, caution is recommended as the development of resistance is anticipated and already being detected in many areas. Syphilis continues to be sensitive to penicillin. This should be administered parenterally. Coexistent human immunodeficiency virus infection may make standard therapy inadequate, and closer follow-up is recommended. Therapy with non-penicillin antibiotics

is still inadequately studied. Chancroid is treated with ceftriaxone, ciprofloxacin, azithromycin, or erythromycin. In some areas, resistance to tetracyclines and TMP-SMX has made these drugs ineffective as first-line treatments. Bacterial vaginosis is effectively treated with a single dose of metronidazole 1 g or 500 mg bid over seven days. Similar regimens are also effective against trichomoniasis. Vulvovaginal candidiasis can be treated with topical imidazole preparations or oral antifungal medications.

Chaney M.A. et al. *Severe incisional pain and long thoracic nerve injury after port-access minimally invasive mitral valve surgery.* Anesth Analg. 2000; 91(2) : 288-90.p Abstract: The authors describe the occurrence of severe postoperative pain and long thoracic nerve injury after Port-Access minimally invasive mitral valve surgery. The potential for these events and the impact on postoperative hospitalization and rehabilitation are emphasized.

Chang F.Y. *Staphylococcus aureus bacteremia and endocarditis.* J Microbiol Immunol Infect. 2000; 33(2) : 63-8.p Abstract: Staphylococcus aureus bacteremia is a serious and common disease often associated with infective endocarditis. It occurs in both healthy, immunologically competent people in the community and compromised patients in the hospitals. For S. aureus bacteremia, questions on clinical issues such as antimicrobial treatment are raised. Is nafcillin/oxacillin superior to vancomycin? Does the addition of rifampin improve outcome? Does addition of aminoglycoside improve the outcome? Does increasing duration of therapy (> 4 weeks versus < 2 weeks) improve outcome? How many cases of community-acquired S. aureus bacteremia have endocarditis on admission? What are the risk factors that would separate bacteremia from endocarditis? What is the role of echocardiography? What are the indications for routine echocardiography? Are methicillin-resistant S. aureus (MRSA) more virulent than methicillin-susceptible S. aureus (MSSA)? What factors predict mortality in S. aureus bacteremia? Herein, the above important issues on S. aureus bacteremia and endocarditis are critically reviewed.

Chang M.C. et al. *Maintaining survivors' values of left ventricular power output during shock resuscitation: a prospective pilot study.* J Trauma. 2000; 49(1) : 26-33; discussion 34-7.p Abstract: OBJECTIVE: Maintaining left ventricular power output (LVP) > 320 mm Hg x L/min/m2 during resuscitation has been retrospectively associated with faster resolution of acidosis and survival after posttraumatic shock. The purpose of this prospective study was to evaluate the effects of maintaining LVP above this threshold during resuscitation on base deficit clearance, organ failure, and survival. METHODS: This was a study of a consecutive series of critically injured patients (PWR) monitored with a pulmonary artery catheter during initial resuscitation. LVP, calculated as cardiac index-(mean arterial pressure-central venous pressure), was maintained >320 mm Hg x L/min/m2 via a predefined protocol by using ventricular pressure-volume diagrams. Outcome was assessed by base deficit clearance (<6 mEq/L) in <24 hours, lowest base deficit in the first 24 hours after admission (24-hr base deficit), organ dysfunctions/patient, and survival. Results were compared with 39 control patients (OXY) with identical enrollment criteria from a previous prospective study who were resuscitated based on oxygen transport criteria. RESULTS: Twenty patients were studied over a 6-month period. Mean LVP during resuscitation in the PWR group was 360 +/- 100 mm Hg x L/min/m2. Admission base deficit was similar between the two groups (PWR 11 +/- 4.2 vs. OXY 11 +/- 5.8 mEq/L;p = 0.66). More PWR patients cleared base deficit in < 24 hours than OXY patients (16 of 20 vs. 17 of 39, p = 0.009, Fisher's exact test), and the PWR patients had a significantly lower 24-hr base deficit (3.9 +/- 3.7 vs. 7.1 +/- 4.6 mEq/L, p = 0.01). Organ dysfunction rate was lower in the PWR group (2.1 +/- 1.5 vs. 3.2 +/- 1.4 organ dysfunctions/patient, p = 0.007). Survival in the PWR group was 15 of 20, versus 21 of 39 in the OXY group (p = 0.10). CONCLUSION: Prospectively maintaining LVP above 320 mm Hg x L/min/m2 during resuscitation is an achievable goal. It is associated with improved base deficit clearance and a lower rate of organ dysfunction after resuscitation from traumatic shock.

Chang S.C. et al. *In vitro activity of meropenem against common pathogenic bacteria isolated in Taiwan.* Diagn Microbiol Infect Dis. 1998; 32(4) : 273-9.p Abstract: The in vitro antimicrobial activity of meropenem, in comparison with nine other antimicrobial agents, against 12 different common pathogenic bacteria were evaluated to know the susceptibility of common bacteria to meropenem in Taiwan. Meropenem was active against most Gram-positive, Gram-negative, and anaerobic bacteria, including methicillin-sensitive Staphylococcus aureus, Streptococcus pyogenes, Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Pseudomonas aeruginosa, Burkholderia cepacia, Acinetobacter baumannii, Haemophilus influenzae, and Bacteroides fragilis. For many of them, meropenem was the most active one in comparison with other broad-spectrum cephalosporins, aztreonam, imipenem, and ciprofloxacin. It is concluded that meropenem is a very active agent against most common pathogenic bacteria. It is uncommon for these common bacteria, except MRSA and Stenotrophomonas maltophilia, to be resistant to meropenem in Taiwan, where a high prevalence of resistance to other antimicrobial agents was found in many of the common bacteria.

Chang S.C. et al. *In vitro activity of quinupristin/dalfopristin against clinical isolates of common gram-positive bacteria in Taiwan.* Diagn Microbiol Infect Dis. 1999; 33(4) : 299-303.p Abstract: The MICs of quinupristin/dalfopristin against common Gram-positive bacteria isolated from various clinical specimens at a university hospital in Taiwan were determined by the agar dilution method. The tested bacteria included methicillin-resistant Staphylococcus aureus (MRSA), methicillin-susceptible S. aureus (MSSA), methicillin-resistant Staphylococcus epidermidis (MRSE), methicillin-susceptible S. epidermidis (MSSE), Streptococcus pyogenes, Streptococcus pneumoniae, and Enterococcus faecalis. With the exception of E. faecalis all bacteria were susceptible to quinupristin/dalfopristin. The MIC50 and MIC90 were, respectively, 0.25 microgram/mL and 0.5 microgram/mL for both MRSA and MSSA; 0.25 microgram/mL and 0.5 microgram/mL for MRSE; 0.25 microgram/mL and 0.25 microgram/mL for MSSE; 0.125 microgram/mL and 0.125 microgram/mL for S. pyogenes; and < or = 0.03 microgram/mL and 0.25 microgram/mL for S. pneumoniae. Eighty-two percent of the tested E. faecalis isolates were intermediately resistant or resistant to quinupristin/dalfopristin, with an MIC50 of 2 micrograms/mL and an MIC90 of 4 micrograms/mL. Quinupristin/dalfopristin seems to be a promising antimicrobial agent against common Gram-positive bacteria other than E. faecalis in Taiwan.

Chang S.C. et al. *High prevalence of antibiotic resistance of common pathogenic bacteria in Taiwan. The Antibiotic Resistance Study Group of the Infectious Disease Society of the Republic of China.* Diagn Microbiol Infect Dis. 2000; 36(2) : 107-12.p Abstract: We analyzed the antimicrobial susceptibilities of all clinical isolates of 14 common pathogenic bacteria recovered from patients in eight medical centers in Taiwan during 1995 and 1996. Susceptibility to commonly used antimicrobial agents was tested by the disk diffusion method as recommended by the National Committee for Clinical Laboratory Standards. Of the Staphylococcus aureus isolates, 59.3% and 62% were oxacillin-resistant in 1995 and 1996, respectively, whereas 63.2% of the coagulase-negative staphylococci isolates during the study period were oxacillin-resistant. The rate of penicillin-resistance among Streptococcus pneumoniae isolates was 39.7% in 1995 and 53.7% in 1996. Macrolide-resistance was found in 71.4%, 42.1%, and 46.7% of S. pneumoniae, beta-hemolytic streptococci, and viridans streptococci, respectively, in 1996. Less than 2% of the enterococcal isolates were vancomycin resistant, but 77% of them were gentamicin resistant. Resistance to gentamicin was also common in Enterobacteriaceae, Pseudomonas aeruginosa, and Acinetobacter

baumannii. Various degrees of resistance to ampicillin, piperacillin, cephalosporins, aztreonam, and ciprofloxacin were detected in Enterobacteriaceae, P. aeruginosa, and A. baumannii. More than 55% of Haemophilus influenzae isolates were ampicillin resistant. In summary, resistance to many antimicrobial agents in various common pathogenic bacteria is very common in Taiwan. Our results implicate that antibiotic resistance in the developing countries need to be monitored closely.

Chaowagul W. et al. *Oral fluoroquinolones for maintenance treatment of melioidosis.* Trans R Soc Trop Med Hyg. 1997; 91(5) : 599-601.p Abstract: Ciprofloxacin (20 mg/kg/d) or ofloxacin (12 mg/kg/d) given for a median of 15 weeks (range 12-40) were used for maintenance treatment of 57 adult patients with melioidosis. The median duration of follow-up in the 45 patients who complied with treatment and were followed for at least 6 months was 28 months (range 6-65). Fluoroquinolone treatment was well tolerated. There were 13 treatment failures (5 failures to respond, 8 relapses), a failure rate of 29% (95% confidence interval 17-43%). The median time to treatment failure was 7 months (range 2-26). These results are inferior to those with courses lasting 20 weeks of amoxycillin/clavulanic acid or the combination of chloramphenicol, doxycycline and trimethoprim/sulphamethoxazole, and suggest that the fluoroquinolones should be reserved as third line agents, and not used for the maintenance treatment of melioidosis unless there is resistance to, or intolerance of, the other available antimicrobial compounds.

Chastre J. et al. *Nosocomial pneumonia in patients with acute respiratory distress syndrome.* Am J Respir Crit Care Med. 1998; 157(4 Pt 1) : 1165-72.p Abstract: To describe the epidemiologic and microbial aspects of ventilator-associated pneumonia (VAP) in patients with acute respiratory distress syndrome (ARDS), we prospectively evaluated 243 consecutive patients who required mechanical ventilation (MV) for > or = 48 h, 56 of whom developed ARDS as defined by a Murray lung injury score > 2.5. We did this with bronchoscopic techniques when VAP was clinically suspected, before any modification of existing antimicrobial therapy. For all patients, the diagnosis of pneumonia was established on the basis of culture results of protected-specimen brush (PSB) (> or = 10(3) cfu/ml) and bronchoalvelolar lavage fluid (BALF) (> or = 10(4) cfu/ml) specimens, and direct examination of cells recovered by bronchoalveolar lavage (BAL) (< or = 5% of infected cells). Thirty-one (55%) of the 56 patients with ARDS developed VAP for a total of 41 episodes, as compared with only 53 (28%) of the 187 patients without ARDS for a total of 65 episodes (p = 0.0005). Only 10% of first episodes of VAP in patients with ARDS occurred before Day 7 of MV, as compared with 40% of the episodes in patients without ARDS (p = 0.005). All but two patients with ARDS who developed VAP had received antimicrobial treatment (mostly with broad-spectrum antibiotics) before the onset of infection, as compared with only 35 patients without ARDS (p = 0.004). The organisms most frequently isolated from patients with ARDS and VAP were methicillin-resistant Staphylococcus aureus (23%), nonfermenting gram-negative bacilli (21%), and Enterobacteriaceae (21%). These findings confirm that microbiologically provable VAP occurs far more often in patients with ARDS than in other ventilated patients. Because these patients are often treated with antibiotics early in the course of the syndrome, the onset of VAP is frequently delayed after the first week of MV, and is then caused mainly by methicillin-resistant S. aureus and other multiresistant microorganisms.

Chatte G. et al. *Aerosolized interferon gamma for Mycobacterium avium-complex lung disease.* Am J Respir Crit Care Med. 1995; 152(3) : 1094-6.p Abstract: It has recently been shown that human alveolar macrophages can be selectively activated without systemic effect by the use of aerosolized interferon-gamma (IFN gamma), a cytokine that enhances macrophage oxidative and antimicrobial activity. We report the case of a 38-yr-old man negative for human immunodeficiency virus (HIV), with silicosis and advanced cavitary lung disease due to Mycobacterium avium intracellulare (MAI), who failed to improve despite 3 yr of continuous medical therapy with three or more drugs. He received three courses of aerosolized IFN gamma (500 micrograms 3 d per week for 5 wk in two courses and 200 micrograms 3 d a week for 5 wk after a short single trial of subcutaneous IFN gamma). The numbers of MAI decreased in the sputum during therapy, but cultures of the organism remained positive at the same level for the first two treatment periods. The patients sputum became AFB smear negative and the number of colonies decreased significantly after the third course of IFN gamma therapy. Cessation of IFN gamma was associated with a rapid increase in the numbers of MAI in the sputum. Aerosolized IFN gamma can be considered as an adjuvant to conventional drug therapy, with a good tolerance, in cases of lung disease caused by resistant MAI.

Chaudhury A. et al. *Biochemical characterisation, enteropathogenicity and antimicrobial resistance plasmids of clinical and environmental Aeromonas isolates.* J Med Microbiol. 1996; 44(6) : 434-7.p Abstract: One hundred and eight strains of Aeromonas from clinical and environmental samples were speciated. Seven species were identified, the most prevalent of which was A. hydrophila. Experimental studies in an animal model with 36 representative strains of different species revealed that all strains could cause significant fluid accumulation in rabbit ileal loops. Of 107 strains showing single or multiple antimicrobial resistance, the highest incidence of resistance was shown for beta-lactam antibiotics other than cefotaxime. Transferable resistance plasmids, encoding resistance to ampicillin, cephalexin, cefoxitin, erythromycin and furazolidone, either alone or in combination, were detected in 35 strains. A further proportion of strains could be cured of one or more resistance markers, including resistance to nalidixic acid, and this was accompanied by the loss of plasmid DNA. The plasmids ranged in size between 85.6 and > 1 50 kb.

Chávez P. A. et al. *Meningitis por streptococcus pneumoniae con sensibilidad disminuída a cefotaxima.* Rev. chil. infectología. 1997; 14(1) : 53-4.p Abstract : Se reporta un lactante de 15 meses de edad, el primer caso de meningitis neumocóccica documentado en el Hospital Exequiel González Cortés, cuyo tratamiento con cefotaxima, en dosis de 200 mg/kg/día, no logró esterilizar el LCR tras 24 horas de aplicación debiendo adicionarse vancomicina según las recomendaciones internacionales vigentes. Las CIM, efectuadas por epsilometría, fueron de 1 æg/ml tanto para penicilina como cefotaxima. El paciente egresó del hospital sin secuelas neurológicas inmediatas aparentes (AU).

Chawla P.G. et al. *Management of hemodialysis catheter-related bacteremia—a 10-year experience.* Pediatr Nephrol. 2000; 14(3) : 198-202.p Abstract: Between January 1986 and December 1995, 18 episodes of bacteremia occurred in our pediatric patients undergoing chronic hemodialysis on an outpatient basis. Seven episodes were caused by coagulase-negative Staphylococcus, 6 by Staphylococcus aureus, 2 by Mycobacterium, and 1 each by Pseudomonas, Xanthomonas, and Enterococcus. In 6 cases, the catheter was retained with antimicrobial therapy alone, whereas 12 cases required removal of the catheter after some period of time. The subset of cases in which catheter removal was necessary included 2 cases of Mycobacterium fortuitum complex and 5 cases of Staphylococcus aureus. We found that Staphylococcus aureus bacteremia may be cleared with antibiotic therapy alone in a minority of cases (17%). In the 6 cases in which catheters were retained and infections cleared, the maximum length of time to sterilization of blood with appropriate antibiotics was 48 h.

Chen C. et al. *Oral food consumption and subgingival microorganisms: subgingival microbiota of gastrostomy tube-fed children and healthy controls.* J Periodontol. 1997; 68(12) : 1163-8.p Abstract: This study examined the effect of oral food consumption on the prevalence and levels of subgingival bacteria and yeasts in 20 gastrostomy tube-fed children and 24 healthy controls. Microbial identification was carried

out using anaerobic culture and 16S rRNA-based PCR identification methods. Streptococcal and Actinomyces species were recovered from 100% and 76% of all subjects and averaged 66% and 11% of total cultivable organisms, respectively. In decreasing order of prevalence, Fusobacterium, enteric rods, Prevotella intermedia/Prevotella nigrescens, Capnocytophaga, Propionibacterium, yeasts, Actinobacillus actinomycetemcomitans, coagulase-negative Staphylococcus, Campylobacter rectus, Bacteroides forsythus, and Porphyromonas gingivalis were detected in 48% to 2% of the study subjects. The cultivable levels of these species varied widely among subjects. PCR detection showed C. rectus and Eikenella corrodens both to occur in 93% of the study subjects and to be the most prevalent putative periodontal pathogens examined. In decreasing order of prevalence, PCR identified Treponema denticola, A. actinomycetemcomitans, P. nigrescens, P. intermedia, B. forsythus, and P. gingivalis in 38% to 21% of the subjects studied. Tube-fed children and healthy controls exhibited similar subgingival microbial compositions. It appears from this study that oral food consumption is not a major determinant for the establishment of subgingival microbiota in children.

Chen D.Z. et al. *Actinonin, a naturally occurring antibacterial agent, is a potent deformylase inhibitor.* Biochemistry. 2000; 39(6) : 1256-62.p Abstract: Peptide deformylase (PDF) is essential in prokaryotes and absent in mammalian cells, thus making it an attractive target for the discovery of novel antibiotics. We have identified actinonin, a naturally occurring antibacterial agent, as a potent PDF inhibitor. The dissociation constant for this compound was 0.3 x 10(-)(9) M against Ni-PDF from Escherichia coli; the PDF from Staphylococcus aureus gave a similar value. Microbiological evaluation revealed that actinonin is a bacteriostatic agent with activity against Gram-positive and fastidious Gram-negative microorganisms. The PDF gene, def, was placed under control of P(BAD) in E. coli tolC, permitting regulation of PDF expression levels in the cell by varying the external arabinose concentration. The susceptibility of this strain to actinonin increases with decreased levels of PDF expression, indicating that actinonin inhibits bacterial growth by targeting this enzyme. Actinonin provides an excellent starting point from which to derive a more potent PDF inhibitor that has a broader spectrum of antibacterial activity.

Chen F.M. et al. *Geocoding and linking data from population-based surveillance and the US Census to evaluate the impact of median household income on the epidemiology of invasive Streptococcus pneumoniae infections.* Am J Epidemiol. 1998; 148(12) : 1212-8.p Abstract: The emergence of drug-resistant Streptococcus pneumoniae poses new clinical challenges and may also reflect a change in the epidemiology of S. pneumoniae infections. A variety of studies have shown that drug-resistant S. pneumoniae infections are linked to antimicrobial use. It has been hypothesized that persons of high socioeconomic status are at increased risk for a drug-resistant infection because of greater access to antimicrobial drugs. To assess whether median household income is associated with increased risk of penicillin-nonsusceptible S. pneumoniae infections, the authors geocoded and linked data from population-based surveillance for invasive pneumococcal disease with data from the 1990 US Census. Among invasive pneumococcal isolates from Atlanta, Georgia, in 1994, increasing proportions of penicillin-nonsusceptible isolates were associated with higher median household incomes (chi2 for trend, 15.17; p=0.002). Despite higher rates of invasive pneumococcal disease among blacks and persons who resided within lower median household income areas, white patients in areas with higher median household income had a higher risk of being infected with strains that were not susceptible to penicillin (Wilcoxon rank sum, Z=2.66, p=0.008). These findings demonstrated the utility of geocoding and US Census data in describing the epidemiology of drug-resistant S. pneumoniae and also provided more evidence that socioeconomic factors may influence the development of drug resistance.

Chen H.Y. et al. *National survey of susceptibility to antimicrobials amongst clinical isolates of Pseudomonas aeruginosa.* J Antimicrob Chemother. 1995; 35(4) : 521-34.p Abstract: Between September and December 1993, each of 24 hospitals in the UK collected up to 100 consecutive clinical isolates of Pseudomonas aeruginosa and sent these to the London Hospital Medical College (LHMC). Of 2184 cultures received, 1991 contained viable P. aeruginosa. Minimum inhibitory concentrations (MICs) of antimicrobials were determined by agar dilution. The frequencies of resistance to low breakpoints were as follows: gentamicin, MIC > 2 mg/L, 11.7%; amikacin, MIC > 4 mg/L, 10.5%, carbenicillin, MIC > 128 mg/L, 11.7%; azlocillin, MIC> 16 mg/L, 10.9%; ceftazidime, MIC > 4 mg/L, 9.6%; ciprofloxacin, MIC > 1 mg/L, 8.1%; imipenem, MIC > 4 mg/L 2.5% and meropenem, MIC > 4 mg/L, 1.1%. Resistance to each antimicrobial except amikacin was commoner among the 134 isolates from patients in intensive care units (ICUs) than amongst the 1042 isolates from other in-patients ($P < 0.01$). Resistance to penicillins and ceftazidime, though not to other agents, was rarer among the 797 isolates from out-patients than amongst those from non-ICU in-patient ($P < 0.01$). Compared to a similar study in 1982, during which 1866 isolates had been examined, the frequency of resistance to the aminoglycosides increased ($P < 0.05$) as had those to the penicillins and ceftazidime ($P < 0.01$). Ciprofloxacin and the carbapenems were not tested in 1982. Cross-resistance patterns suggested that the increases in resistance to aminoglycosides and beta-lactams were largely a reflection of greater numbers of isolates with barrier or efflux mechanisms and were not due to an increase in isolates with antibiotic-degrading enzymes. The participating hospitals mostly employed Stokes' disc diffusion method and, when the results were compared to the MICs determined at the LHMC, fewer than 9% of the isolates reported as susceptible were found to be resistant. However, up to 72% of those reported by the hospitals as resistant were found to be susceptible.

Chen H.Y. et al. *Mechanisms of resistance to beta-lactam antibiotics amongst Pseudomonas aeruginosa isolates collected in the UK in 1993.* J Med Microbiol. 1995; 43(4) : 300-9.p Abstract: Antimicrobial resistance among 1991 Pseudomonas aeruginosa isolates collected at 24 UK hospitals during late 1993 was surveyed. Three-hundred and seventy-two of the isolates were resistant, or had reduced susceptibility, to some or all of azlocillin, carbenicillin, ceftazidime, imipenem and meropenem, and the mechanisms underlying their behaviour were examined. Only 13 isolates produced secondary beta-lactamases: six possessed PSE-1 or PSE-4 enzymes and seven had novel OXA enzyme types. Those with PSE types were highly resistant to azlocillin and carbenicillin whereas those with OXA enzymes were less resistant to these penicillins. Chromosomal beta-lactamase derepression was demonstrated in 54 isolates, most of which were resistant to ceftazidime and azlocillin although susceptible to carbenicillin and carbapenems. beta-Lactamase-independent "intrinsic" resistance occurred in 277 isolates and is believed to reflect some combination of impermeability and efflux. Two forms were seen: the classical type, present in 195 isolates, gave carbenicillin resistance (MIC > 128 mg/L) and reduced susceptibility to ciprofloxacin and to all beta-lactam agents except imipenem; a novel variant, seen in 82 isolates, affected only azlocillin, ceftazidime and, to a small extent, meropenem. Resistance to imipenem was largely dissociated from that to other beta-lactam agents, and probably reflected loss of D2 porin, whereas resistance to meropenem was mostly associated with intrinsic resistance to penicillins and cephalosporins. Comparison of the present results with those of a similar study in 1982 revealed significant increases in the proportions of isolates with intrinsic resistance or stable derepression ($p < 0.01$, chi 2 test).(ABSTRACT TRUNCATED AT 250 WORDS).

Chen S.H. et al. *High-dose cytarabine-containing chemotherapy with or without granulocyte colony-stimulating factor for children with acute leukemia.* Am J Hematol. 1998; 58(1) : 20-3.p Abstract: We sought to determine the role of granulocyte colony-stimulating factor (G-CSF) as

an adjunct therapy in high-dose cytarabine-containing chemotherapy (HD C/T) for children with acute leukemia. Seventeen patients, aged 9 months to 18 years old, 8 ALL and 9 AML, were treated with cytarabine (Ara-C) 1 g/m2 q12h for 8 doses with mitoxantrone, idarubicin, VP-16, or asparaginase. A total of 71 courses of HD C/T was given. G-CSF was not used in 14 courses (Group A). Prophylactic G-CSF was given in 57 courses (Group B) as 200 microg/m2/d SC started one day after the completion of HD C/T and continued until the neutrophil recovery was maintained. The incidences of sepsis per course in Group A and Group B were 35.7% (5/14) and 40.4% (23/57), respectively. While 2 patients in Group A died of sepsis or pneumonia, none in Group B died. The mortality and delay in chemotherapy were fewer in Group B (P = 0.037 and 0.0006, respectively, Fisher exact test). There was a shorter average number of days of neutrophil <500/cumm, antibiotic usage, fever, and hospital stay in Group B (11, 8, 5, 17 days in Group B vs. 21, 17, 10, 37 days in Group A; P = 0.0001, log-rank test; 0.0006, 0.0023, 0.0001, Wilcoxon rank sum test, respectively). The incidence of neutropenic fever was lower in Group B, but the difference did not reach statistical significance (P = 0.06, Fisher exact test). We conclude that G-CSF as an adjunct therapy in HD C/T is effective in reducing mortality, days of neutropenia, antibiotic usage, fever, hospital stay, and frequency of delay in chemotherapy. The efficacy of this treatment approach requires further testing in a randomized, controlled trial.

Chen Y. et al. *Percutaneous implantation of a Port-Catheter System using the left subclavian artery.* Cardiovasc Intervent Radiol. 2000; 23(1) : 22-5.p Abstract: PURPOSE: To evaluate the safety and feasibility of a percutaneous Port-Catheter System (PCS) implanted via the subclavian artery (SCA) for regional chemotherapy or chemoembolization of thoracic, abdominal, and pelvic malignant tumors. METHODS: Percutaneous puncture of the SCA was performed in 256 patients with thoracic, abdominal, or pelvic malignant tumors; then a catheter was inserted into the target artery. After the first transcatheter chemotherapy or chemoembolization with an emulsion of lipiodol and anticancer agents, an indwelling catheter was introduced with its tip placed in the target artery and its end subcutaneously connected to a port. RESULTS: The procedure was successfully completed in all 256 cases (100%). The indwelling catheter tip was satisfactorily placed in the target arteries in 242 cases (98%). Complications attributable to the procedure occurred in 20 (7.8%) cases, including pneumothorax (n = 10, 4%), hemothorax (n = 1, 0.4%), infections in the pocket (n = 4, 1.6%), and hematoma at the puncture site (n = 5, 2%). There were no severe sequelae or deaths. The duration of PCS usage was 1-36 months (median 9.5 months). During the course of treatment, occlusion of the target artery occurred in 20 cases (7.8%). Dislocation of the tip of the indwelling catheter occurred in 12 cases (4.7%); in 10 of the 12, the tip of the indwelling catheter was repositioned into the target artery. In all 10 cases no large symptomatic hematomas developed after the PCS was removed. CONCLUSION: Percutaneous PCS implantation via the left SCA, a relatively new procedure, is a safe and less invasive treatment approach than surgical placement for malignancies.

Chen Y. et al. *Microbial models of soil metabolism: biotransformations of danofloxacin.* J Ind Microbiol Biotechnol. 1997; 19(5-6) : 378-84.p Abstract: Danofloxacin is a new synthetic fluoroquinolone antibacterial agent under development for exclusive use in veterinary medicine. Such use could lead to deposition of low levels of danofloxacin residues in the environment in manure from treated livestock. This study was conducted to evaluate the potential for indigenous soil microorganisms to metabolize danofloxacin. Cultures of 72 soil microorganisms representing a diverse panel of bacteria, fungi and yeast were incubated with danofloxacin mesylate substrate and samples analyzed periodically by high performance liquid chromatography for loss of danofloxacin and formation of metabolites. Some samples were further analyzed by liquid chromatography-mass spectrometry and mass spectrometry to confirm metabolite identification. Twelve organisms, representing eight different genera, biotransformed danofloxacin to metabolites detectable by the chromatographic methods employed. Two Mycobacterium species, two Pseudomonas species, and isolates of Nocardia sp, Rhizopus arrhizus and Streptomyces griseus all formed N-desmethyldanofloxacin. The formation of the 7-amino danofloxacin derivative, 1-cyclopropyl-6-fluoro-7-amino-4-oxo-1,4-dihydroquinoline-3-carboxylic acid by cultures of Candida lipopytica, Pseudomonas fluorescens, two Mycobacterium species and three Penicillium species demonstrates the propensities of these cultures to completely degrade the piperazine ring. At least two additional and unidentified metabolite peaks were observed in chromatograms of Aspergillus nidulans and Penicillium sp cultures. Radiolabled [2-14C]danofloxacin added to cultures of the fungus Curvularia lunata was apparently mineralized, with approximately 31% of the radiolabel recovered as volatile metabolites after 24 h of incubation, indicating the susceptibility of the quinolone ring to microbial metabolic degradation.

Chen Y.H. et al. *Salmonella choleraesuis bacteremia in southern Taiwan.* Kao Hsiung I Hsueh Ko Hsueh Tsa Chih. 1999; 15(4) : 202-8.p Abstract: Within a 6-year period from January 1991 to December 1996, 19 patients with Salmonella choleraesuis bacteremia were enrolled for clinical and microbiological analysis. Young children, the elderly and patients with hematological malignancy (36.8%), liver cirrhosis (26.3%), systemic lupus erythematosus (10.5%), chronic renal impairment (10.5%), and peptic ulcer (10.5%) were at high risk of this infection. The ratio of male to female was 3:1. Three cases (15.8%) were nosocomially acquired. Fever (89.5%), chills (57.9%) and anorexia (52.6%) were the most common clinical manifestations. Seven patients (36.8%) presented no gastrointestinal manifestations. Normal white blood cell count was noted in seven patients (36.8%), and neutropenia caused by underlying diseases or severe infection was found in six cases (31.6%). Various types of metastatic focal infections were found, such as septic arthritis, cutaneous infection, spontaneous bacterial peritonitis, and pneumonia. The severe immunocompromised status of patients and the high virulence of this pathogen may contribute to the high case fatality rate (21%). Higher resistance rate to commonly used antimicrobial agents was noted in ampicillin (94.7%), chloramphenicol (89.5%), and TMP/SMZ (63.8%). All strains of S. choleraesuis were susceptible to third-generation cephalosporins and fluoroquinolones. Generally, S. choleraesuis bacteremia should be taken into account in the differential diagnosis of sepsis in immunocompromised patients, even without gastrointestinal manifestations. The third-generation cephalosporins and fluoroquinolones may be the first choice for treatment of this invasive infections.

Chen Y.H. et al. *Epidemiological study of human salmonellosis during 1991-1996 in southern Taiwan.* Kao Hsiung I Hsueh Ko Hsueh Tsa Chih. 1999; 15(3) : 127-36.p Abstract: Within a 6-year period from January 1991 to December 1996, 249 patients of salmonellosis admitted to Kaohsiung Medical College Hospital were enrolled for clinical and microbiological analysis. The number of patients increased by year from 1991 (14 patients) to 1996 (79 patients), especially in the case of nontyphoid salmonellosis. There were 57 different serotypes isolated during these period. Salmonella typhimurium was the most common clinical serotype of human origin in southern Taiwan, followed by S. choleraesuis, S. schwanzengrund, and S. derby. Fever (81.1%), diarrhea (68.9%), and anorexia (44.6%) were the most common manifestations of human salmonellosis. Relative bradycardia was a more important feature in S. typhi group (100%) than nontyphoid salmonellosis. Leukocytosis, especially lymphocytosis, was found especially in nontyphoid, but not in typhoid salmonellosis. Elevated liver function tests were found in the most severe patients, such as S. choleraesuis and S. typhi infections. Malignancy (8.8%), especially hematological malignancy (5.2%), gastrointestinal diseases (8.8%), and diabetes mellitus (6.4%) were the common underlying diseases. Case fatality rate of human salmonellosis was 8% (20/249), especially high in S. choleraesuis group. The severity of

underlying diseases may be the major cause in S. choleraesuis group. There was no fatal case with typhoid fever. Very high resistance rate to commonly used antimicrobial agents in nontyphoid Salmonella was noted in southern Taiwan with overall rates of resistance to ampicillin, 67.9%, chloramphenicol, 66.7%, and TMP/SMZ, 42.2%. The emergence of ciprofloxacin-resistant and multiresistant strains was also a major therapeutic problem in this study.

Cheng K.I. et al. *A novel approach of intravenous electrocardiograph technique in correct position the long-term central venous catheter.* Kaohsiung J Med Sci. 2000; 16(5) : 241-7.p Abstract: Intravenous electrocardiograph (IVECG) can correctly positioning the catheter tip by enlarging p wave as it is moved toward right atrium, and it is a safe, reliable and accurate technique. To evaluate the efficacy of wire-conducted IVECG signal and IVECG signal from the port with sodium bicarbonate (NaHCO3) flushed catheter and to compare those with conventional anatomy landmark method was the propose of this study. This prospective study was carried out in 216 patients who suffered from malignant diseases. The correct position of the catheter tip among these groups was confirmed as follows. In group 1 (n = 80), the anatomy landmark method and portable chest radiograph recognized the correct position. In group 2 (n = 72), IVECG signal was conducted from guide wire to identify the tip position. In group 3 (n = 64), IVECG signal was conducted from the port with NaHCO3 (0.8 mEq/mL) flushed catheter to ascertain the tip position. The patient characteristics did not differ significantly among the groups. The duration of operation was significantly ($P < 0.001$) longer in group 1 than in group 2 and group 3 (45.4 +/- 9.3 minutes vs 35.7 +/- 8.0 minutes and 35.2 +/- 9.7 minutes, respectively). Catheter tip placement times were shorter in group 2 and group 3 than in group 1 (5.3 +/- 2.9 minutes and 6.4 +/- 3.0 minutes vs 16.7 +/- 5.7 minutes, respectively); there was a statistically significant difference between the group 1 and group 2 and group 3 ($p < 0.001$). Nonetheless, the duration of operation and catheter tip placement time was similar in group 2 and group 3. Early and late complications within the subsequent 3 months showed no significant difference among groups. We concluded that IVECG signal conducted from guide wire obtained a similar efficiency to that signal from the port with NaHCO3 flushed catheter on positioning the catheter tip of the venous Port-A-Cath system. It is recommended to use these methods to facilitate implanting long-term central venous devices.

Cheng Q. et al. *Novel purification scheme and functions for a C3-binding protein from Streptococcus pneumoniae.* Biochemistry. 2000; 39(18) : 5450-7.p Abstract: To isolate microbial proteins capable of binding the third component of complement (C3), we coupled the free sulfhydryl group of methylamine-inactivated C3 to a thiolSepharose matrix. This simple technique facilitated the purification of the first C3-binding protein isolated from a bacterium (Streptococcus pneumoniae). Both metastable (native) and thioester-disrupted C3 were recognized by this protein; binding of C3 was noncovalent, independent of thioester conformation, and preferential for the C3 alpha-chain. Sequencing of amino-terminal and internal peptides from the C3-binding protein disclosed a proline-rich region spanning approximately 20 amino acids and a signal peptide that had not been previously reported. The gene was isolated from a library of genomic DNA from laboratory strain CP1200 by screening with a 1200 bp PCR product amplified from degenerate oligonucleotides encoding the amino terminal sequence and the internal proline-rich sequence. The open reading frame spanned 1692 bp; all peptide sequences were identified in the translated gene product, which also contained at least three choline-binding repeats at the carboxy-terminus. The gene was conserved, and the translated protein was functionally active in pneumococcal clinical isolates of serotypes 1, 3, 4, 14, and 19F. Serum from a patient recovering from acute pneumococcal infection contained IgG antibodies specific for this protein by immunoblot. Wide conservation among clinical isolates, saturable binding of C3, and the ability to stimulate the human immune response have not previously been reported for this choline-binding protein. A similar biochemical approach should enable the identification of other C3-binding proteins in microorganisms able to elude complement-mediated host defense.

Chenia H.Y. et al. *Antibiotic susceptibility patterns and plasmid profiles of penicillinase-producing Neisseria gonorrhoeae strains in Durban, South Africa, 1990-1993.* Sex Transm Dis. 1997; 24(1) : 18-22.p Abstract: BACKGROUND AND OBJECTIVES: The appearance of strains of Neisseria gonorrhoeae resistant, both chromosomally and plasmid-mediated, to penicillin and other antibiotics makes this versatile pathogen difficult to treat. There is, therefore, a need for surveillance of N. gonorrhoeae strains to determine the efficacy of current therapeutic measures. GOALS: To survey the antibiotic susceptibilities and plasmid profiles of penicillinase-producing N. gonorrhoeae strains isolated over a 4-year period. STUDY DESIGN: Penicillinase-producing N. gonorrhoeae strains were detected by the chromogenic cephalosporin test. Minimum inhibitory concentrations to penicillin G, tetracycline, ceftriaxone, and ciprofloxacin were determined using the E-test. Plasmid DNA was obtained by the alkaline lysis method and profiles generated. RESULTS: Penicillinase-producing N. gonorrhoeae strains increased from 16.4% to 19.0% in the period from 1990 through 1993. Although all strains were resistant to penicillin, strains were susceptible to varying levels of ciprofloxacin, ceftriaxone, and even tetracycline. All penicillinase-producing N. gonorrhoeae strains possessed the 2.6-megadalton cryptic plasmid, and in addition 87.7% contained the 24.5-megadalton conjugative plasmid. Of the six known gonococcal beta-lactamase plasmids, the 4.4-megadalton Asian and 3.2-megadalton African plasmids were predominant. The most prevalent plasmid profile contained the 2.6-megadalton cryptic, 24.5-megadalton conjugative, and 4.4-megadalton Asian plasmids. CONCLUSIONS: To ensure effective treatment of gonorrhea, continued surveillance of the antimicrobial susceptibilities and plasmid profiles of penicillinase-producing N. gonorrhoeae strains is necessary.

Chenoweth C. et al. *Antimicrobial resistance: implications for managing respiratory failure.* Curr Opin Pulm Med. 1997; 3(2) : 159-69.p Abstract: The prevalence of antibiotic resistance in respiratory pathogens is increasing rapidly. In the community, resistance to beta-lactam antibiotics has escalated dramatically among Moraxella catarrhalis, Haemophilus influenzae, and Streptococcus pneumoniae. Resistance to penicillin among S. pneumoniae has developed at an alarming rate over the past two decades. Recent studies in the United States have cited rates of penicillin resistance as high as 23.6%, with 9.5% exhibiting high-level resistance. Many of these strains are resistant to multiple antibiotics. Antimicrobial resistance in hospital-acquired pathogens is a problem, which in large part reflects patterns of antibiotic use. Antimicrobial resistance may arise via multiple mechanisms. Pseudomonas aeruginosa and other gram-negative bacilli have become increasingly resistant to beta-lactam antibiotics, including imipenem. Extended-spectrum beta-lactamases are seen with increasing frequency in Enterobacteriaceae, primarily Klebsiella spp. Fluoroquinolone resistance has increased in P. aeruginosa and Staphylococcus aureus and has now been identified in Escherichia coli isolated from hematology wards. Excessive use of antibiotics may promote the emergence and spread of resistant microorganisms. Rigorous infection control measures and modification of antibiotic use patterns may limit or reduce the prevalence of resistant organisms.

Cheong Y.M. et al. *Antimicrobial resistance pattern of bacteria isolated from patients seen by private practitioners in the Klang Valley.* Singapore Med J. 1995; 36(1) : 43-6.p Abstract: Data on bacterial resistance in patients seen by general practitioners are usually not readily available. The objective of this paper is to present the antimicrobial resistance pattern of bacteria isolated from patients seen by private practitioners in the Klang Valley. A total of 18 clinics participated in this study. From mid August 1991 to end of June 1993, 2,823 specimens were

received. Throat swabs and urine specimens constituted 56% of all the specimens. A large proportion of the specimens (55%) yielded no growth or just normal flora. The common bacteria encountered were Staphylococcus aureus (18.4%), Escherichia coli (16.2%), Klebsiella spp (13.7%) and Neisseria gonorrhoeae (9.3%). The S. aureus strains were mainly isolated from wound, pus and ear swabs. Not one out of the 218 strains tested was resistant to methicillin. In vitro susceptibility tests showed that 91% were resistant to penicillin while 23% were resistant to tetracycline and 13% to erythromycin. Eighty-two percent of the E. coli were isolated from urine. It was also the most common isolate from urine. Fifty percent of these strains were resistant to ampicillin, 33% to cotrimoxazole, 17% to cephalothin, 21% to ampicillin-sulbactam, 18% to amoxycillin-clavulanic acid while only 2.3% were resistant to nalidixic acid and nitrofurantoin and none to cefuroxime. Generally the gram negative bacilli encountered in general practice are less resistant to the third generation cephalosporins and aminoglycosides when compared to the hospital strains.

Chertow G.M. *Ochrobactrum anthropi bacteremia in a patient on hemodialysis.* Am J Kidney Dis. 2000; 35(6) : E30.p Abstract: Although newer tunneled dialysis catheters offer improved capacity for blood flow and efficiency of dialysis, catheter-associated bacteremia remains an extremely important complication of this access strategy. This is a report of a case of catheter-associated bacteremia with Ochrobactrum anthropi, a water-borne gram-negative rod with an unusual pattern of antibiotic resistance. Given the organism's hydrophilic property and the frequency of catheter use in debilitated individuals with end-stage renal disease, Ochrobactrum anthropi infection should be considered in the differential diagnosis of a hemodialysis patient with unexplained fever.

Chesky M. et al. *Polymerase chain reaction for the laboratory diagnosis of aseptic meningitis and encephalitis.* Arq Neuropsiquiatr. 2000; 58(3B) : 836-842.p Abstract: A protocol for testing cerebrospinal fluid specimens using a range of PCR assays for the diagnosis of central nervous system infection was developed and used to test prospectively 383 specimens. PCR assays were used for the detection of adenovirus, Borrelia burgdorferi, enteroviruses, Epstein Barr virus, cytomegalovirus, herpes simplex virus, human herpes virus type 6, JC virus, Leptospira interrogans, Listeria monocytogenes, lymphocytic choriomeningitis virus, measles virus, mumps virus, Mycobacterium sp., Mycoplasma pneumoniae, Toxoplasma gondii and varicella zoster virus. Of the 383 specimens tested in this study, 46 (12.0%) were found to be positive. The microorganisms detected were CMV, enterovirus, Epstein Barr virus, herpes simplex virus, human herpes virus type 6, JC virus, L. monocytogenes, Mycobacterium genus, Toxoplasma gondii and varicella zoster virus. The introduction of the PCR protocol described has improved the diagnosis of a range of central nervous system infections in our laboratory. We believe however that further evaluation of these assays in immunocompromised patients is necessary to better determine the predictive value of positive PCR results in these patient groups.

Chesney P.J. et al. *Penicillin- and cephalosporin-resistant strains of Streptococcus pneumoniae causing sepsis and meningitis in children with sickle cell disease.* J Pediatr. 1995; 127(4) : 526-32.p Abstract: OBJECTIVE: We investigated the possibility that antimicrobial-resistant pneumococci were causing invasive disease in children with sickle-cell disease (SCD). STUDY DESIGN: Records of all children with SCD observed at the Mid-South Sickle Cell Center (MSSCC) at LeBonheur Children's Medical Center were reviewed from January 1990 to June 1994. Children with SCD and pneumococcal sepsis were identified. The Streptococcus pneumoniae isolates from these children were examined for serotype and antimicrobial susceptibilities. Two additional children not observed in the MSSCC had pneumococcal sepsis caused by penicillin-resistant isolates and were also included. RESULTS: Antimicrobial susceptibility testing of the six penicillin-resistant isolates revealed that four were resistant to trimethoprim-sulfamethoxazole, two to erythromycin, and one to clindamycin. The two isolates that were resistant to ceftriaxone also were multiply resistant. From the MSSCC, 26 children had pneumococcal sepsis during the 4 1/2-year period studied. Five of these children (19%) died. Four (15%), including one who died, were infected with penicillin-resistant strains. CONCLUSION: Pneumococcal sepsis, meningitis, and infections of other foci in children with SCD may be caused by S. pneumoniae that is resistant to one or more antimicrobial agents, including penicillin. The addition of vancomycin to the antibiotics currently used for initial management should be considered in areas where the antibiotic resistance of S. pneumoniae is prevalent.

Cheung J. et al. *Microbial etiology and predisposing factors among patients hospitalized for corneal ulceration.* Can J Ophthalmol. 1995; 30(5) : 251-5.p Abstract: OBJECTIVE: To report the spectrum of microorganisms causing corneal ulceration in patients treated on an inpatient basis and to characterize the predisposing factors. DESIGN: Case series. SETTING: Large university-affiliated hospital in Toronto. PATIENTS: All inpatients with corneal ulcers managed between February 1991 and February 1993 (n = 95). RESULTS: Coagulase-negative staphylococci (30% of the 60 culture-positive cases), Staphylococcus aureus (23%), Streptococcus pneumoniae (12%), Pseudomonas aeruginosa (12%) and Moraxella (7%) were the predominant isolates. Previous eye surgery (cataract extraction in 30 cases [32%], penetrating keratoplasty in 12 [13%] and both procedures in 9 [9%]) was a common predisposing factor. Eleven cases (12%) were associated with the use of contact lenses, in all cases extended-wear soft contact lenses; six patients wore bandage lenses and five wore contact lenses for cosmetic reasons. Pseudomonas was the predominant isolate among contact lens wearers (four cases). Most of the 95 cases involved older patients (average age 62.5 years) with concomitant eye or systemic disease. Sixteen patients (17%) ultimately required penetrating keratoplasty. CONCLUSIONS: Recognition of the risk factors for corneal ulceration and prompt, intensive therapy are important to decrease the morbidity associated with this potentially blinding disease.

Chiew Y.F. *Vancomycin-resistant enterococci.* Ann Acad Med Singapore. 1997; 26(6) : 808-14.p Abstract: Vancomycin-resistant enterococci (VRE) are gaining much attention in the West, chiefly because of the lack of available antimicrobial therapy for VRE infections as most VRE are also resistant to drugs previously used to treat such diseases (e.g. aminoglycosides and ampicillin), the possibility that the vancomycin-resistant genes present in VRE can be transferred to methicillin-resistant Staphylococcus aureus (MRSA), and increasing reports of VRE and the trend towards endemicity in North America. There are three case reports and a study showing stool carriage of more than 10% from Singapore. One of the case reports is notable as the VRE isolated from the urinary tract is community-acquired. In Europe, there is a strong association between the use of avoparcin (a glycopeptide) in animal feeds and the emergence of VRE. Clonal dissemination resulting in nosocomial transmission is also demonstrated. Prior vancomycin use is a risk factor for the subsequent development of VRE bacteraemia. The laboratory plays an important role, namely, a) detection of VRE, and b) determination of susceptibilities of antimicrobials whereby possible therapeutic options may be instituted when antimicrobial intervention is indicated. There is a need to evaluate existing infection control measures against VRE to prevent it from becoming endemic in Singapore as had happened in North America.

Chikindas M.L. et al. *Mutacin II, a bactericidal antibiotic from Streptococcus mutans.* Antimicrob Agents Chemother. 1995; 39(12) : 2656-60.p Abstract: Mutacin II is an antibiotic that is produced by group II Streptococcus mutans. It inhibits the growth of other streptococci as well as many other gram-positive microorganisms by a hitherto unknown mechanism. Mutacin II possess bactericidal activity against susceptible cells. It transiently depolarizes the transmembrane elec-

trical potential (delta psi) and the transmembrane pH gradient (delta pH) and partially inhibits amino acid transport. However, it rapidly depletes the intracellular ATP pool in glucose-energized cells and prevents the generation of ATP. It is concluded that mutacin II does not belong to the group of pore-forming antibiotics (type A) or to the type B antibiotics, which inhibit phospholipases or interfere with peptidoglycan biosynthesis. Mutacin II acts by inhibiting essential enzyme functions at the level of metabolic energy generation, an activity that has not yet been classified for antibiotics.

Chin A.E. et al. *Tracking drug-resistant Streptococcus pneumoniae in Oregon: an alternative surveillance method*. Emerg Infect Dis. 1999; 5(5) : 688-93.p Abstract: With the emergence of drug-resistant Streptococcus pneumoniae, community-specific antimicrobial susceptibility patterns have become valuable determinants of empiric therapy for S. pneumoniae infections. Traditionally, these patterns are tracked by active surveillance for invasive disease, collection of isolates, and centralized susceptibility testing. We investigated whether a simpler and less expensive method aggregating existing hospital antibiograms—could provide community-specific antimicrobial susceptibility data. We compared 1996 active surveillance data with antibiogram data from hospital laboratories in Portland, Oregon. Of the 178 S. pneumoniae active surveillance isolates, 153 (86% [95% confidence interval (CI) = 80% to 91%]) were susceptible to penicillin. Of the 1,092 aggregated isolates used by hospitals to generate antibiograms, 921 (84% [95% CI = 82%-87%]) were susceptible to penicillin. With the exception of one hospital's erythromycin susceptibility results, hospital-specific S. pneumoniae susceptibilities to penicillin, cefotaxime, trimethoprim-sulfamethoxazole, and erythromycin from the two methods were statistically comparable. Although yielding fewer data than active surveillance, antibiograms provided accurate, community-specific drug-resistant S. pneumoniae data in Oregon.

Chiou C.C. et al. *Extremely high prevalence of nasopharyngeal carriage of penicillin-resistant Streptococcus pneumoniae among children in Kaohsiung, Taiwan*. J Clin Microbiol. 1998; 36(7) : 1933-7.p Abstract: Resistance (intermediate and high) to penicillin among Streptococcus pneumoniae strains is an emerging problem worldwide. From 1995 to 1997, isolates of S. pneumoniae not susceptible to penicillin were seen with increasing frequency from blood, cerebrospinal fluid, pleural fluid, and middle ear fluid from pediatric patients at the Veterans General Hospital-Kaohsiung. To determine the prevalence of carriage of these penicillin-nonsusceptible S. pneumoniae isolates, we obtained nasopharyngeal swab specimens from 2,905 children (ages, 2 months to 7 years) attending day-care centers or kindergartens or seen in our outpatient clinic. S. pneumoniae was isolated from 611 children, and 584 strains were available for analysis. The oxacillin disc test was used as a screening test to evaluate penicillin susceptibility. The MICs of 11 antibiotics (penicillin, cefaclor, cefuroxime, ceftriaxone, cefotaxime, imipenem, chloramphenicol, clarithromycin, rifampin, vancomycin, and teicoplanin) were determined by the E-test. Only 169 (29%) of the strains were susceptible to penicillin; 175 (30%) strains were intermediately resistant and 240 (41%) were highly resistant. The isolates also demonstrated high rates of resistance to other beta-lactams (46% were resistant to cefaclor, 45% were resistant to cefuroxime, 45% were resistant to ceftriaxone, 31% were resistant to cefotaxime, and 46% were resistant to imipenem). The rate of resistance to macrolide antimicrobial agents was strikingly high; 95% of the isolates were not susceptible to clarithromycin. However, 97% were susceptible to rifampin and 100% were susceptible to the two glycopeptides (vancomycin and teicoplanin). While reports of penicillin-resistant S. pneumoniae increased worldwide through the 1980s, the high prevalence (71%) of resistance reported here is astonishing. Surveillance of nasopharyngeal swab specimen cultures may provide useful information on the prevalence of nonsusceptible strains causing invasive disease. Such information could be used to guide therapy of pneumococcal infections.

Chiu C.H. et al. *A pilot study of seven days of ceftriaxone therapy for children with Salmonella enterocolitis.* Chang Keng I Hsueh. 1997; 20(2) : 115-21.p Abstract: BACKGROUND: The most effective therapy for non-typhoid Salmonella enterocolitis is still unknown. Traditionally, unless extraintestinal complications are present, antimicrobial drugs are not recommended, since earlier trials have shown that antibiotics such as ampicillin, chloramphenicol, or co-trimoxazole, do not shorten the duration of diarrhea and may even prolong convalescent fecal carriage of the bacteria. However, the recently-developed third generation cephalosporin ceftriaxone has been used successfully in the treatment of typhoid fever and other systemic salmonellosis. A controlled, pilot study was therefore undertaken to evaluate the efficacy of intravenous ceftriaxone in the treatment of children with non-typhoid Salmonella enterocolitis. METHODS: Fifteen children with Salmonella enterocolitis and bacteremia who were eligible for antibiotic therapy were given ceftriaxone intravenously for 7 days and 15 children with enterocolitis but without bacteremia who were admitted for supportive treatment during the study period were selected as the control group. Available stool samples collected on days, 7, 14, and 30 after the completion of the drug therapy were checked for the presence of the bacteria using polymerase chain reaction (PCR) and culture methods. RESULTS: The result showed that the duration of diarrhea was not significantly affected by ceftriaxone treatment. However, the difference in the rate of clearance of Salmonella from stools, as defined by negative stool cultures and PCR, was statistically significant between the two groups on post-treatment days 7 and 14. Only one patient given ceftriaxone was shown to have recrudescence of the bacteria in feces on day 14. One month after therapy, PCR was positive in two of the ten cases tested and one of these two experienced a relapse of diarrhea, whereas bacterial carriage was maintained in 63% of the control patients. CONCLUSION: A prompt eradication of Salmonella in feces was observed in most of the patients treated with ceftriaxone in this study. If further studies confirm the efficacy of this therapy and the risk of inducing drug resistance is minimal, the epidemiologic problem created by convalescent fecal bacterial carriage may justify a short-course of ceftriaxone therapy for children with Salmonella enterocolitis.

Chiu C.H. et al. *Typhoid fever in children: a fourteen-year experience.* Acta Paediatr Taiwan. 2000; 41(1) : 28-32.p Abstract: From 1982 to 1995, 71 children admitted in our medical center were diagnosed to have typhoid fever by culture or serology. Of the 71 children, most (83%) were aged 5-15 years. These children usually presented with fever and gastrointestinal symptoms, including abdominal pain, diarrhea, nausea or vomiting, and constipation. Hepatosplenomegaly was the most common physical sign observed and abdominal tenderness ranked the second. Thrombocytopenia occurring in 9 patients (13%) was the most common mode of complication. Other complications included intestinal perforation (3%), rectal bleeding (3%), ascites or pleural effusion (4%), and meningitis (1%). The incidence of complications tended to be higher among children 5 years of age or older ($p = 0.31$). Most patients responded well to appropriate antimicrobial therapies. There was no mortality. Relapse was observed in two children, although both had received 10 days of chloramphenicol therapy. The clinical isolates of Salmonella typhi were susceptible in vitro to all the antibiotics tested, including chloramphenicol, which, however, showed a higher MIC90 level than other drugs tested. In conclusion, there were age-specific differences of typhoid fever in children in terms of the incidence and morbidity and antibiotic resistance of S. typhi has not been a problem in this area at least up to 1995.

Chong L.Y. et al. *Clinical evaluation of ceftibuten in gonorrhea. A pilot study in Hong Kong.* Sex Transm Dis. 1998; 25(9) : 464-7.p Abstract: BACKGROUND: The escalating rates of gonococcal resistance to quinolone in Hong Kong have prompted a search for an alternative first-line antimicrobial agent for use in treating uncomplicated gonococcal urethritis. Ceftibuten is an orally active third-generation

cephalosporin with potent in vitro activity against Neisseria gonorrhoeae. Its pharmacokinetic properties allow single-dose administration. OBJECTIVE: To evaluate the efficacy, safety, and tolerability of ceftibuten in the treatment of uncomplicated gonorrhea in men. STUDY DESIGN: Ceftibuten was evaluated in an open-label, noncomparative, multicenter study. Eligible men with uncomplicated gonococcal urethritis were treated with a single 400-mg oral dose of ceftibuten and reassessed 1 week and 3 weeks after treatment. The main outcome measures were the isolation of N. gonorrhoeae, patient-reported side effects, and other safety parameters (e.g., blood counts and renal and hepatic function tests). RESULTS: One hundred twenty-five men were enrolled in the study. The overall cure rate was 98.2% (110 of 112 evaluable patients). Adverse events, which occurred in 4.5% of patients, were all mild, well tolerated, and of short duration. No significant changes in laboratory test results were noted. Of the 125 isolates, 4.8% were -lactamase positive. Susceptibility to ofloxacin was found to be low in 59.2% of isolates (MIC 0.1 to < 1g/mL) and 25.6% of isolates were resistant (MIC1g/mL) to ofloxacin. CONCLUSIONS: A single 400-mg oral dose of ceftibuten is highly effective and well tolerated in the treatment of uncomplicated gonococcal urethritis in men.

Chong Y. et al. *Capsular types and antimicrobial resistance of Streptococcus pneumoniae isolated in Korea.* Eur J Clin Microbiol Infect Dis. 1995; 14(6) : 528-31.p Abstract: The capsular types and the MICs of penicillin G and other antimicrobial agents were determined for 89 isolates of Streptococcus pneumoniae. MICs of penicillin G ranged from 0.015 to 2 mg/l, with 29% and 48% of the isolates exhibiting intermediate resistance and complete resistance, respectively. All isolates were susceptible to teicoplanin and vancomycin, but 81% and 43% of the penicillin G-resistant strains were intermediately resistant to cefotaxime and imipenem, respectively. Strains belonged to 16 different capsular types: 73% belonged to types 19F and 23F, and 97% of strains belonging to these two types exhibited either intermediate or complete resistance to penicillin G.

Chopra I. et al. *Molecular action of anti-mycobacterial agents.* Tuber Lung Dis. 1997; 78(2) : 89-98.p Abstract: In terms of the paradigms for antibacterial action presented in the introduction, there is good evidence that broad spectrum agents exert their anti-mycobacterial activity by interaction with classical targets occurring in a wide range of organisms including the mycobacteria. This is supported either by direct evidence (e.g., inhibition by rifampicin of mycobacterial RNA polymerase), or indirectly by the characterization of drug-resistant mycobacteria where mutations conferring resistance have been mapped to target sites homologous to those found in other bacteria (fluoroquinolones, macrolides, rifampicin, streptomycin). On the other hand, although the mode of action of some of the agents with an anti-mycobacterial spectrum is not fully understood, it is evident that the restricted spectrum is likely to arise from the possession of unique targets, or specific pro-drug conversion systems, or to a combination of both mechanisms. In several cases the narrow spectrum of the agents can be attributed to inhibition of molecular targets involved in the biosynthesis of the mycobacterial cell envelope that contains many unique polymers. The recent re-emergence of tuberculosis as an important human pathogen has led to improved methods for exploring the structure, biochemistry and genetics of the mycobacteria. These technical advances can now be used to gain a better understanding of the molecular basis of drug action in mycobacteria.

Choque C. R. *Revisión clínica del paludismo; Hospital de Clínicas Servicio de Enfermedades Infecciosas; años 1991-1995.* Rev. med. (Bolivia). 1995; 2(3/4) : 203-6.p Abstract: Se describen los resultados de una revision de historias clinicas de pacientes internados en el Servicio de Enfermedades Infecciosas del Hospital de Clinicas Universitario de la ciudad de La Paz, con el diagnostico de Paludismo, desde enero de 1991 a octubre de 1995, caracterizando las manifestaciones clinicas, signos y sintomas, diagnostico laboratorial asi como la respuesta terapeutica, habiendose encontrado variaciones importantes que son motivo de analisis del presente articulo. (AU).

Chou Y.H. et al. *The use of prophylactic intravenous immunoglobulin therapy in very low birthweight infants.* Chang Keng I Hsueh Tsa Chih. 1998; 21(4) : 371-6.p Abstract: BACKGROUND: Nosocomial infections are a major cause of death in premature infants, especially in very low birthweight (VLBW) infants. The VLBW infants have low serum immunoglobulin G levels, which may have an effect on infections in early infancy. Thus, prophylactic administration of intravenous immunoglobulin (IVIG) is proposed to maintain higher immunoglobulin G and reduce the rate of hospital-acquired infection. MATERIALS AND METHODS: A study for the effects of prophylactic IVIG therapy in VLBW infants was performed. A total of 61 VLBW infants were enrolled, and divided into the IVIG group (n = 31) and the control group (n = 30). The dose for each infant was 750-1000 mg/kg for those whose birthweight was less than 1000 g, and 500-750 mg/kg for infants whose birthweight was between 1001 and 1500 g. The control group received saline infusion. The infusions were given every 2 weeks until the infant weighed 1800 g, or was discharged. RESULTS: The results showed: there were no major differences in the perinatal and neonatal characteristics between the two groups, consistently higher IgG levels were found in the IVIG group, and the age of first documented sepsis was earlier in the control group. CONCLUSION: In this study, the prophylactic IVIG therapy may give substantially higher IgG levels, which may last for 2 months. However, a prophylactic effect for hospital-acquired infections was not observed.

Chover Lara J.L. et al. *[Outbreak of shigellosis in a lower-class district].* Rev Esp Salud Publica. 1999; 73(3) : 393-401.p Abstract: BACKGROUND: The outbreaks of Shigella sonnei in our environment frequently involve day care centers and elementary schools. An outbreak of shigellosis in a lower-class district is reported. The purpose of this study is that of pinpointing the center of infection, the means of contagion, the characteristics of those infected and of assessing the suitability of the measures taken. METHODS: For monitoring the outbreak over time, a combined observational timeline study was conducted within a territory the bounds of which were marked by means of the conventional epidemiological monitoring variables (time, place and individual). The infectivity of the center of infection (contagion rate) is analyzed by age, gender and school; rate ratio and percentage attributable thereto. RESULTS: On a time-related basis, the outbreak in question started on week 46/97 and ended on week 8/98. This outbreak involved 218 individuals (110 males and 108 females) totaling 5.46% of the district. The highest frequency was found among the 0-4 age group (43.6%), 29.4% in day care (70.32% contagion rate) with a relative risk of 3.9 (95% CI: 2.57-5.93) and 74.36% attributable percentage. The rate ratio between day care and the schools in the district in question is 5.62 (95% CI: 4.33-7.31). Stool cultures were taken and analyzed in 84 cases (38.5%), Shigella sonnei being detected in 38 cases (17.4%). Antibacterial treatment (amoxicillin-clavulan) was set out and individual and group health and safety measures were employed. CONCLUSIONS: The long communicability period and the small number of viable microorganisms necessary for causing this disease fostered its being passed on from one person to another at school and in the home. The measures employed effectively confined the contagion of the infectious agent at the schools.

Christensen A. et al. *[Antibiotic resistance of blood culture isolates in Buskerud in 1994 and 1998].* Tidsskr Nor Laegeforen. 2000; 120(15) : 1727-30.p Abstract: BACKGROUND: The increase of antimicrobial resistance has caused general concern world-wide. There is a high risk that this development will also occur in Norway. Several efforts have been made to prevent the emergence of antimicrobial resistance. A national surveillance programme for antimicrobial resistance has been started, and new legislation has made resistance surveillance programmes compulsory in every Norwegian hospital. Local surveillance of resistance is among the most important measures.

MATERIAL AND METHODS: We have undertaken surveillance of all blood culture isolates from the County of Buskerud in 1994 and 1998. Detection of antibiotic resistance-patterns were undertaken for all blood culture isolates in the two years using disc diffusion method (Rosco diagnostics, Taastrup, Denmark). We also looked at the consumption of antimicrobial agents in Buskerud Central Hospital in 1998. A total of 628 isolates from 572 patients were included in the study, 279 isolates from 1994 and 349 from 1998. RESULTS: We still have low occurrence of resistance in Buskerud, and there has been no significant increase during the four-year period. INTERPRETATION: The low prevalence of antibiotic resistance reflects the restrictive antibiotic policy in Norway. Therefore, we find it important to continue this policy and to continue close surveillance of the development of antibiotic resistance.

Christenson J.C. et al. *Detection of vancomycin-resistant enterococci colonization in a children's hospital*. Am J Infect Control. 1998; 26(6) : 569-71.p Abstract: BACKGROUND: Vancomycin-resistant enterococci (VRE) are important nosocomial pathogens in many hospitals. The true prevalence of VRE in pediatric hospitals is not known. METHODS: A surveillance study was performed at a pediatric tertiary care medical center by using vancomycin-containing screening media. RESULTS: Six children (of 112 screened) were found to be colonized with VRE. Colonized patients had a history of receiving broad-spectrum antimicrobial agents. CONCLUSION: In the absence of VRE infections, surveillance studies can help determine the extent of VRE colonization and support infection control measures.

Christiano A.P. et al. *Double-blind randomized comparison of single-dose ciprofloxacin versus intravenous cefazolin in patients undergoing outpatient endourologic surgery.* Urology. 2000; 55(2) : 182-5.p Abstract: OBJECTIVES: To compare the efficacy of single-dose oral ciprofloxacin with intravenous cefazolin as a prophylactic agent in patients undergoing outpatient endourologic surgery. METHODS: One hundred patients were enrolled in a double-blind, randomized study to receive either ciprofloxacin (500 mg) or cefazolin (1 g) before surgery. A postoperative clinical evaluation and urine cultures were performed 5 to 10 days after surgery. Patients undergoing ureteral stent insertion or exchange, ureteroscopy, bladder biopsy, retrograde pyelography, collagen injection, and internal urethrotomy were included. RESULTS: Postoperative urinary tract infection occurred in 7 (9.1%) of 77 patients, including 3 (8.1%) of 37 and 4 (10.0%) of 40 of those who received ciprofloxacin and cefazolin, respectively (P = 0.77). There were no episodes of sepsis, and no patient with infection required hospitalization. The total cost associated with the administration of prophylactic antibiotics in the study population was $3657 less in those 50 patients who received ciprofloxacin than in the 50 patients who received cefazolin. CONCLUSIONS: A single oral dose of ciprofloxacin in patients undergoing outpatient endourologic surgery was equally effective as cefazolin in preventing postoperative urinary tract infection, but was associated with markedly lower overall costs.

Christou N.V. et al. *Management of intra-abdominal infections. The case for intraoperative cultures and comprehensive broad-spectrum antibiotic coverage. The Canadian Intra-abdominal Infection Study Group.* Arch Surg. 1996; 131(11) : 1193-201.p Abstract: OBJECTIVE: To test the hypothesis that comprehensive broad-spectrum empirical antimicrobial therapy is superior to limited-spectrum empirical antimicrobial therapy in intra-abdominal infections. DESIGN: Prospective, randomized, double-blinded study. SETTING: University-affiliated hospitals in Canada. PATIENTS: Two hundred thirteen patients with intra-abdominal infections and planned operative or percutaneous drainage. INTERVENTION: Limited-spectrum empirical antimicrobial therapy consisted of cefoxitin sodium, 2 g, intravenously, every 6 hours (n = 109). Comprehensive broad-spectrum empirical antimicrobial therapy consisted of a combination of imipenem and cilastatin sodium, 500 mg, intravenously, every 6 hours (n = 104). MAIN OUTCOME MEASURES: Failure to cure the intra-abdominal infection (persistence of infection or death). RESULTS: Of initial isolates, 98% were sensitive to imipenem plus cilastin sodium compared with 72% for cefoxitin. No difference was found in the failure rate between treatment groups. Among various reasons for failure (including technical), 12 of 80 patients in the limited-spectrum empirical antimicrobial therapy group had resistant organisms at a second intervention compared with 1 of 74 in the comprehensive broad-spectrum empirical antimicrobial therapy group (P <.003, chi 2). One death in the limited-spectrum empirical antimicrobial therapy group was due to autopsy-proved disseminated Pseudomonas aeruginosa (blood, peritoneum, lung, and pleural fluid) that was resistant to cefoxitin, and the other was associated with peritonitis due to cefoxitin-resistant Enterobacter cloacae. One death in the comprehensive broad-spectrum empirical antimicrobial therapy group was associated with peritonitis from Clostridium perfringens that was sensitive to imipenem plus cilastin sodium, and the other was associated with peritonitis from Pseudomonas aeruginosa that was resistant to imipenem plus cilastin sodium. CONCLUSION: Treatment failure of intra-abdominal infection may be due, in part, to the presence of resistant pathogens at the site of infection. Therefore, routine culture of these sites seems worthwhile and empirical therapy should be as comprehensive as possible and should cover all potential pathogens.

Chu Y.I. et al. *Colorimetric indicators of microbial contamination in corneal preservation medium*. Cornea. 2000; 19(4) : 517-20.p Abstract: PURPOSE: To compare acid-base and oxidation-reduction indicators and to investigate the effect of buffer and temperature on the colorimetric detection of microbial growth in corneal preservation media. METHODS: Corneal preservation media containing gentamicin, without or with HEPES buffer, were prepared with either phenol red or AlamarBlue indicators (AccuMed International, Westlake, OH, U.S.A.). Both media were inoculated with Staphylococcus aureus, Streptococcus sanguis, Pseudomonas aeruginosa, Serratia marcescens, or Candida albicans and then incubated at 4 degrees C, 22 degrees C, or 35 degrees C. The pH or percent reduction were determined hourly for eight hours, then daily for one week. RESULTS: The length of time before a confirmed change in pH or reduction occurred varied by microorganism, storage temperature, and buffering capacity. At 4 degrees C, none of the microorganisms caused a detectable pH change in buffered medium within one day after inoculation, although two bacterial species reduced AlamarBlue within four hours. At 22 degrees C and 35 degrees C, all bacteria except P. aeruginosa produced a pH shift within a few hours, and all tested bacterial species reduced AlamarBlue. For bacteria producing detectable pH changes, HEPES-buffered medium took longer to change than medium without HEPES. C. albicans was not detectable in HEPES-buffered medium at any temperature by phenol red and was only detectable by AlamarBlue after 2-3 days at 22 degrees C and 35 degrees C. CONCLUSION: Acidic shifts in refrigerated corneal preservation medium do not occur during contamination by several microorganisms. AlamarBlue, a redox indicator, is more sensitive than phenol red in detecting some bacteria. C. albicans is not reliably detected by pH or redox indicators.

Chu Y.W. et al. *Antimicrobial resistance in Shigella flexneri and Shigella sonnei in Hong Kong, 1986 to 1995*. Antimicrob Agents Chemother. 1998; 42(2) : 440-3.p Abstract: Three hundred and thirty-three Shigella isolates obtained in 1986 to 1995 were tested for their susceptibilities to 19 antimicrobial agents. Nalidixic acid resistance had emerged in 59.6% of Shigella flexneri isolates during 1994 to 1995, with all tested resistant isolates having the mutation in gyrA encoding the Ser-83 alteration. Multiresistance (resistance to four or more agents) was more common in S. flexneri than in Shigella sonnei.

Chung T.A. et al. *A clinical, microbiological, and histopathologic study of trichostasis spinulosa*. J Dermatol. 1998; 25(11) : 697-702.p Abstract:

Trichostasis spinulosa (TSS) is a relatively common follicular disorder that can occur on the face and trunk, especially in the interscapular area. Its cause remains unclear. We examined clinically 30 patients with TSS and follicular materials extracted from each patient were examined microscopically. Bacterial culture and skin biopsy were done in 12 and 10 patients, respectively. Periodic acid Schiff (PAS) and Brown-Brenn Gram stain were used for detection of pityrosporum (malassezia) and bacteria. The interscapular area (14/30), nose (8/30), and cheek (4/30) were common sites of TSS. Pityrosporum and bacteria in the extracted follicular material were found at the rates of 82.6% and 73.3%, respectively. In histologic examination, follicular hyperkeratosis and numerous vellus hairs enveloped within keratotic sheath were common features. Pityrosporum and bacteria were found at the rate of 70% in biopsied specimens on PAS and Brown-Brenn Gram stain. In bacterial culture, Propionibacterium acne was most commonly identified in 75% (9 out of 12 patients). Pityrosporum and bacteria, especially Propionibacterium acne, were commonly found in the extracted follicular material and biopsied specimens. Thus, they may be related to the induction of follicular hyperkeratosis with retention of vellus hairs, and we suggest that these microorganisms may be one of the possible etiologic factors of TSS.

Ciabatti R. et al. *Semisynthetic glycopeptides: chemistry, structure-activity relationships and prospects.* Farmaco. 1997; 52(5) : 313-21.p Abstract: Glycopeptides are a class of naturally occurring antibiotics produced by fermentation of microorganisms. They inhibit cell wall biosynthesis in bacteria by forming a complex with the C-terminal D-alanyl-D-alanine of growing peptidoglycan chains. Glycopeptides are active against Gram-positive bacteria including the major pathogens. Among all the glycopeptides that have been discovered, only vancomycin and teicoplanin are on the market for the clinical use. By modification of the natural glycopeptide it is possible to increase its activity against methicillin-resistant Staphylococcus aureus and coagulase-negative staphylococci. Basic amides of teicoplanin aglycon have produced one compound endowed with interesting activity against Gram-negative bacteria because of its ability to cross the outer membrane of this last bacteria. Selective degradation of teicoplanin has given a tetrapeptide, a key intermediate that has been used as starting material for the synthesis of new non natural glycopeptides. One of them has shown a weak but promising activity against Van A Enterococci highly resistant to natural glycopeptides.

Cinat M.E. et al. *New advances in the use of antimicrobial agents in surgery: intra-abdominal infections.* J Chemother. 1999; 11(6) : 453-63.p Abstract: Advances in both technical methods and antimicrobial therapy have significantly reduced morbidity and mortality for secondary (enterogenous) or community-acquired intra-abdominal infections. Presumptive antimicrobial therapy for most community-acquired intra-abdominal infection can be safely initiated with a single broad-spectrum antimicrobial effective against the expected Enterobacteriaceae and anaerobic flora. Beta-lactams and carbapenems are effective against gram-negative rods and anaerobes, achieve therapeutic levels rapidly, and have low toxicity in the absence of penicillin allergy. Second generation cephalosporins (e.g. cefoxitin and cefotetan) remain useful in surgical prophylaxis and treatment of mild community-acquired pneumonia, but limitations in their spectra and antimicrobial resistance restrict their utility in more serious infections. The fourth generation cephalosporins are also effective, but should be combined with other antimicrobials such as metronidazole for adequate anaerobic coverage. Preliminary data on new fluoroquinolones are scant, but promising results were obtained in one clinical trial. We predict the current trend toward the use of broad-spectrum single agent antimicrobials for therapy of intra-abdominal infection will continue.

Cirrincione G. et al. *Derivatives of the new ring system indolo[1,2-c]benzo[1,2,3]triazine with potent antitumor and antimicrobial activity.* J Med Chem. 1999; 42(14) : 2561-8.p Abstract: Derivatives of the new ring system indolo[1,2-c]benzo[1,2,3]triazine 5 were synthesized by diazotization of substituted 2-(2-aminophenyl)indoles followed by an intramolecular coupling reaction of the diazonium group with the indole nitrogen. To obtain the indolobenzotriazine system it was necessary to protect the 3 position of the indole nucleus to avoid cyclization into the indolo[3,2-c]cinnoline system 4. Indolobenzotriazines 5a-g were evaluated in vitro for antitumor activity against a panel of leukemia-, lymphoma-, carcinoma-, and neuroblastoma-derived cell lines. Some compounds inhibited the proliferation of T and B cell lines at submicromolar concentrations, whereas their activity against solid tumor cell lines was in the micromolar range. When evaluated for their antifungal potential 5a,d inhibited some of the fungi tested, although at concentrations very close to those inhibiting the proliferation of human cells. On the contrary, all indolobenzotriazines proved fairly potent and selective inhibitors of Streptococcus and Staphylococcus. In particular 5b,c,g were up to 80 times more potent than the reference drug streptomycin and inhibited the growth of the above Gram-positive bacteria at concentrations far lower than those cytotoxic for animal cells.

Cisneros J.M. et al. *Bacteremia due to Acinetobacter baumannii: epidemiology, clinical findings, and prognostic features.* Clin Infect Dis. 1996; 22(6) : 1026-32.p Abstract: The number of nosocomial infections caused by Acinetobacter baumannii has increased in recent years. During a 12-month study, there were 1.8 episodes of A. Baumannii bacteremia per 1,000 adults admitted to a hospital in Seville, Spain. Seventy-nine patients were included in the study. A. baumannii bacteremia occurred after a mean (+/- SD) hospitalization of 18 +/- 20 days. In all cases the infections were acquired nosocomially; 71% wee acquired in intensive care units. Ampicillin/ sulbactam was found to be the most active agent against A. baumannii. The common source of the bacteremia was the respiratory tract (32 cases [71%]). Twenty patients (25%) had septic shock, and 24 (30%) had disseminated intravascular coagulation (DIC). Treatment with imipenem or ampicillin/sulbactam was most effective (cure rates, 87.5% and 83%, respectively). The deaths of 27 patients (34%) were related to A baumannii bacteremia. The presence of DIC (odds ratio [OR] = 116.4; P <.0001) and inappropriate antimicrobial treatment (OR = 15.2; P <.01) were independently associated with mortality. We conclude that most A. baumannii isolates are multiresistant and that nosocomial A. baumannii bacteremia may cause severe clinical disease that is associated with a high mortality.

Cizman M. et al. *Antimicrobial resistance of invasive Streptococcus pneumoniae in Slovenia, 1993-1995. The Slovenian Meningitis Study Group.* Scand J Infect Dis. 1997; 29(3) : 251-4.p Abstract: The susceptibility of 108 Streptococcus pneumoniae strains isolated from normally sterile body sites during 1993-1995 in Slovenia has been studied. Overall resistance to penicillin, erythromycin, trimethoprim-sulfamethoxazole, cefuroxime, cefaclor and chloramphenicol was 16.6, 0.9, 26.8, 0, 4.5 and 4.6%, respectively. All penicillin-resistant isolates (intermediate resistance) were susceptible to cefotaxime, ceftriaxone and vancomycin. Isolates less susceptible to penicillin were also significantly less sensitive to chloramphenicol, cefaclor and trimethoprim-sulfamethoxazole than penicillin-sensitive strains. Pneumococci isolated in children were significantly ($p < 0.05$) more resistant to trimethoprim-sulfamethoxazole than those isolated in adults. The study demonstrated moderate resistance rate of S. pneumoniae to penicillin and trimethoprim-sulfamethoxazole and a low-level resistance rate to erythromycin, cefaclor and chloramphenicol. No straightforward correlation between overall consumption of antibiotics and antimicrobial resistance was found.

Clark N.C. et al. *Detection and differentiation of vanC-1, vanC-2, and vanC-3 glycopeptide resistance genes in enterococci.* J Clin Microbiol. 1998; 36(8) : 2294-7.p Abstract: The VanC phenotype, as found in Enterococcus gallinarum, E. casseliflavus, and E. flavescens, is characterized by intrinsic low-level resistance to vancomycin. The

nucleotide sequences of the vanC-1 gene in E. gallinarum, the vanC-2 gene in E. casseliflavus, and the vanC-3 gene in E. flavescens have been reported, although there is some disagreement as to whether E. flavescens is a legitimate enterococcal species. Previous attempts to differentiate the vanC-2 and vanC-3 genes by PCR analysis have been unsuccessful. The purpose of the present study was to detect and differentiate the three vanC determinants and examine the distribution of these genes in a collection of both typical and atypical enterococci. The 796-bp vanC-1 PCR product was amplified only from E. gallinarum isolates. As expected, due to the extensive homology in the vanC-2 and vanC-3 gene sequences, all of the E. casseliflavus and E. casseliflavus/flavescens isolates produced the 484-bp vanC-2 PCR product, although the E. gallinarum isolates were negative. Only the E. casseliflavus/flavescens isolates produced the 224-bp vanC-3 product. Using the three sets of primers, we were able to detect and distinguish the vanC-1, vanC-2, and vanC-3 genes from both typical and atypical enterococci strains. Antimicrobial susceptibility tests and analysis of genomic DNA by pulsed-field gel electrophoresis were also performed, but the results indicated that they were not able to distinguish among strains possessing the three vanC genotypes.

Clark P.J. et al. *Contamination of diagnostic ophthalmic solutions in primary eye care settings.* Mil Med. 1997; 162(7) : 501-6.p Abstract: Pharmaceutical agents and irrigating solutions are widely used in both optometric and ophthalmologic practices. Contamination of these containers or solutions could possibly pose some risk of infection to a patient. We set out to investigate the possible contamination of a representative sample of these containers in small office practices. Representative bottles of two diagnostic pharmaceutical agents and an irrigating solution were obtained from primary care optometric and ophthalmologic practices in the San Francisco-Oakland Bay area. These bottles were tested to investigate the rate of contamination and to identify the types of microorganisms in the contaminated solutions. Sixty total samples (proparacaine, tropicamide, and an irrigating solution) were randomly cultured, and 11.7% of the samples showed contamination. Pseudomonas cepacia, Staphylococcus epidermidis, Pseudomonas putida, and Streptococcus species were the predominant organisms isolated from the contaminated bottles. In addition, 17 of the original 60 containers were further cultured for investigation of the dried residue particles around the threads of the containers. Of these 17 containers, 13 (76.5%) tested positive for Staphylococcus and Micrococcus species.

Clarke N.M. et al. *Effect of antimicrobial factors in human milk on rhinoviruses and milk-borne cytomegalovirus in vitro.* J Med Microbiol. 2000; 49(8) : 719-23.p Abstract: Various antimicrobial factors present in human milk were tested for in-vitro antiviral activity against three rhinoviruses (two clinical isolates and rhinovirus 2) and an isolate of cytomegalovirus (CMV) from human milk. These factors included the gangliosides GM1, 2 and 3, sialyl-lactose, chondroitin sulphates A, B and C, prostaglandins E2 and F2alpha, monolaurin, vitamin A and the protein lactoferrin. All were tested for their ability to inhibit growth of the viruses in cell culture. Human milk was also tested for antiviral activity against these viruses. Only vitamin A, monolaurin and lactoferrin inhibited the growth of CMV, whereas both prostaglandins enhanced the growth of this virus at least four-fold. CMV infects infants from milk but, nevertheless, the milk-borne CMV isolate showed no special resistance to any of the antiviral factors tested. None of the compounds inhibited or enhanced the growth of the rhinoviruses. However, human milk decreased the growth of some of the rhinoviruses and specific secretory immunoglobulin A (sIgA) neutralised the virus.

Claros M.C. et al. *Characterization of indole-negative Bacteroides fragilis group species with use of polymerase chain reaction fingerprinting and resistance profiles.* Clin Infect Dis. 1996; 23 Suppl 1 : S66-72.p Abstract: Biochemical tests alone do not adequately differentiate the various Bacteroides species, groups, and antimicrobial-resistant variants. Consequently, we used a polymerase chain reaction (PCR) fingerprinting technique, with either a single nonspecific primer derived from the t-DNA intergenic spacer region (T3B) or a single primer that anneals to minisatellite DNA sequences (M13 core), to identify and characterize 58 clinical isolates of Bacteroides fragilis group species (B. fragilis, B. distasonis, and B. caccae). In addition to species- and subspecies-specific differences, 4 strains of B. fragilis, 1 of B. distasonis, and 3 of B. caccae that showed increased resistance to imipenem, ampicillin, and ampicillin/sulbactam also produced unique PCR fingerprint profiles. Analysis by the clinical source of isolation (i.e. blood or intraabdominal, skin, or soft-tissue infection) indicated that no particular PCR fingerprint type was associated with greater pathogenicity of any individual clinical source. The PCR fingerprinting technique proves to be a useful tool for species identification and taxonomic studies, as well as for epidemiological studies of Bacteroides species.

Clemett D. et al. *Linezolid.* Drugs. 2000; 59(4) : 815-27; discussion 828.p Abstract: Linezolid is an oxazolidinone antibacterial agent that acts by inhibiting the initiation of bacterial protein synthesis. Cross-resistance between linezolid and other inhibitors of protein synthesis has not been demonstrated. Linezolid has a wide spectrum of activity against gram-positive organisms including methicillin-resistant staphylococci, penicillin-resistant pneumococci and vancomycin-resistant Enterococcus faecalis and E. faecium. Anerobes such as Clostridium spp., Peptostreptococcus spp. and Prevotella spp. are also susceptible to linezolid. Linezolid is bacteriostatic against most susceptible organisms but displays bactericidal activity against some strains of pneumococci, Bacteroides fragilis and C. perfringens. In clinical trials involving hospitalised patients with skin/soft tissue infections (predominantly S. aureus), intravenous/oral linezolid (up to 1250 mg mg/day) produced clinical success in >83% of individuals. In patients with community-acquired pneumonia, success rates were >94%. Preliminary clinical data also indicate that twice daily intravenous/oral linezolid 600 mg is as effective as intravenous vancomycin 1 g in the treatment of patients with hospital-acquired pneumonia and in those with infections caused by methicillin-resistant staphylococci. Moreover, linezolid 600 mg twice daily produced >85% clinical/microbiological cure in vancomycin-resistant enterococcal infections. Linezolid is generally well tolerated and gastrointestinal disturbances are the most commonly occurring adverse events. No clinical evidence of adverse reactions as a result of monoamine oxidase inhibition has been reported.

Cleveland J.L. et al. *Multidrug-resistant Mycobacterium tuberculosis in an HIV dental clinic.* Infect Control Hosp Epidemiol. 1995; 16(1) : 7-11.p Abstract: OBJECTIVE: To investigate possible transmission of multidrug-resistant tuberculosis (MDR-TB) in a dental setting. DESIGN: A retrospective, descriptive study of dental workers (DWs), patients, and practice characteristics. PATIENTS: Two dental workers (DW1 and DW2) with acquired immunodeficiency syndrome and MDR-TB. SETTING: A hospital-based (Hospital X) human immunodeficiency virus (HIV) dental clinic in New York City. METHODS: To identify dental patients with tuberculosis (TB), patients treated in the dental clinic at Hospital X during 1990 were cross-matched with those listed in the New York City Department of Health Tuberculosis Registry. Mycobacterium tuberculosis isolates from both DWs and from dental patients with TB were tested for antimicrobial susceptibility and typed by restriction fragment length polymorphism (RFLP) analysis. Infection control practices were reviewed. RESULTS: M tuberculosis isolates infecting DW1 and DW2 were resistant to isoniazid and rifampin and had identical RFLP patterns. DW1 and DW2 worked in close proximity to each other in a small HIV dental clinic in Hospital X during 1990. Of 472 patients treated in the dental clinic in 1990, 41 (8.7%) had culture-proven M tuberculosis infection. Of these 41, 5 had isolates with resistance patterns similar to both DWs; however, for four available isolates, the RFLP patterns were different from the patterns

of the DWs. Sixteen of the 41 patients received dental treatment while potentially infectious. Dental patients were not routinely questioned about TB by dental staff, nor were all dental staff screened routinely for TB. No supplemental environmental measures for TB were employed in the dental clinic in 1990. CONCLUSIONS: Our investigation suggests that MDR-TB transmission may have occurred between two DWs in an HIV dental clinic. Opportunities for transmission of TB among dental staff and patients were identified. TB surveillance programs for DWs and appropriate infection control strategies, including worker education, are needed to monitor and minimize exposure to TB in dental settings providing care to patients at risk for TB.

Climo M.W. et al. *Hospital-wide restriction of clindamycin: effect on the incidence of Clostridium difficile-associated diarrhea and cost.* Ann Intern Med. 1998; 128(12 Pt 1) : 989-95.p Abstract: BACKGROUND: Widespread antibiotic use has been associated with increases in both bacterial resistance and nosocomial infection. OBJECTIVE: To characterize the impact of hospital-wide clindamycin restriction on the incidence of Clostridium difficile-associated diarrhea and on antimicrobial prescribing practices. DESIGN: Prospective, observational cohort study. SETTING: University-affiliated Veterans Affairs Medical Center. PATIENTS: Hospitalized patients with symptomatic diarrhea. MEASUREMENTS: Clinical data on individual patients and data on antibiotic use were obtained from hospital pharmacy records. Hospital-wide use of antimicrobial agents was monitored. Isolates of C. difficile underwent antimicrobial susceptibility testing and molecular typing. RESULTS: An outbreak of C. difficile-associated diarrhea was caused by a clonal isolate of clindamycin-resistant C. difficile and was associated with increased use of clindamycin. Hospital-wide requirement of approval by an infectious disease consultant of clindamycin use led to an overall reduction in clindamycin use, a sustained reduction in the mean number of cases of C. difficile-associated diarrhea (11.5 cases/month compared with 3.33 cases/month; $P < 0.001$), and an increase in clindamycin susceptibility among C. difficile isolates (9% compared with 61%; $P < 0.001$). A parallel increase was noted in the use of and costs associated with other antibiotics with antianaerobic activity, including cefotetan, ticarcillin-clavulanate, and imipenem-cilastin. The hospital realized overall cost savings as a result of the decreased incidence of C. difficile-associated diarrhea. CONCLUSIONS: Hospital formulary restriction of clindamycin is an effective way to decrease the number of infections due to C. difficile. It can also lead to a return in clindamycin susceptibility among isolates and can effect cost savings to the hospital.

Clouatre Y. et al. *Outpatient CAPD catheter salvage for persistent exit-site/tunnel infection.* Nephrol Dial Transplant. 2000; 15(2) : 231-4.p Abstract: BACKGROUND: Partial replantation (i.e. replacement of the extraperitoneal portion of the catheter with creation of a new subcutaneous tunnel) has been suggested to avoid catheter removal in patients with persistent exit-site/tunnel infection (ESTI). However, published experience with this technique is limited. METHODS: Partial replantation was performed on an outpatient basis under local anesthesia for seven patients with persistent ESTI of >3 months duration. All patients resumed CAPD immediately following surgery. RESULTS: One patient had dialysate leakage less than 1 week after surgery that required catheter removal. The other patients had no complications and mean catheter survival following surgery was 7. 7 months (range 3.5-13 months). There was no recurrence of ESTI after surgery, although two patients presented with exit-site infection unrelated to the initial episode (i.e. different organism, long latency). Three other patients presented with episodes of peritonitis unrelated to surgery (i.e. delay >1 month) or ESTI (i.e. different organism). CONCLUSIONS: Partial replantation allows significant prolongation of catheter survival without major complications or interruption of CAPD. This novel procedure appears to be an appropriate alternative to catheter removal for the management of persistent ESTI. However, further studies are needed to prospectively compare partial replantation with catheter removal.

Cockerill F.R. 3rd. *Conventional and genetic laboratory tests used to guide antimicrobial therapy.* Mayo Clin Proc. 1998; 73(10) : 1007-21.p Abstract: Detection of antimicrobial resistance is important so that clinicians can make rational decisions about optimal antimicrobial therapy for their patients. During the past decade, new types of antimicrobial resistance have emerged, some of which present new challenges for the clinical microbiology laboratory. In most cases, conventional culture-based testing methods continue to be useful. In other situations in which the organism responsible for infection grows slowly (for example, Mycobacterium tuberculosis), culture methods are technically difficult (such as for human immunodeficiency virus), or genotypes are inconsistently expressed (for instance, methicillin resistance in staphylococci), genetic susceptibility testing methods may offer special advantages. Determining serum concentrations of antimicrobial agents may be useful both to ensure adequacy of treatment and to prevent toxicity. In this review, methods are described for conventional and genetic tests used to guide antimicrobial therapy.

Cockerill F.R. 3rd et al. *Clinical comparison of BACTEC 9240 plus aerobic/F resin bottles and the isolator aerobic culture system for detection of bloodstream infections.* J Clin Microbiol. 1997; 35(6) : 1469-72.p Abstract: The Plus Aerobic/F resin bottle of the BACTEC 9240 automated blood culture system (Becton Dickinson Diagnostic Instrument Systems, Sparks, Md.) was compared with aerobic culture of the Isolator system (Wampole Laboratories, Cranbury, N.J.) for the detection of bloodstream microorganisms from 6,145 blood cultures collected from adult patients with suspected septicemia. The BACTEC resin bottles were incubated for 7 days, and the sediment from the Isolator tube was inoculated to sheep blood and chocolate agars which were incubated for 72 h and to inhibitory mold, brain heart infusion, and Sabouraud agars which were incubated for 21 days. A total of 622 microorganisms were recovered from 583 blood cultures. The BACTEC resin bottle recovered statistically significantly more pathogens overall than the Isolator system ($P = 0.0006$). When individual pathogens isolated from either system for a 7-day study period were assessed, it was determined that the BACTEC resin bottle detected statistically significantly more isolates of Staphylococcus aureus ($P = 0.0113$) and coagulase-negative Staphylococcus spp. ($P = 0.0029$) than the Isolator system. The BACTEC resin bottle also detected statistically significantly more bloodstream infections (septic episodes) caused by coagulase-negative Staphylococcus spp. ($P = 0.0146$). The Isolator system recovered statistically significantly more contaminants overall ($P < 0.0001$), and among this group of microorganisms, recovered statistically significantly more Bacillus spp. ($P < 0.0001$), coagulase-negative Staphylococcus spp. ($P < 0.0001$), and viridans group Streptococcus spp. ($P = 0.0156$). The Isolator system detected statistically significantly more isolates of Histoplasma capsulatum ($P = 0.004$), but all of these isolates were detected at > or = 7 days of incubation of fungal plates, i.e., after the system to system comparison study period (7 days). In blood culture sets which produced growth of the same pathogen in both systems, there was a statistically significant difference in median time to detection for all pathogens combined favoring the BACTEC resin bottle over the Isolator tube ($P < 0.05$). When assessing individual microorganisms, the median times for detection of S. aureus, Enterococcus spp., and Pseudomonas spp. were all statistically significantly less for the BACTEC system ($P < 0.05$). The BACTEC instrument had 79 (1.3%) false positive signals. The BACTEC system required less processing time than the Isolator system and eliminates the hands-on time for detection of positive cultures required with the Isolator system.

Cockerill F.R. 3rd et al. *Clinical comparison of difco ESP, Wampole isolator, and Becton Dickinson Septi-Chek aerobic blood culturing systems.* J Clin Microbiol. 1996; 34(1) : 20-4.p Abstract: The ESP 80A aerobic blood culture of the ESP automated blood culture system (Difco

Laboratories. Detroit, Mich.) was compared with two manual aerobic blood culture systems, the Isolator (Wampole Laboratories, Cranbury, N.J.) and the Septi-Chek (Becton Dickinson, Cockeysville, Md.) systems, for the detection of bloodstream microorganisms from 5,845 blood samples for culture collected from adult patients with suspected septicemia. The bottles were incubated for 7 days, and the sediment from the Isolator tube was inoculated onto solid medium and this medium was incubated for 72 h. A total of 609 microorganisms were recovered from 546 blood cultures. There was no statistically significant difference in the total recovery of microorganisms for the ESP 80A system when compared with that for the Septi-Chek system ($P = 0.083$); however, the Isolator system recovered significantly more microorganisms overall than either the ESP 80A ($P < 0.001$) or the Septi-Chek ($P < 0.001$) system. When assessing individual probable pathogens, the Isolator system detected statistically significantly more Staphylococcus aureus and Candida spp. than either the ESP 80A or the Septi-Chek system ($P < 0.05$). Similarly, the Isolator system detected statistically significantly more bloodstream infections (septic episodes) caused by S. aureus and Candida spp. than either the ESP 80A or the Septi-Chek system ($P < 0.05$). In blood culture sets which produced growth of the same probable pathogens in the ESP 80A and the Isolator systems, there was no statistically significant difference in the median times to detection for all pathogens combined ($P = 0.067$). However, a similar comparison showed the Isolator and the ESP 80A systems to have statistically significantly shorter median detection times for all pathogens combined ($P < 0.001$) when they were independently compared with the Septi-Chek system. The ESP 80A system had 29 (0.5%) false-positive signals. The ESP system required less processing time than the Isolator system and eliminates the hands-on time for the detection of positive cultures required by the manual systems.

Cohen G.S. et al. *External beam irradiation as an adjunctive treatment in failing dialysis shunts.* J Vasc Interv Radiol. 2000; 11(3) : 321-6.p Abstract: PURPOSE: To evaluate the utility of low-dose irradiation as adjunctive treatment for failing dialysis shunts related to stenoses. MATERIALS AND METHODS: Thirty-one patients with 41 lesions in their dialysis shunts were successfully enrolled for this study. After imaging of the shunt and calculation of venous stenoses, each patient was randomized into one of two segments of the protocol: (i) angioplasty and/or stent placement alone, and (ii) angioplasty and/or stent placement followed by external beam irradiation. All patients with significant venous stenoses (> or =50%) were treated with appropriately sized PTA (percutaneous transluminal angioplasty) and Wallstents. Patients randomized to the external irradiation segment underwent localized irradiation via a Theratron cobalt unit of 7 Gy 0-24 hours and 24-48 hours after intervention. Those patients randomized to the control group received no additional treatment. Clinical follow-up included resumption of successful dialysis with appropriate hemodynamic parameters. Two follow-up shunt images were obtained, follow-up 1 (fu-1) from 90 to 179 days and follow-up 2 (fu-2) from 180 to 365 days. Percentages of significant recurrent stenoses, defined as greater than 50%, were recorded and re-treated as needed. RESULTS: Sixteen of the 31 patients underwent external beam irradiation. There were 21 lesions in the test group that underwent irradiation after intervention, and 20 lesions were treated with intervention alone. There were seven native arteriovenous fistulas and 24 Gore-tex grafts. All stenoses were either venous outflow stenoses (68%) or central stenoses (32%). The authors utilized chi2 analysis to compare restenoses rates between the control and irradiated groups at fu-1 ($P<.99$) and fu-2 ($P<.10$). CONCLUSIONS: Although the results show that external beam irradiation has minimal effects on the restenoses of dialysis grafts when used in conjunction with PTA and stent placement, further studies with a larger, more homogenous population are needed to assess the trend of improving patency rates after external beam irradiation.

Cohen H.A. et al. *Stethoscopes and otoscopes—a potential vector of infection?* Fam Pract. 1997; 14(6) : 446-9.p Abstract: OBJECTIVES: We aimed to determine whether stethoscopes and otoscopes used in community paediatric clinics harboured pathogenic micro-organisms, and, if so, which measures could prevent this. METHODS: Fifty-five stethoscopes belonging to paediatric physicians working in 12 community clinics were sampled for bacterial cultures by two methods: (i) direct impression of the diaphragm and bell section of each stethoscope for 5 seconds onto blood agar plates and a mannitol-salt-agar plate; (ii) swabbing the entire surface of the diaphragm of the stethoscope with a sterile cotton-tipped applicator. Forty-two otoscopes from the same physicians were sampled by rubbing the handles of the otoscopes with cotton-tipped swabs. The plates were incubated at 37 degrees C for 48 hours and examined for colony growth at 24 and 48 hours of incubation. Culture results were recorded as mean numbers of colony-forming units (CFUs). Eight additional stethoscope diaphragms were chosen at random at the participating clinics and cultured as described above. They were then wiped with alcohol swabs (isopropyl alcohol 70%), allowed to air dry for approximately 10 minutes and cultured a second time. RESULTS: All the stethoscopes and 90% of the otoscope handles were colonized by microorganisms. Staphylococci were isolated from 85.4% of the stethoscopes and 83.3% of the otoscopes, with 54.5% and 45.2% respectively being S. Aureus. Methicillin-resistant S. aureus were found in four each of the stethoscopes (7.3%) and otoscopes (9.5%). Cleaning with alcohol reduced the colony count by an average of 96.3%. CONCLUSIONS: Fomites can harbour potentially pathogenic bacteria, and with the increasing trend for children with more complex medical problems to be managed in an ambulatory setting, often by physicians who also work in hospitals, there is a real risk of spreading potentially serious infections to such patients. Simple cleansing with alcohol effectively eliminates the bacterial contamination of the fomites, and should be encouraged.

Cohen H.A. et al. *Handwashing patterns in primary pediatric community clinics.* Infection. 1998; 26(1) : 45-7.p Abstract: Handwashing is acknowledged as a critical factor in the prevention of nosocomial infection. Nonetheless, health care personnel often wash their hands inadequately. The purpose of this study was to examine the flora of hands and the frequency of handwashing of physicians working in primary care pediatric community clinics. The fingers of the dominant hand of 55 physicians working in 12 clinics were sampled for bacterial cultures. Only 354/720 (49%) of the expected handwashings by 17 board-certified pediatricians were recorded as having been performed. None of them washed their hands after each contact with an examined child. All physicians' hands were found to be contaminated with microorganisms. Staphylococcus species were isolated from 47 (85.4%) of the physicians' hands. Methicillin-resistant Staphylococcus aureus was found on the hands of 9.1% of the physicians. Such contaminated hands may serve as a potential vector of community-acquired infection with highly resistant organisms. Compliance with handwashing recommendations among these physicians was low. An active educational infection control program must be introduced in ambulatory pediatric community clinics.

Cohen M.L. *Changing patterns of infectious disease.* Nature. 2000; 406(6797) : 762-7.p Abstract: Despite a century of often successful prevention and control efforts, infectious diseases remain an important global problem in public health, causing over 13 million deaths each year. Changes in society, technology and the microorganisms themselves are contributing to the emergence of new diseases, the re-emergence of diseases once controlled, and to the development of antimicrobial resistance. Two areas of special concern in the twenty-first century are food-borne disease and antimicrobial resistance. The effective control of infectious diseases in the new millennium will require effective public health infrastructures that will rapidly recognize and respond to them and will prevent emerging problems.

Cohen M.L. *Epidemiological factors influencing the emergence of antimicrobial resistance.* Ciba Found Symp. 1997; 207 : 223-31; discussion 231-7.p Abstract: Antimicrobial resistance is becoming an important public health problem for both hospital- and community-acquired infections. In the hospital, infections caused by drug-resistant Staphylococcus aureus, Mycobacterium tuberculosis, enterococci, and a variety of Gram-negative rods are resulting in increased morbidity, mortality and costs, in part because of prolonged hospitalization and the use of more expensive antimicrobial agents. Drug-resistant, community-acquired infections are also causing important problems in both the developed and the developing world. Although the relative importance of specific pathogens varies with the geographical area, community-acquired pathogens including Salmonella, Shigella, Neisseria gonorrhoeae, Haemophilus influenzae and Streptococcus pneumoniae are causing both sporadic cases and outbreaks of drug-resistant illness. The emergence of antimicrobial resistance is being attributed to a series of societal, technological, environmental and microbial changes. These include increasing populations of susceptible hosts, international travel and commerce, changes in technology and industry, microbial adaptation and change, and the breakdown of public health measures. Addressing emerging problems and antimicrobial resistance will require enhanced surveillance, prudent use of existing antimicrobial drugs, development of new antimicrobial agents, increased emphasis on infection control and hygienic practices, effective disease control programs, better use of existing vaccines, and development of more and better vaccines.

Cohen Tervaert J.W. et al. *The role of superantigens in vasculitis.* Curr Opin Rheumatol. 1999; 11(1) : 24-33.p Abstract: Multiple risk factors are involved in susceptibility to vasculitis. Inherited determinants may increase the risk but are insufficient to induce the disease. Environmental factors, such as infections, are important modulators and probably trigger the disease in most cases. One of the possible triggers may be a bacterial superantigen (SAg). SAgs may activate autoreactive T cells that mediate autoimmune vessel wall destruction. Furthermore, SAgs may activate autoreactive B cells to produce autoantibodies that are involved in the pathophysiology of vasculitis, such as antineutrophil cytoplasmic autoantibodies or anti-endothelial cell antibodies. In patients with Kawasaki disease, Wegener's granulomatosis, and infection-related forms of vasculitis, SAg-producing microorganisms have regularly been found. Activation of circulating T cells and skewing of the T-cell repertoire have been reported in most forms of vasculitis. In the past year, for the first time, patients were described in which T-cell receptor V beta expansions were documented simultaneously with the typing of the microbial SAgs, providing evidence that the observed changes in the T-cell repertoire could be caused by these bacterial SAgs. In the future, elucidation of the immunologic mechanisms by which SAgs may play a role in the pathophysiology of vasculitis will provide more effective methods for the treatment of vasculitis.

Colizza S. et al. *Monitoring of antimicrobial prophylaxis in general surgery.* J Chemother. 1999; 11(6) : 573-6.p Abstract: The incidence of infections in general surgery is related to different factors. Cost-benefit analysis of antimicrobic prophylaxis is positive, even though incorrect use may be even dangerous (development of resistance and/or superinfections, for instance). The authors report data on a study concerning a total of 316 patients divided into two series, who had antimicrobic prophylaxis before a surgical operation. 274 patients out of 316 (or 86.7%) had an ultra-short (one-shot-only) or short (<24 hours) prophylaxis, 42 (13.3%) standard (>24 hours). The operations performed were classified following class of contamination, i.e. I (clean), II (potentially contaminated), III (contaminated). Antibiotics used were ceftizoxime, cefepime, ceftriaxone, piperacillin and gentamicin in combination. A total of 16 postoperative infections was observed (5%); 11 of these 16 belonged to class III operations. Escherichia coli and Staphylococcus aureus were isolated in most of the infected wounds. The data confirm what is reported in the literature. The authors conclude that a preoperative single-shot 3rd or 4th generation cephalosporin reduces the incidence of wound infections in clean and clean-contaminated surgery.

Collignon P.J. et al. *Drug-resistant Streptococcus pneumoniae: the beginning of the end for many antibiotics? Australian Group on Antimicrobial Resistance (AGAR).* Med J Aust. 1996; 164(2) : 64-7.p Abstract: OBJECTIVE: To determine the levels of antibiotic resistance in Streptococcus pneumoniae in Australia. DESIGN: Prospective, Australia-wide, laboratory-based survey. SETTING: 27 hospital and private laboratories around Australia, from January 1994 to August 1995. SUBJECTS: First 100 patients with clinically significant isolates of S. pneumoniae at each laboratory. OUTCOME MEASURES: Resistance to penicillin (determined from penicillin minimum inhibitory concentration [MIC] measured by the Etest), erythromycin, trimethoprim-sulfamethoxazole, tetracycline, chloramphenicol, cefotaxime and ceftriaxone. RESULTS: A total of 2396 isolates were tested (including 537 invasive isolates and 740 from children). Penicillin resistance was seen in 161 isolates (6.7%), including 17 with high level resistance. Penicillin resistance rates were significantly lower in invasive than in non-invasive strains (3.7% versus 7.6%; odds ratio [OR], 0.47; 95% confidence interval [CI], 0.28-0.77; P = 0.001). There was no significant difference in penicillin resistance rates between children (< 15 years) and adults (7.3% versus 6.5%; OR, 1.14; 95% CI, 0.80-1.63; P = 0.47). Resistance rates were higher for most other antibiotics than for penicillin (chloramphenicol, 6%; erythromycin, 11%; tetracycline, 15%; and trimethoprim-sulfamethoxazole, 42%). No high level resistance was seen to third generation cephalosporins, but 17 of 109 penicillin-resistant isolates tested (16%) displayed intermediate resistance to cefotaxime. Rates of antibiotic resistance varied between States, with the lowest rates in Tasmania. CONCLUSIONS: Antibiotic resistance levels in S. pneumoniae are increasing in Australia and high level penicillin resistance is being encountered for the first time (including in invasive strains). This will lead to an increasing number of therapeutic dilemmas and possible therapeutic failures, especially important in meningitis.

Colmenero J.L.M. et al. *Infecção genital pelo papiloma vírus: como diagnosticar? como tratar?* An. paul. med. cir. 1995; 122(1) : 11-6.p Abstract: O encontro de lesões genitais malignas e suas formas precursoras em associação com a infecção genital pelo Papiloma Vírus Humano, assim como a identificação de subtipos virais pertencentes ao grupo de alto risco oncogenético, tornou necessária uma revisão dos aspectos diagnósticos e terapêuticos. As formas clínica, subclínica e latente da moléstia são discutidas em relação aos métodos de diagnóstico. nfase aos fatores de escolha da terapêutica, tais como a localização e extensão das lesões, o tipo de infecção e sua associação com atipias epiteliais. Descrição dos métodos químicos, cirúrgicos e a imunoterapia utilizados no tratamento. Prognóstico quanto … recidiva e cancerização(AU).

Colom K. et al. *Five-year survey of cefotaxime resistance in Spain.* Microb Drug Resist. 1995; 1(4) : 327-30.p Abstract: During 1991-1995 a Spain collaborative study group surveyed the resistance to cefotaxime both in community as well as in hospital isolates of bacteria. The isolates tested during the study period of 5 years were 813, 875, 3631, 3184, and 3050 strains, respectively. Antimicrobial activity of cefotaxime was assayed by broth or agar microdilution, in accordance with criteria of the National Committee of Clinical Laboratory Standards (NCCLS). Cefotaxime resistance included 2.5% of all isolates: 2.6% Enterobacteriaceae, 1.7% Streptococcus pneumoniae, 0.5% Haemophilus influenzae, 0.0% Haemophilus spp., and 0.0% Moraxella catarrhalis. The overall incidence of resistance to cefotaxime decreased fro member of Enterobacteriaceae from 3.6% in 1991 to 2.5% in 1995. The incidence of resistance varied with the species and was highest in Enterobacter and in Citrobacter freundii.

Conces D.J. Jr. *Bacterial pneumonia in immunocompromised patients.* J Thorac Imaging. 1998; 13(4) : 261-70.p Abstract: Immunocompromised patients develop infections resulting from a wide range of organisms. The most commonly encountered type of infection is bacterial in origin. Many of the infections are community-acquired pneumonias in which most of the infections are caused by organisms that typically produce disease in the healthy person. Hospital-acquired pneumonias are particularly serious, being caused by the highly virulent gram-negative bacilli and Staphylococcus aureus. Immunocompromised patients frequently have indwelling intravascular catheters. These catheters may become infected and seed the lung with septic emboli, producing a hematogenous pneumonia. Underlying conditions and therapy increase the risk for aspiration in the immunocompromised patient. These aspirations can result in the development of an aspiration pneumonia and lung abscess formation. The majority of pneumonias resulting from Legionella and Nocardia occur in immunocompromised patients.

Conterno L.O. et al. *Risk factors for mortality in Staphylococcus aureus bacteremia.* Infect Control Hosp Epidemiol. 1998; 19(1) : 32-7.p Abstract: OBJECTIVE: To analyze risk factors for, and the role of methicillin resistance in, mortality in Staphylococcus aureus bacteremia. DESIGN: Nested case-control study. SETTING: General teaching hospital with a high prevalence of methicillin-resistant Staphylococcus aureus (MRSA) strains, in Sao Paulo, Brazil. PATIENTS: 136 patients over 14 years old with documented S aureus bacteremia. Those who died were compared with those who survived at least 14 days. RESULTS: Mortality within 14 days of bacteremia was 39% (53/136). Mean age was 47 years. Hospital-acquired bacteremia represented 86% (117/136) of episodes. In 26% (35/136), infection was related to an intravascular catheter and in 13% (17/136) to the respiratory tract. Septic shock occurred in 22% (30/136) of cases. MRSA was isolated in 66% (90/136). Multivariate analysis identified three variables that were significantly and independently associated with mortality: site of entry (lung, odds ratio [OR], 17.0; unknown, OR, 12.3; others, OR, 6.6); occurrence of shock (OR, 8.9), and resistance of S aureus to methicillin (OR, 4.2). CONCLUSION: Our study shows that S aureus bacteremia has a high mortality, especially when the lung is the source of infection and when shock develops; resistance to methicillin may be another risk factor for poor outcome.

Conti S. et al. *In vitro activity of monoclonal and recombinant yeast killer toxin-like antibodies against antibiotic-resistant Gram-positive cocci.* Mol Med. 2000; 6(7) : 613-9.p Abstract: BACKGROUND: Monoclonal (mAbKT) and recombinant single-chain (scFvKT) anti-idiotypic antibodies were produced to represent the internal image of a yeast killer toxin (KT) characterized by a wide spectrum of antimicrobial activity, including Gram-positive cocci. Pathogenic eukaryotic and prokaryotic microorganisms, such as Candida albicans, Pneumocystis carinii, and a multidrug-resistant strain of Mycobacterium tuberculosis, presenting specific, although yet undefined, KT-cell wall receptors (KTR), have proven to be killed in vitro by mAbKT and scFvKT. mAbKT and scFvKT exert a therapeutic effect in vivo in experimental models of candidiasis and pneumocystosis by mimicking the functional activity of protective antibodies naturally produced in humans against KTR of infecting microorganisms. The swelling tide of concern over increasing bacterial resistance to antibiotic drugs gives the impetus to develop new therapeutic compounds against microbial threat. Thus, the in vitro bactericidal activity of mAbKT and scFvKT against gram-positive, drug-resistant cocci of major epidemiologial interest was investigated. MATERIALS AND METHODS: mAbKT and scFvKT generated by hybridoma and DNA recombinant technology from the spleen lymphocytes of mice immunized with a KT-neutralizing monoclonal antibody (mAb KT4) were used in a conventional colony forming unit (CFU) assay to determine, from a qualitative point of view, their bactericidal activity against Staphylococcus aureus, S. haemolyticus, Enterococcus faecalis, E. faecium, and Streptococcus pneumoniae strains. These bacterial strains are characterized by different patterns of resistance to antibiotics, including methicillin, vancomycin, and penicillin. RESULTS: According to the experimental conditions adopted, no bacterial isolate proved to be resistant to the activity of mAbKT and scFvKT. CONCLUSIONS: scFvKT exerted a microbicidal activity against multidrug resistant bacteria, which may represent the basis for the drug modeling of new antibiotics with broad antibacterial spectra to tackle the emergence of microbial resistance.

Contreras Larrabe M.d.C. et al. *Detección de marcadores parasitarios y virales en embarazadas adolescentes y sus recién nacidos de riesgo.* Rev. chil. obstet. ginecol. 1995; 60(2) : 85-9.p Abstract: Las embarazadas adolescentes constituirían por su condición etárea una población de alto riesgo de infección por agentes relevantes en el binomio madre-hijo. Se investigó en 139 embarazadas adolescentes, la prevalencia de anticuerpos anti Toxoplasma gondii, Trypanosoma cruzi, Virus hepatitis B (VHB), citomegalovirus (CMV), Virus rubéola (VR) y Virus de la Inmunodeficiencia humana (VIH), así como la presencia de marcadores de infección en sus recién nacidos (RN) de riesgo. Se utilizaron las técnicas de Sabin y Feldman, fijación del complemento, ELISA, hemoaglutinación indirecta y xenodiagnóstico. Se detectó 30.9 por ciento de seropositivas para T. gondii, siendo estas madres y sus RN IgM negativos. Se detectaron dos madres con Acs anti T. cruzi (1.4 por ciento) y uno de los RN presentaba parásitos circulantes. En relación al estudio virológico, se detectó un 93,5 por ciento de madres seropositivas para CMV siendo sus RN IgM negativos, un 90,6 por ciento de las adolescentes eran antirrubéola positivas y se detectó un caso de adolescentes positiva para VIH. Las prevalencias establecidas en este grupo de embarazadas, no son significativamente diferentes a las encontradas en la población general de embarazadas (AU).

Contreras R. et al. *Resistencia de enterococos a los antimicrobianos en Venezuela.* Bol. Soc. Venez. Microbiol. 1995; 15(1) : 11-5.p Abstract: Se analiza la resistencia de Enterococcus sp., según los datos del Proyecto de Vigilancia a la Resistencia Bacteriana en Venezuela. Se utilizó el método de difusión en agar, siguiendo las normas de eficiencia de la NCCLS, en 1925 cepas durante 1988, 1990, 1992 y 1994. El uso de ampicilina o sulbactam/ampicilina en infecciones simples, y la combinación ampicilina más aminoglicósido en infecciones severas, siguen siendo la primera opción. La utilización de eritromicina (48 por ciento), clindamicina (88 por ciento) y tetraciclinas (62 por ciento), al igual que a nivel mundial, no está justificado, debido a los altos porcentajes de resistencia. Venezuela es el primer país latinoamericano en reportar resistencia a vancomicina y, al contrario de lo que ocurre en otros países, se ha mantenido estable en el período estudiado. La alta resistencia de Enterococcus faecalis a los aminoglicósidos es un problema mundial, pero su detección se realiza mediante pruebas especiales, que escapan a los objetivos del proyecto de vigilancia(AU).

Conville P.S. et al. *Effect of PANTA on growth of Mycobacterium kansasii in BACTEC 12B medium.* J Clin Microbiol. 1995; 33(8) : 2012-5.p Abstract: Mycobacterium kansasii isolates from two patients showed relatively slow growth in BACTEC 12B medium (12B) (Becton Dickinson Diagnostic Instrument Systems, Sparks, Md.) compared with the more rapid growth of these isolates on solid media. This finding prompted an evaluation of the effect of PANTA (Becton Dickinson) on the growth rate of these isolates. Suspensions of one isolate from each of these two patients (A and B), six additional isolates from six other patients (C through H), and one M. kansasii American Type Culture Collection isolate were inoculated into 12B with PANTA, 12B with reconstituting fluid only, and Middlebrook 7H11 agar plates (Remel, Lenexa, Kans.). For the isolates from patients A and B, the average times to detection for 12B with PANTA, 12B with reconstituting fluid, and Middlebrook 7H11 agar were 12.3, 7.4, and 9.0 days, respectively. For the remaining six patient isolates and the American Type Culture Collection strain, the average times to detection for these media were 9.2, 8.1, and 9.6

days. Susceptibility tests performed with the isolates from patients A and B with the individual component antibiotics of PANTA and testing of four of the other isolates with nalidixic acid alone suggested that nalidixic acid exerts some degree of inhibition on the growth of M. kansasii. The eight patient isolates were also inoculated onto Lowenstein Jensen medium (Remel) and onto a variety of selective mycobacterial media containing nalidixic acid and other antimicrobial agents. All isolates showed some degree of inhibition on at least one of these selective media.

Cookson B.D. *Nosocomial antimicrobial resistance surveillance.* J Hosp Infect. 1999; 43 Suppl : S97-103.p Abstract: The global threat of antimicrobial resistance and potentially untreatable infections is a serious matter under review currently by the WHO and many countries throughout the world. I consider the optimal surveillance scheme and point out the various biases in the systems that we have been using in the UK over the last decade. MRSA are used as an example where similar trends have been identified in these systems and the information has, once again, proved to be of value to the MRSA control working party.

Cookson S.T. et al. *Study to determine the ability of clinical laboratories to detect antimicrobial-resistant Enterococcus spp. in Buenos Aires, Argentina.* Diagn Microbiol Infect Dis. 1997; 29(2) : 107-9.p Abstract: Few reports of vancomycin-resistant enterococci have appeared outside the USA. Therefore, we evaluated the ability of five laboratories in Buenos Aires, Argentina, to perform susceptibility testing using the disk diffusion method. Laboratories had difficulty identifying the low- and intermediate-level vancomycin-resistant phenotypes. This suggests that the disk diffusion method used by laboratories abroad may fail to detect some vancomycin-resistant enterococci.

Corbella X. et al. *Efficacy of sulbactam alone and in combination with ampicillin in nosocomial infections caused by multiresistant Acinetobacter baumannii.* J Antimicrob Chemother. 1998; 42(6) : 793-802.p Abstract: From March 1995 to March 1997, sulbactam was prospectively evaluated in patients with non-life-threatening multiresistant Acinetobacter baumannii infections. During this period, 47 patients were treated with sulbactam; of them, five were excluded because they had received < or =48 h of sulbactam therapy. A total of 42 patients, 27 males and 15 females with a mean age of 60+/-15 years, were finally evaluated. Infections were as follows: surgical wound, 19; tracheobronchitis, 12; urinary tract, 7; catheter-related bacteraemia, 2; and pneumonia, 2. Eighteen patients received intravenous sulbactam alone (1 g every 8 h) and 24 patients received intravenous sulbactam/ampicillin (1 g:2 g every 8 h) with no major adverse effects. Of the 42 patients, 39 improved or were cured and showed A. baumannii eradication and one patient had persistence of wound infection after 8 days of sulbactam/ampicillin requiring surgical debridement. Two patients died after 3 days of therapy (one of the deaths was attributable to A. baumannii infection). The in-vitro activity of the sulbactam/ampicillin combination was by virtue of the antimicrobial activity exhibited by sulbactam. Killing curves showed that sulbactam was bacteriostatic; no synergy was observed between ampicillin and sulbactam. Our results indicate that sulbactam may prove effective for non-life-threatening A. baumannii infections. Its role in the treatment of severe infections is unknown. However, the current formulation of sulbactam alone may allow its use at higher doses and provide new potential synergic combinations, particularly for those infections by A. baumannii resistant to imipenem.

Cordero L. et al. *Bloodstream infections in a neonatal intensive-care unit: 12 years' experience with an antibiotic control program.* Infect Control Hosp Epidemiol. 1999; 20(4) : 242-6.p Abstract: OBJECTIVE: To assess the prevalence of gram-positive coccal (GPC), gram-negative bacillary (GNB), and fungal blood-stream infections (BSIs) during a 12-year period in which a consistent antibiotic treatment protocol was in place; to evaluate the efficacy of these antibiotic policies in relation to treatment, to the emergence of bacterial or fungal resistance, and to the occurrence of infection outbreaks or epidemics. STUDY DESIGN: Case series. METHODS: Demographic, clinical, and bacteriological information from 363 infants born during 1986 through 1991 and 1992 through 1997 who developed 433 blood-culture-proven BSIs was analyzed. Early-onset BSIs were defined as those infections discovered within 48 hours of birth, and late-onset BSIs as those that occurred thereafter. Suspected early-onset BSIs were treated with ampicillin and gentamicin, and suspected late-onset BSIs with vancomycin and gentamicin. Antibiotics were changed on the basis of organism antimicrobial susceptibility. RESULTS: Early-onset BSIs were noted in 52 of 21,336 live births and 40 of 20,402 live births during 1986 through 1991 and 1992 through 1997, respectively. GPC (83% due to group B streptococcus [GBS]) accounted for approximately one half of early-onset BSI cases and GNB (68% Enterobacteriaceae) for the remainder. Early-onset GBS declined from 24 to 11 cases (P=.04) and late-onset BSI increased from 111 to 230 cases (P<.01) from the first to the last study period. Sixty-eight percent of late-onset BSIs were due to GPC (primarily coagulase-negative Staphylococcus), 18% to GNB, and 14% to fungus. Over the study period, Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, and Pseudomonas aeruginosa isolated from the newborn intensivecare unit (unlike those strains from other hospital units) remained fully susceptible to ceftazidime and gentamicin. Although the hospitalwide prevalence of methicillin-resistant Staphylococcus aureus increased, all 17 newborn BSI cases were due to methicillin-sensitive strains. Prevalence of methicillin-resistant coagulase-negative Staphylococcus increased, although all strains remained vancomycin-susceptible, as did the 16 Enterococcus faecalis isolates. All fungi recovered (from 48 patients) were susceptible to amphotericin. CONCLUSION: We observed a decrease in the prevalence of early-onset BSIs due to GBS and an increase in late-onset BSIs due to GPC, GNB, and fungi. The combination of ampicillin and gentamicin for suspected early-onset BSIs and vancomycin and gentamicin for late-onset BSIs has been successful for treatment of individual patients without the occurrence of infection outbreaks or the emergence of resistance. Controlled antibiotic programs and periodic evaluations based on individual unit and not on hospital-wide antibiograms are advisable.

Cordero Thompson J. et al. *Meningitis por streptococcus pneumoniae resistente.* Rev. chil. infectología. 1997; 14(1) : 55-6.p Abstract: Se comunica caso de lactante que adquirió meningitis neumocóccica causada por una cepa medianamente sensible a penicilina-CIM 1 æg/ml y resistente a ceftriaxona- CIM 3 æg/ml. El tratamiento inicial incluyó ceftriaxona 100 mg/kg/día y dexametasona. Hubo una esterilización tardía del LCR y graves secuelas neurológicas al egreso pese al tratamiento con vancomicina sistémica e intraventricular. Este es el primer caso documentado de resistencia a cefalosporinas de tercera generación, relacionado a fracaso terapéutico en meningitis, en nuestro hospital (AU).

Cordoba M.G. et al. *Evaluation of microbial hazards during processing of Spanish prepared Flamenquin.* J Food Prot. 1998; 61(6) : 693-9.p Abstract: Flamenquin is a traditional, prepared, frozen meat product from the south of Spain made with minced pork, chicken, and cooked ham. Since it is a prepared raw meat product some microbial hazards could be associated with the process of making it. Microbiological analyses have been performed throughout the various steps of processing over a 1-year period to evaluate microbial hazards in the commercial process. High levels of microorganisms were observed all through the processing of this product, the mincing and mixing steps being where major microbial contamination was observed. Pathogenic bacteria such as Staphylococcus aureus, Clostridium perfringens, Escherichia coli and Pseudomonas aeruginosa were detected during processing. Raw materials and food handlers were the principal sources of microbial contamination. A modification of processing to include a heating step after mincing and mixing and an improvement in hygiene practices could eliminate the microbial hazards. Both modifications should be noted for the

implementation of a hazard analysis of critical control points (HACCP) program in commercial flamenquin processing.

Cormican M.G. et al. *Avoparcin, a glycopeptide used in animal foods: antimicrobial spectrum and potency tested against human isolates from the United States.* Diagn Microbiol Infect Dis. 1997; 29(4) : 241-8.p Abstract: Avoparcin is a glycopeptide antimicrobial that is widely used as a growth promoter in animal feeds in portions of Western Europe. Recently, concern has emerged about the possible contribution of avoparcin use to the emergence of glycopeptide resistance in enterococci. Relatively little information exists on the spectrum of activity and potency of avoparcin. We studied the activity of avoparcin compared to vancomycin, teicoplanin, and 3 other antimicrobials against 814 recent human clinical isolates, including Staphylococcus spp. (240 strains), Streptococcus spp. (90 strains), and Enterococcus spp. (60 strains), using reference susceptibility test methods. Our results indicate that avoparcin was less potent than either vancomycin or teichoplanin against staphylococci (MIC50, 4 micrograms/ mL). There was a good correlation of avoparcin MICs with the MICs for vancomycin and teichoplanin for most species; however, the avoparcin MICs for Enterococcus spp. of the vanB phenotype were quite variable (MIC range, 2 to > 16 micrograms/mL). For Staphylococcus haemolyticus, high avoparcin MICs (> or = 16 micrograms/mL) were associated with oxacillin resistance. These results are relevant to the debate concerning the appropriateness of continued use of avoparcin as a growth promoter in animal husbandry. In particular, avoparcin as a glycopeptide with limited potency against some staphylococci seems to represent a theoretically greater risk for selecting glycopeptide resistance among staphylococci, but may not represent any greater threat for the selection of resistance in enterococci.

Cormican M.G. et al. *Antimicrobial activity of cefotaxime tested against infrequently isolated pathogenic species (unusual pathogens).* Diagn Microbiol Infect Dis. 1995; 22(1-2) : 43-8.p Abstract: The cefotaxime sodium spectrum of activity is very broad and includes many common species and a variety of less frequently isolated pathogens. We have reviewed the clinical microbiology literature (44 references) and the data base of the University of Iowa Hospitals and Clinics (Iowa City, IA) to collect data on the activity of cefotaxime against the less common species. Cefotaxime was consistently active against Actinobacillus actinomycetemcomitans, Capnocytophaga spp., Eikenella corrodens, Erysipelothrix rhusiopathiae, Pasteurella multocida, Plesiomonas shigelloides, and Fusobacterium nucleatum. The species Alcaligenes xylosoxidans, Flavobacterium spp., Stenotrophomonas (Xanthomonas) maltophilia, Bacillus cereus, Listeria monocytogenes, and Rhodococcus equi were uniformly cefotaxime resistant. For many other species there was considerable variation in reported minimum inhibitory concentrations. These data may be helpful in guiding therapy of unusual infections, particularly in the case of fastidious species, where the appropriate susceptibility testing methodology may not be immediately or routinely available.

Cormican M.G. et al. *Emerging resistance to antimicrobial agents in gram-positive bacteria. Enterococci, staphylococci and nonpneumococcal streptococci.* Drugs. 1996; 51 Suppl 1 : 6-12.p Abstract: Staphylococci (Staphylococcus aureus and coagulase-negative Staphylococcus species) and enterococci are the aetiological organisms in 47 to 52% of nosocomial blood stream infections and approximately 30% of all nosocomial infections in the US. In European intensive care units, almost half of all infections are attributed to staphylococci. The streptococci have also become increasingly important because of the modified virulence of Streptococcus pyogenes strains, and the emerging role of the viridans group streptococci as a cause of potentially fatal bacteraemia in the neutropenic host. Resistance to available antimicrobial agents is increasing and includes, in particular, resistance to the glycopeptides (vancomycin and teicoplanin) amongst enterococci, resistance to penicillinase-resistant penicillins (oxacillin and methicillin) and fluoroquinolones (ciprofloxacin and ofloxacin) amongst staphylococci, and resistance to penicillin and some other beta-lactams amongst viridans group streptococci. New compounds for effective therapy of infection with antimicrobial-resistant Gram-positive species are needed urgently. To this end, the streptogramin combinations [quinupristin/dalfopristin (RP 59500; Synercid)], everninomycin derivatives (SCH 27899), oxazolidinones (U-100572, U-100766) and several newer fluoroquinolones (clinafloxacin, DU 6859a, grepafloxacin, levofloxacin, sparfloxacin, trovafloxacin) are under rapid development and clinical investigation.

Cornaglia G. et al. *Resistance of Streptococcus pyogenes to erythromycin and related antibiotics in Italy. The Italian Surveillance Group for Antimicrobial Resistance.* Clin Infect Dis. 1998; 27 Suppl 1 : S87-92.p Abstract: A survey of antimicrobial resistance in Streptococcus pyogenes, performed within the framework of a national surveillance program, has revealed a dramatic increase in resistance of S. pyogenes to erythromycin in most areas of Italy. In virtually all the centers that provided data for 3 consecutive years, the incidence of erythromycin-resistant strains increased twofold to 20-fold from 1993 to 1995 and was greater than 30% in five of the 14 centers participating in the study. The clonality of erythromycin-resistant isolates was studied in 15 strains isolated from different patients at the Institute of Microbiology of Verona University (Verona). The features of the Verona isolates and the substantially different rates of erythromycin and clindamycin resistance observed in most centers suggest that the spread of different resistance genes in multiple clones might be occurring throughout the country.

Cornaglia G. et al. *Rapid increase of resistance to erythromycin and clindamycin in Streptococcus pyogenes in Italy, 1993-1995. The Italian Surveillance Group for Antimicrobial Resistance.* Emerg Infect Dis. 1996; 2(4) : 339-42.p Abstract: A survey of antibiotic resistance in Streptococcus pyogenes in Italy showed a sharp increase in erythromycin resistance. In 1993, the incidence of erythromycin-resistant strains was on average 5.1%, with marked variations by geographic area. Two years later, the incidence of these strains had registered a 1.5- to roughly 20-fold increase, with a mean value of 25.9%, exceeding 40% in three centers out of 13 and 30% in another four. For all the strains studied, normal levels of susceptibility to penicillin were reported.

Cornelissen C.N. et al. *The transferrin receptor expressed by gonococcal strain FA1090 is required for the experimental infection of human male volunteers.* Mol Microbiol. 1998; 27(3) : 611-6.p Abstract: Iron, an essential nutrient for most microorganisms, is sequestered by the host to decrease the concentration of iron available to bacterial pathogens. Neisseria gonorrhoeae, the causative agent of gonorrhoea, can acquire iron by direct interaction with human iron-binding proteins, including the serum glycoprotein, transferrin. Iron internalization from host transferrin requires the expression of a bacterial receptor, which specifically recognizes the human form of transferrin. Two gonococcal transferrin-binding proteins have been implicated in transferrin receptor function, TbpA and TbpB. We constructed a gonococcal transferrin receptor mutant without the introduction of additional antibiotic resistance markers and tested its ability to cause experimental urethritis in human male volunteers. The transferrin receptor mutant was incapable of initiating urethritis, although the same inoculum size of the wild-type parent strain, FA1090, causes urethritis in >90% of inoculated volunteers. To our knowledge, this is the first experimental demonstration that a bacterial iron acquisition system is an essential virulence factor for human infection.

Coronado B.E. et al. *Antibiotic-induced D-lactic acidosis.* Ann Intern Med. 1995; 122(11) : 839-42.p Abstract: OBJECTIVE: To describe a case of oral antibiotic-induced D-lactic acidosis in a patient with enteric overgrowth of Lactobacillus acidophilus. DESIGN: Single case study. SETTING: University-affiliated community hospital.

INTERVENTION: Oral carbohydrate challenge test with 4000 kcal/d. MAIN RESULTS: A patient had several episodes of D-lactic acidosis after receiving oral antibiotics. Stool cultures yielded Lactobacillus acidophilus resistant to the implicated agents. Provocative challenge with dietary carbohydrate alone, in the absence of antibiotics, failed to reproduce the syndrome. CONCLUSIONS: Oral antibiotics may induce D-lactic acidosis in patients with the short-bowel syndrome by promoting the overgrowth of resistant D-lactate-producing organisms. Interactions between carbohydrate intake and antibiotic use are likely determinants in the development of this syndrome. Periodic use of stool cultures with antimicrobial susceptibility testing may assist in the management of these patients by optimizing the selection of antimicrobial agents.

Corso A. et al. *[Determination of serum aminoglycoside and vancomycin concentrations by the microbiological method in the presence of other antimicrobials].* Rev Argent Microbiol. 1996; 28(3) : 123-31.p Abstract: The determination of serum concentrations of antimicrobials with a narrow therapeutic range by microbiological method requires some modifications when the patient is under combined antimicrobial therapy. The methodological conditions for the appraisal of aminoglycosides and vancomycin in the presence of other drugs were evaluated by using strains with selective sensitivity to the antimicrobial to be tested or by the adding crude extracts of beta-lactamases for the inactivation of the beta-lactam antimicrobials. These beta-lactamases were obtained from Enterobacter cloacae P99 (derepressed mutant) cultures for the inactivation of penicillins and first, second and third generation cephalosporins, as well as from Stenotrophomonas (Xanthomonas) maltophilia M 1484 cultures for the hydrolysis of imipenem. The strains allowing vancomycin appraisal and indifferent to the synergic activity of other drugs in the mixture were S. aureus M 2120, when the accompanying antimicrobials were gentamicin, ciprofloxacin or rifampicin, and E. faecalis M 2113, E. avium M 2091 and S. aureus M 2101 when the drugs in the mixture were amikacin, lincomycin or trimethoprim-sulfamethoxazole, respectively. For the appraisal of gentamicin in the presence of vancomycin or fluoroquinolones (ciprofloxacin or norfloxacin), E. coli M 1376 was the most suitable strain, while the use of K. pneumoniae ATCC 10031 was required for the appraisal of amikacin or netilmicin. When rifampicin was the accompanying antimicrobial, E. coli M 1495 turned out more adequate. E. coli M 1462 proved to be more satisfactory for gentamicin, amikacin and netilmicin dosages in samples also containing chloramphenicol, trimethoprim-sulfamethoxazole or tetracycline.

Corwin A. et al. *Emerging disease surveillance in Southeast Asia.* Ann Acad Med Singapore. 1997; 26(5) : 628-31.p Abstract: The emergence of infectious disease causing agents/pathogens necessitates a rational surveillance approach leading to early detection and appropriate intervention. Surveillance activities with support from the US Naval Medical Research Unit No. 2 (NAMRU-2), targeting susceptible populations/areas in Southeast Asia, have been organised using a multi-design strategy: 1) systematic multi-size (usually hospital-based) study; 2) investigation of (suspected) outbreak events involving significant case populations (and associated fatalities); and 3) monitoring of unique "risk opportunities" that include pre- and post-screening of immunologically naive (susceptible) persons (including military personnel and tourists) travelling in groups to areas of likely disease transmission/occurrence. Recognition of new (or old) disease agents or emerging antimicrobial resistance requires a standardised study effort with complementary advanced diagnostic capabilities. Collaborative research involving NAMRU-2 includes surveillance of 01 and non-01 Vibrio cholerae strains in epidemic and sporadic transmission, profiling regional patterns of antimicrobial resistance associated with Mycobacterium tuberculosis, describing the molecular epidemiology of HIV genotypic spread, and investigating foci of epidemic hepatitis E virus transmission. Focused surveillance efforts, as described, provide for recognition of emerging and/or re-emerging diseases, optimising the investment of generally scarce public health resources.

Cosseron-Zerbib M. et al. *A control programme for MRSA (methicillin-resistant Staphylococcus aureus) containment in a paediatric intensive care unit: evaluation and impact on infections caused by other micro-organisms.* J Hosp Infect. 1998; 40(3) : 225-35.p Abstract: Methicillin-resistant Staphylococcus aureus (MRSA) is increasingly reported as a hospital-acquired pathogen in intensive care units (ICUs). The inconsistent application of hygiene measures by healthcare workers accounts largely for the epidemic dissemination of such resistant strains. The efficacy of a control programme to prevent spread of MRSA was assessed in our paediatric ICU (PICU) from April 1992 to December 1995. Patients initially had weekly MRSA cultures taken from samples of anterior nares and perineum, but from January 1994, cultures were also obtained upon admission. Immediately after notification, all MRSA carriers were isolated. Education of hospital staff was an essential component of our programme. Nosocomial infection rates were recorded retrospectively in 1992 and 1993, and prospectively in 1994 and 1995. Incidence rates between 'pre-programme' and 'programme' periods were compared. The rate of MRSA infection decreased from 5.9-0.8/1000 Patient-Days (PD), ($P < 10(-7)$. MRSA carriage also decreased from 34-2% ($P < 10(-9)$ and the ratio of MRSA to all S. aureus fell from 71-11% ($P < 10(-4)$. The decrease in the global incidence of infection from 20.1-13.9/1000 PD ($P = 0.002$) was due only to the decrease in MRSA infection. However, between 1994 and 1995, there was a significant increase in the number of transplant patients despite a constant patient/nurse ratio. The nosocomial infection rates caused by other micro-organisms decreased among the transplant patients from 64.8-33.2/1000 transplanted PD ($P = 0.009$) between 1994 and 1995. At the same time, we observed a slight increase of infections in non-transplanted patients, which may have been due to the effect of increased overall workload on those patients who were supposed to have fewer nosocomial risk factors. We conclude that implementation of infection control measures directed towards limiting person-to-person spread was effective in controlling high MRSA infection rates in a PICU, but it is important to allow enough time for staff to carry out hygiene practices thoroughly.

Costa L.M.D. et al. *Vancomycin-Resistant Enterococcus faecium: first case in Brazil.* Braz. j. infect. dis. 1998; 2(3) : 160-3.p Abstract: We report a fatal case of septicemia due to a vancomycin-resistant Enterococcus faecium in a 9 year-old girl with aplastic anemia. The isolate was also resistant to amplicillin, teicoplanin, gentamicin (high level), and streptomycin (high level). We believe that this is the first case of vancomycin-resistant Enterococcus (VRE) reported from a clinical specimen in Brazil. (AU);.

Costa S. de M et al. *[Scanning electronic microscopy of the small intestine in persistent diarrhea].* Arq Gastroenterol. 1997; 34(2) : 112-20.p Abstract: Persistent diarrhea very often leads children to malnutrition. It has become the major cause of death resulting from acute diarrhea episodes in developing countries. In order to determine the ultrastructural alterations of the small bowel that occur in the syndrome, 16 infants with severe persistent diarrhea were studied, utilizing light microscopy and the scanning electron microscope. Stool and jejunal fluid samples were collected for culture, rotavirus, ova and parasite search. Enteropathogenic agents were isolated in stools from 11 (68.7%) patients and bacterial proliferation in the small bowel was detected in 11 (68.7%) patients. EPEC strains were the most frequent enteropathogenic agent isolated both from stool and jejunal fluid cultures. The stool cultures revealed the presence of the following enteropathogenic microorganisms: EPEC 0111 in four, EPEC 0119 in one, EAggEC in five, Shigella flexneri in two, and Shigella sonnei in one; mixed infections due to EAggEC associated with EPEC 0111 were seen in two patients. The light microscopic analysis revealed that 56.2% of the patients suffered moderate villous atrophy most frequently associated with effacement of the microvil-

li, intracytoplasmatic vacuolization, increased number of multivesicular bodied and increased lymphocytic and eosinophylic infiltration in the lamina propria. The scanning electron microscopic analysis revealed in all cases shortening of the villi and enterocyte derangements; very often there was a total lack and/or effacement of the microvilli; in half of the patients there was a mucoid material covering the enterocytes tightly adhered to the apical epithelium surface. The scanning ultrastructural alterations observed in these patients are probably due to an association of factors brought about by the presence of enteropathogenic microorganisms and the resulting food intolerance that is responsible for perpetuation of diarrhea.

Costa S.F. et al. *Nosocomial fungaemia: a 2-year prospective study.* J Hosp Infect. 2000; 45(1) : 69-72.p Abstract: Eighty-six consecutive patients with fungaemia were studied during a period of 2 years, 81% had two or more positive blood cultures. Gastrointestinal tract (28%) and haematological diseases (17%) were the most common underlying conditions. The majority of cases had received vancomycin and/or imipenem (87%) and a central venous catheter (78%). Candida albicans (50%) and Candida parapsilosis (17%) were the most frequent isolates. Overall mortality was 41%, and for patients with Candida tropicalis was 71%. There was not significant difference in survival with gender, age and days of treatment with antifungal drugs. Haematological diseases, neutropenia and a higher number of positive blood cultures were associated with poor outcome.

Coudron P.E. et al. *In-vitro evaluation of nitrofurantoin as an alternative agent for metronidazole in combination antimicrobial therapy against Helicobacter pylori.* J Antimicrob Chemother. 1998; 42(5) : 657-60.p Abstract: Increasing metronidazole resistance suggests the need for alternative antibiotics for combination therapy of Helicobacter pylori infections. We evaluated a metronidazole-resistant and a clarithromycin-resistant strain of H. pylori under stationary growth phase conditions that favoured physiological conditions in order to determine if nitrofurantoin might be a suitable alternative for metronidazole in combination therapy. The results demonstrated that the triple combination of bismuth, tetracycline and nitrofurantoin achieved greater bactericidal activity against these two strains than did the combination of bismuth, tetracycline and metronidazole. These results suggest that further evaluation is warranted.

Coulton S. et al. *Recent advances in the chemistry and biology of carbapenem antibiotics.* Prog Med Chem. 1996; 33 : 99-145.p Abstract: The discovery of the olivanic acids and thienamycin aroused considerable interest amongst medicinal chemists and microbiologists around the world. The susceptibility of these agents to metabolic degradation has, however, been a major obstacle in their development. For many years the only notable success from such intensive research was the combination of imipenem with cilastatin, an inhibitor of the renal dipeptidase enzyme DHP-1. The enormous success of Primaxin for the treatment of a range of life-threatening bacterial infections provided the impetus for the discovery of totally synthetic, non-natural carbapenem derivatives that combine the broad spectrum of antimicrobial activity with stability to enzymatic degradation. This has indeed been realised in the development of meropenem; it possesses the broad spectrum of activity and resistance to beta-lactamases that are embodied in imipenem as well as displaying increased stability to human dehydropeptidases. Most recent research has focused upon the development of carbapenem antibiotics which combine broad spectrum antimicrobial activity and metabolic stability with oral absorption, for the treatment of community-acquired infections. Indeed, the pro-drug esters of the tricyclic carbapenems represent the first significant advance in this respect. However, the increased use of carbapenem antibiotics would undoubtedly accelerate the emergence of carbapenem-hydrolysing enzymes. The ultimate challenge could therefore be the design and synthesis of carbapenem derivatives that are resistant to these metallo-beta-lactamases. Due to the enormous problems encountered in the development of the carbapenem antibiotics, this area of research has, in the past, been described as a battlefield that did not bode well for the future [181]. Primaxin and meropenem proved however that these problems were not insurmountable, and are therefore a testimony to the persistence and dedication of those scientists in their war against bacterial infection.

Courcoux M.F. et al. *[Intravascular rupture of a central venous catheter in a premature infant: retrieval by a nonsurgical technique].* Arch Pediatr. 2000; 7(3) : 267-70.p Abstract: Central venous access is a frequent procedure in pediatric intensive care and neonatology. Catheter fracture with migration of the distal portion into the vessels is rare but may have side effects such as thrombosis. CASE REPORT: We report the case of a premature infant who had at three weeks of age a retained central venous catheter fragment in the pulmonary artery. The fragment was successfully retrieved by a percutaneous endovascular technique. No complication was observed during the procedure and afterward. CONCLUSION: This technique has avoided either delicate surgery or thrombotic risk due to a persistent intravascular foreign body. The authors prompted this interventional procedure within 36 hours after catheter migration in a center experienced in neonatal interventional catheterization.

Couroucli X.I. et al. *Detection of microorganisms in the tracheal aspirates of preterm infants by polymerase chain reaction: association of adenovirus infection with bronchopulmonary dysplasia.* Pediatr Res. 2000; 47(2) : 225-32.p Abstract: Bronchopulmonary dysplasia (BPD) is recognized as an important cause of morbidity and mortality in preterm infants. Because the role of congenital infections in BPD has been debated, the purpose of this study was to test the hypothesis that detection of infectious agents in tracheal aspirate samples was associated with the development of BPD. Tracheal aspirate samples were obtained within the 1st week of life and screened by polymerase chain reaction for adenovirus, cytomegalovirus, parvovirus, enteroviruses, Ureaplasma urealyticum, Mycoplasma hominis, Mycoplasma pneumoniae, and Chlamydia species. BPD was defined as persistent oxygen dependence at 28 d of age and 36 wk postconceptional age (PCA). Infants that expired before these time points were excluded from statistical analysis. Out of 89 infants studied, at 28 d of life, 13 had expired, 45 had BPD, and 31 had no BPD (controls). At 36 wk PCA, 15 infants expired, 39 still had BPD, and 35 did not. A significant increase in the frequency of adenovirus genome was identified in BPD patients compared with controls, both at 28 d of life (12/45 = 27% versus 1/31 = 3%: p< or =0.01) and at 36 wk PCA (10/39 = 29% versus 2/35 = 6%: p = 0.01). Other microorganisms were rarely detected and not associated with the development of BPD. This is the first study reporting the frequency of detection of adenovirus DNA in tracheal aspirate samples obtained during the 1st week of life from infants with BPD and suggests that prenatal acquisition may be important in the development of BPD.

Courtois P.H. et al. *Purification of NADH: hypothiocyanite oxidoreductase in Streptococcus sanguis.* Biochem Mol Med. 1996; 57(2) : 134-8.p Abstract: NADH: hypothiocyanite oxidoreductase (NHOR) activity, found in some oral Streptococci, is postulated to protect these microorganisms against salivary peroxidase-produced hypothiocyanite. NHOR, however, has not been purified so far. The purification of NHOR from crude extracts of Streptococcus sanguis NCTC 7863 strain (by ultrafiltration and anion-exchange chromatography) revealed one fraction of 125 +/- kDa. However, SDS-PAGE electrophoresis provided a single protein of 21.1 +/- 1.2 kDa. This last discovery suggests that NHOR enzyme is a hexameric complex having six subunits.

Cox C.E. *Cost-effective management of complicated urinary tract infections.* Adv Ther. 1995; 12(4) : 222-35.p Abstract: Complicated urinary tract infection (UTI), which often requires hospitalization or prolongs a hospital stay, presents numerous diagnostic and therapeutic challenges. Implementation of effective antimicrobial treatment is vital because of the risk of adverse sequelae due to persistence of infec-

tion, relapse, or reinfection. Further, the increasing resistance of common uropathogens, such as Pseudomonas aeruginosa, Klebsiella pneumoniae, and Enterobacter species, can complicate the therapeutic outcome. Economic factors also mandate cost-effective therapy. The costs of managing adverse sequelae have placed a significant liability on an already overburdened health care system. Estimates for prolonged hospitalization due to nosocomial UTI are reported as high as $2 billion a year in the United States. When parenteral rather than oral antimicrobial therapy is used, additional health care costs approximate $1000 per day per patient. Given the resistance to commonly used medications and the risk of serious adverse sequelae, clinicians are seeking more appropriate therapy. New oral antimicrobial agents now permit outpatient management of complicated UTIs that formerly required hospitalization for prolonged treatment. Currently, quinolones are recommended as first-line agents for complicated UTI. Reviews of pharmacokinetics, antimicrobial activity, efficacy, and safety of these drugs have noted equipotence or superiority to other antimicrobials, including trimethoprim/sulfamethoxazole. When used appropriately, quinolones provide effective and safe therapy for complicated UTI and offer in vitro efficacy against a broad range of pathogens.

Cox T.R. *Vascular infections: exceeding the threshold.* Mil Med. 1995; 160(12) : 609-11.p Abstract: During fiscal year 1988, our hospital infection control practitioner identified a 400% increase in the incidence of vascular surgery nosocomial infections. The six graft and six amputation infections were validated as nosocomial against hospital definitions adopted from the Centers for Disease Control. Our Infection Control Committee mandated an audit of the infected vascular surgery patients using a case/control design to identify and examine associated variables that may need attention. The significant finding was microbial resistance to prophylactic antibiotics used during surgery ($p > 0.0001$, Fisher's exact). The use of vancomycin as a prophylactic antimicrobial agent for all major vascular cases was recommended to the surgeons.

Crabtree T.D. et al. *Gender-dependent differences in outcome after the treatment of infection in hospitalized patients.* JAMA. 1999; 282(22) : 2143-8.p Abstract: CONTEXT: While it is established that management strategies and outcomes differ by gender for many diseases, its effect on infection has not been adequately studied. OBJECTIVE: To investigate the role of gender among hospitalized patients treated for infection. DESIGN: Observational cohort study conducted during a 26-month period from December 1996 through January 1999. SETTING: University-affiliated hospital. PARTICIPANTS: A total of 892 patients in the surgical units of the hospital with 1470 consecutive infectious episodes (782 in men and 688 in women). MAIN OUTCOME MEASURES: Mortality during hospitalization by gender for infection episodes overall and for specific infectious sites, including lung, peritoneum, bloodstream, catheter, urine, surgical site, and skin/soft tissue. RESULTS: Among all infections, there was no significant difference in mortality based on gender (men, 11.1% vs women, 14.2%; P =.07). After logistic regression analysis, factors independently associated with mortality included higher APACHE (Acute Physiology and Chronic Health Evaluation) II score, older age, malignancy, blood transfusion, and diagnosis of infection more than 7 days after admission, but not gender (female odds ratio [OR] for death, 1.32; 95% confidence interval [CI], 0.90-1.94; P =.16). Mortality was higher in women for lung (men, 18% vs women, 34%; P =.002) and soft tissue (men, 2% vs women, 10%; P < or =.05) infection; for other infectious sites, mortality did not differ by gender. Factors associated with mortality due to pneumonia by logistic regression included higher APACHE II score, malignancy, diabetes mellitus, diagnosis of infection more than 7 days after admission, older age, transplantation, and female gender (OR for death, 2.25; 95% CI, 1.17-4.32; P =.02). CONCLUSIONS: Although gender may not be predictive of mortality among all infections, women appear to be at increased risk for death from hospital-acquired pneumonia, even after controlling for other comorbidities.

Craig W.A. *Antimicrobial resistance issues of the future.* Diagn Microbiol Infect Dis. 1996; 25(4) : 213-7.p Abstract: Increasing antimicrobial resistance among respiratory pathogens has the potential to reduce the efficacy of standard dosage regimens for many oral drugs. The goal of antimicrobial therapy is to maximize bactericidal activity. The duration of time that serum concentrations exceed the MIC is the pharmacokinetic/pharmacodynamic parameter that determines efficacy for beta-lactams, macrolides, and trimethoprim/sulfamethoxazole. Studies in animal models suggest that serum levels of beta-lactams need to exceed the MIC for about half of the dosing interval to obtain maximum antimicrobial efficacy. Studies in children with acute otitis media also demonstrate that serum concentrations need to exceed the MIC for 40% or more of the dosing interval to obtain bacteriologic cure in over 85% of patients. With the oral beta-lactams used against penicillin-resistant Streptotoccus pneumoniae, this goal is obtained only with amoxicillin and amoxicillin/clavulanate. For Haemophilus influenzae, several beta-lactams including cefixime, cefpodoxime, and amoxicillin/clavulanate provide serum levels with the longest durations above the MIC. Antimicrobial resistance has also stimulated the search for new potent antimicrobials, altered but effective dosing regimens, and resistance control measures, such as the prudent use, optimal infection control practices, and vaccines to reduce colonization and subsequent infection.

Craig W.A. *The future—can we learn from the past?* Diagn Microbiol Infect Dis. 1997; 27(1-2) : 49-53.p Abstract: We know that the current problems of resistance among bacterial pathogens to commonly prescribed antibiotics is, in part, attributable to inappropriate prescribing. If we are to rectify matters, we must learn from past mistakes and take appropriate measures to ensure that community-acquired infections do not become as untreatable as certain nosocomial infections are now. This means that we must be able to predict efficacy outcomes better so that we can make more effective use of available antibiotics. Animal studies suggest that the duration of time that an antibiotic exceeds the MIC of the causative pathogen (i.e., at least 40 to 50% of the dosing interval) is a good prognostic indicator for the efficacy of beta-lactam antibiotics. Clinical studies are now being published that confirm the value of time above MIC. Use of this information should enhance efficacy and may delay the pace of developing antibiotic resistance, allowing time for new antimicrobial agents to be researched and brought to market.

Craven D.E. et al. *Hospital-acquired pneumonia: perspectives for the healthcare epidemiologist.* Infect Control Hosp Epidemiol. 1997; 18(11) : 783-95.p Abstract: Nosocomial pneumonia is defined as an infection of lung parenchyma that was neither present nor incubating at the time of the patient's admission to the hospital. In the United States, hospital-acquired pneumonia is the second most common nosocomial infection and accounts for the most deaths from nosocomial infection. We describe how infection control personnel can use targeted surveillance to identify clusters of cases and to prevent pneumonia. We also discuss common pathogens that cause nosocomial pneumonia; ventilator-associated pneumonia; and strategies for prevention of hospital-acquired pneumonia.

Cravens D.D. et al. *Urinary catheter management.* Am Fam Physician. 2000; 61(2) : 369-76.p Abstract: The use of urinary catheters should be avoided whenever possible. Clean intermittent catheterization, when practical, is preferable to long-term catheterization. Suprapubic catheters offer some advantages, and condom catheters may be appropriate for some men. While clean handling of catheters is important, routine perineal cleaning and catheter irrigation or changing are ineffective in eliminating bacteriuria. Bacteriuria is inevitable in patients requiring long-term catheterization, but only symptomatic infections should be treated. Infections are usually polymicrobial, and seriously ill patients require therapy with two antibiotics. Patients with spinal cord injuries and those using catheters for more than 10 years are at greater risk of bladder cancer

and renal complications; periodic renal scans, urine cytology and cystoscopy may be indicated in these patients.

Crawford M. et al. *Peripherally inserted central catheter program*. Nurs Clin North Am. 2000; 35(2) : 349-60.p Abstract: The peripherally inserted central catheter (PICC) is a safe and less costly option to centrally inserted, tunneled, or implanted central vascular access devices. Support for PICC services and reports of results vary among organizations. A comprehensive PICC Program, guided by the Center for Advanced Nursing Practice's Evidence-Based Practice Model, was designed and implemented with successful outcomes. Key program components include administrative, education, clinical practice, and data monitoring to enhance best practice.

Crawford M.J. et al. *Regulation of the Salmonella typhimurium flavohemoglobin gene. A new pathway for bacterial gene expression in response to nitric oxide.* J Biol Chem. 1998; 273(51) : 34028-32.p Abstract: Flavohemoglobins, a family of two-domain proteins with homology to vertebrate hemoglobins, are found in a variety of prokaryotic and eukaryotic microorganisms. Recent studies suggest a role for these proteins in nitrogen oxide metabolism. We now show that nitric oxide donors positively regulate a chromosomal flavohemoglobin (hmp)/lacZ operon fusion in Salmonella typhimurium. hmp gene expression in the presence of NO. is independent of the SoxS, OxyR, and FNR transcription factors and instead relies on inactivation of the iron-dependent Fur repressor. Other Fur-repressed promoters in S. typhimurium are also activated by an NO. donor. In contrast to the wild-type strain, an hmp- mutant requires markedly lower concentrations of NO to induce the hmp/lacZ fusion, whereas its response to iron chelation is equivalent to wild type. These data unveil a new pathway for NO-dependent gene expression in S. typhimurium.

Crewe-Brown H.H. et al. *Streptococcus pneumoniae blood culture isolates from patients with and without human immunodeficiency virus infection: alterations in penicillin susceptibilities and in serogroups or serotypes.* Clin Infect Dis. 1997; 25(5) : 1165-72.p Abstract: We performed a 3-year retrospective study of Streptococcus pneumoniae blood culture isolates recovered at Baragwanath Hospital, Soweto, South Africa, from 1993 to 1995. The study group comprised 457 patients, including 98 children, of known human immunodeficiency virus (HIV) serostatus. Of these patients, 70 (30 [8.4%] of 359 adults and 40 [40.8%] of the 98 children) were infected with penicillin-resistant S. pneumoniae strains (minimal inhibitory concentration, > or = 0.12 microg/mL); 56 of these strains were intermediately resistant to penicillin. HIV-positive patients had significantly more penicillin-resistant isolates than did HIV-negative patients (43 [29.7%] of 145 HIV-positive patients vs. 27 [8.6%] of 312 HIV-negative patients; P <.001); this difference was found for both adults (19% vs. 4.3%; P <.001) and children (53.3% vs. 30.2%; P <.0343). Multiple resistance occurred more frequently in HIV-positive children (P =.02). HIV-positive adults had a statistically significant increase in the percentage of serogroups and serotype usually found in children and commonly associated with antimicrobial resistance, i.e., serotype 14 and serogroups 6, 19, and 23 (48% vs. 28.6%; P <.001). The increased prevalence of serogroups or serotypes usually found in children was also found among penicillin-susceptible strains. These data suggest that HIV-infected adults may again become susceptible to the serogroups or serotypes found in children.

Cristino J.M. et al. *[Multicenter study of isolated micro-organisms resistant to antimicrobials in 10 Portuguese hospitals in 1994].* Acta Med Port. 1996; 9(4-6) : 141-50.p Abstract: In 1994, Microbiology Laboratories of ten Portuguese hospitals analysed isolated microorganisms found in blood and urine samples and studied antimicrobial susceptibilities of the most frequent bacterial pathogens. From 63780 blood samples, the most frequent were Staphylococcus spp. and from 69189 urine samples significant numbers of Escherichia coli, Enterococcus spp., Pseudomonas aeruginosa and Candida spp. were isolated. Escherichia coli strains (c.7000) revealed a low percentage of resistance to antibiotics with the exceptions of ampicillin (48%) and co-trimoxazol (25%). Klebsiella pneumoniae isolates (c.2000) revealed important resistance to ampicillin (98%), cephalotin (31%), co-trimoxazol (38%) and gentamicin (28%), while values for 3rd generation cephalosporins varied among hospitals, with several strains showing phenotype of extended-spectrum beta-lactamase. A great variation in resistance values of P. aeruginosa (c.4000) was found in relation to the antibiotics as well as to the hospitals. Resistance to methicillin in S. aureus (c.6000) was high, reaching an average of 47%, and it was even higher with S. epidermidis (c.3000) and S. haemolyticus (c.650). Only vancomycin was always active against these strains. In E. faecalis (c.2500) resistance was of 2% to ampicillin, 35% to gentamicin, 45% to streptomycin and 1% to vancomycin. E. faecium isolates (c.300) showed the most worrying results with 70% resistance to ampicillin, 42% to gentamicin, 59% to streptomycin and 9% (30 strains isolated in 5 hospitals) to vancomycin. Vancomycin resistant strains were also resistant to all other antibiotics.

Cristino J.M. et al. *[The diversity of Staphylococcus aureus strains isolated in a Lisbon hospital over a 4-year period].* Acta Med Port. 1999; 12(4-6) : 169-76.p Abstract: Over a 4-year period, 2020 Staphylococcus aureus strains isolated in Santa Maria Hospital were studied, 26.3% of which were methicillin-resistant (MRSA). The main specimens from which the strains were isolated included pus, blood and sputum/bronchial secretions. Isolation in blood cultures was the most common source among patients from medical units. Antimicrobial susceptibility studies showed that while in methicillin susceptible strains sensitivity to other antimicrobial agents (apart from penicillin resistance) was the rule, in MRSA strains there was resistance to most antibiotics. Only vancomycin was active against all strains. Phage typing showed that 75.5% of the strains were typable with phages at 100 x R.T.D. Among methicillin sensitive strains, a big diversity of phage patterns was observed, including phage groups I, II, III and V, as well as with phage association D11/95. The large majority of MRSA strains were lysed by group III phages, although several distinct patterns were observed. Within these strains, lysis by groups II and V phages was not observed. Plasmid profiling was the least discriminant issue in the characterization of these micro-organisms because most of the strains harboured only one plasmid (or none). These results showed that a dominant MRSA strain did not exist in this hospital, but rather several distinct strains. The importance, as well as the difficulties in controlling the spread of MRSA strains in the present conditions of high prevalence, are highlighted.

Cross J.T. Jr et al. *Drug-resistant pathogens in community- and hospital-acquired pneumonia.* Clin Chest Med. 1999; 20(3) : 499-506.p Abstract: Antimicrobial resistance has been a problem since the early days of the antibiotic era, but in recent years, this resistance has increased in the hospital and is being recognized more in the community setting. Respiratory pathogens such as S. pneumoniae and H. influenzae, for example, have developed resistance to traditional antimicrobial therapy, often over a very short period of time. This increase in resistance patterns requires physicians to closely monitor antimicrobial resistance in their community and to appreciate that some antimicrobial resistance mechanisms may result in resistance for a complete class of antibiotics or different classes of antibiotics with similar mechanisms of action.

Crowcroft N.S. et al. *Methicillin-resistant Staphylococcus aureus and antimicrobial use in Belgian hospitals.* Infect Control Hosp Epidemiol. 1999; 20(1) : 31-6.p Abstract: OBJECTIVE: To investigate relationships between the incidence of methicillin-resistant Staphylococcus aureus (MRSA) and the use of different classes of antimicrobials in Belgian hospitals. DESIGN: Using Pearson correlation coefficients, the number of new nosocomial MRSA-colonized or -infected patients in the second half of 1994 and the first half of 1995 reported by the national MRSA surveillance program was compared with

use of various antimicrobial classes as reported by the National Institute for Sickness and Disability Insurance. Relationships between different classes of antimicrobials were evaluated in a correlation matrix. MRSA incidence, antimicrobial use, and potential confounding factors were included in a multiple linear regression analysis. SETTING: 50 hospitals in Belgium. RESULTS: The use of a number of different classes of antimicrobials was interrelated. In the multivariate analysis, the incidence of nosocomial MRSA increased with increasing use of ceftazidime and cefsulodin (P=.0003), amoxicillin with clavulanic acid (P=.02), and quinolones (P=.005). No association was found between MRSA incidence and total antimicrobial use. CONCLUSIONS: The relationships between antimicrobial use and MRSA are complex. Interventions aimed at promoting more rational prescribing patterns should be supported by adequate experimental and epidemiological evidence. Advice for preventing and controlling MRSA has focused mainly on hygienic measures and precautions to avoid cross-transmission; the role of relieving antimicrobial pressure needs to be clarified.

Crowe M. et al. *Bacteraemia in the adult intensive care unit of a teaching hospital in Nottingham, UK, 1985-1996.* Eur J Clin Microbiol Infect Dis. 1998; 17(6) : 377-84.p Abstract: Bacteraemia is an important cause of morbidity and mortality in the intensive care unit. In this study the distribution of organisms causing bacteraemic episodes in patients in the adult intensive care unit of a large teaching hospital was determined. Particular emphasis was placed on the type of organisms isolated from community- and hospital-acquired bacteraemia, the suspected source of infection, the possible risk factors associated with bacteraemia, and outcome. The incidence of bacteraemia and fungaemia increased from 17.7 per 1000 admissions in 1985 to 80.3 in 1996. A total of 315 episodes of bacteraemia and fungaemia were documented over a 12-year period, of which 18% were considered community-acquired and 82% hospital-acquired. Gram-positive and gram-negative bacteria accounted for 46.9% and 31.5% of the episodes, respectively. Polymicrobial infection accounted for 17.8% and fungi for 3.8% of the episodes. Staphylococcus aureus (22.5%), Staphylococcus epidermidis (7.6%), and Streptococcus pneumoniae (7.9%) were the predominant gram-positive bacteria implicated, whereas Escherichia coli (6%), Enterobacter cloacae (7%), Klebsiella aerogenes (3.8%), Pseudomonas aeruginosa (5.1%), and Acinetobacter spp. (3.8%) were the predominant gram-negative bacteria isolated. The two most common sources of infection were the respiratory tract (39.7%) and an intravascular line (24.5%), but in 8.9% of episodes the focus of infection remained unknown. Bacteraemic patients stayed in the unit for a longer period (12 days) than did non-bacteraemic patients (3 days). The overall mortality related to bacteraemia and candidaemia was 44.4%. Surveillance of bacteraemia in the intensive care unit is important in detecting major changes in aetiology, e.g., the increasing incidence of gram-positive bacteraemia, the emergence of methicillin-resistant Staphylococcus aureus in 1995, and the emergence of Enterobacter cloacae. It is of value in determining empirical antimicrobial therapy to treat presumed infection pending a microbiological diagnosis and in directing the development of guidelines for infection prevention, e.g., guidelines for central venous catheter care.

Crowther J. et al. *Growth of microorganisms in propofol, thiopental, and a 1:1 mixture of propofol and thiopental.* Anesth Analg. 1996; 82(3) : 475-8.p Abstract: To assess and compare the growth of four microorganisms in solutions of intravenous anesthetics, known quanta of Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Candida albicans were inoculated into propofol, thiopental, a 1:1 mixture of propofol and thiopental, and normal saline. All microorganisms were taken from standard stock cultures and incubated for 24 h (48 h for C. albicans). Growth of microorganism in each drug was compared by counting the number of colony forming units (CFUs) grown from a subculture of each inoculated anesthetic at 0, 3, 6, 12, and 24 h. The study shows that propofol strongly supports the growth of E. coli and C. albicans but is bacteriostatic toward S. aureus and weakly bactericidal toward P. aeruginosa. In contrast, both thiopental and the 1:1 mixture of propofol and thiopental behaved differently, exhibiting markedly bactericidal properties toward E. coli, S. aureus, and P. aeruginosa and a bacteriostatic effect on C. albicans. This finding supports recommendations that a strict aseptic technique should be used when handling propofol and that the contents of an ampoule should be used within 6 h of aspirating. The measured high pH of both thiopental and the 1:1 mixture of propofol and thiopental compared to propofol alone suggests pH to be a major factor in determining whether a given drug will support microbial growth.

Cruchaga S. et al. *[Antimicrobial susceptibility of a selection of Salmonella enterica strains of various origins isolated in Spain].* Rev Esp Quimioter. 1999; 12(3) : 250-4.p Abstract: The widespread use of antimicrobials in human and veterinary practice is increasingly causing the emergence of different multidrug-resistant human pathogens. This situation makes treating infections caused by these microorganisms difficult. Salmonella enterica is an ubiquitous organism and may be a good indicator of the influence of the use and abuse of antimicrobials on the appearance of multiresistant strains. One hundred and ninety S. enterica strains of different origins isolated in Spain in 1996 were randomly selected. The minimal inhibitory concentration (MIC) was studied using the agar dilution method according to NCCLS criteria in the following antimicrobials: ampicillin, ticarcillin, amoxicillin-clavulanic acid, cefazolin, cefuroxime, cefotaxime, imipenem, gentamicin, apramycin, ciprofloxacin, streptomycin, chloramphenicol, tetracycline, sulfamethoxazole and co-trimoxazole. Sixty-three percent of the S. enterica tested were resistant and 24% were multiresistant. The percentage of resistant and multiresistant strains of S. enterica of human origin was slightly higher than those of nonhuman origin. Statistically, ampicillin, ticarcillin and amoxicillin-clavulanic acid were significantly more resistant in strains of human origin. Ninety-one percent of the strains of Typhimurium serotype and phagotype 104 were multiresistant. The Salmonella Typhimurium serotype and phagotype 104 ACSTSu-resistant clone, which is widespread in various Western countries, was also isolated in this study. The use of different antimicrobials in human and veterinary practice needs to be rationalized.

Crump J.A. et al. *Intravascular catheter-associated infections.* Eur J Clin Microbiol Infect Dis. 2000; 19(1) : 1-8.p Abstract: Serious infections associated with intravascular catheters are common. The available data suggests there are likely to be more than 500 000 cases of catheter-associated bloodstream infections occurring annually in Western Europe and the USA. These may be associated with as many as 100 000 deaths. The pathophysiology of this common condition is still not fully elucidated. With catheters that are in place for short periods (a few days), microbial migration down the outer surface of the device to the intravascular tip predominates. For catheters that are in place for longer periods, migration occurs more often via the internal lumen. After being in place for more than 8 days, nearly all central vein catheters will have microorganisms embedded in a biofilm within the catheter lumen. In some catheters, microorganisms will proliferate to sufficient numbers for systemic sepsis to result. The occurrence and rate of this proliferation is dependent on microbial virulence factors, host factors, and characteristics of the catheter. Diagnosis of intravascular device-associated sepsis remains problematic because the pathophysiology of the condition changes with time and because standard culture techniques rarely detect organisms embedded in biofilms. The semiquantitative roll method on blood agar remains in common use because of its simplicity. However, the method only samples the external surface of the catheter. For catheters that have been in place for extended periods of time, methods that better sample the internal lumen, such as sonication and quantitative broth methods, should be developed and used.

Cruz M.C. et al. *Immunosuppressive and nonimmunosuppressive cyclosporine*

analogs are toxic to the opportunistic fungal pathogen Cryptococcus neoformans via cyclophilin-dependent inhibition of calcineurin. Antimicrob Agents Chemother. 2000; 44(1) : 143-9.p Abstract: Cyclosporine (CsA) is an immunosuppressive and antimicrobial drug which, in complex with cyclophilin A, inhibits the protein phosphatase calcineurin. We recently found that Cryptococcus neoformans growth is resistant to CsA at 24 degrees C but sensitive at 37 degrees C and that calcineurin is required for growth at 37 degrees C and pathogenicity. Here CsA analogs were screened for toxicity against C. neoformans in vitro. In most cases, antifungal activity was correlated with cyclophilin A binding in vitro and inhibition of the mixed-lymphocyte reaction and interleukin 2 production in cell culture. Two unusual nonimmunosuppressive CsA derivatives, (gamma-OH) MeLeu(4)-Cs (211-810) and D-Sar (alpha-SMe)(3) Val(2)-DH-Cs (209-825), which are also toxic to C. neoformans were identified. These CsA analogs inhibit C. neoformans via fungal cyclophilin A and calcineurin homologs. Our findings identify calcineurin as a novel antifungal drug target and suggest nonimmunosuppressive CsA analogs warrant investigation as antifungal agents.

Cuadra Fernández, R. et al. *Respuesta social de la población frente a los problemas de salud, en dos barrios de Managua, 1995*; Managua. UNAM/CIES. 1996; 167.p Abstract: Estudio descriptivo de corte transversal y de carácter cuanti-cualitativo de dos barrios marginales de Managua; el Barrio Hilario Sánchez y el Barrio Las Torres, que presentan condiciones socio-económicas, ambientales y problemas de salud similares y con diferentes nivel de desarrollo comunitario. Se caracteriza por encontrar la respuesta social de la población de los barrios estudiados; valorando la organización y participación de la población frente a sus problemas de salud; así como en qué medida el desarrollo comunitario facilita el proceso de solución a los principales problemas de salud de la comunidad. Se utilizaron diferentes instrumentos en la recolección de la información como: grupos focales, entrevistas a informantes claves, encuestas a Madres de familia y revisión bibliográfica. Se encontró que el desarrollo de las organizaciones comunitarias produce un impacto positivo en la salud de la población, pero hay limitantes que impiden que ese impacto sea mayor y logre un cambio de actitudes que permita la autosostenibilidad, autogestión y empoderamiento. Las principales limitantes encontradas para lograr una respuesta social más eficaz se centran en la falta de un concepto amplio de participación de parte de las Instituciones, organismos y organizaciones comunitarias, que permita el empoderamiento de la comunidad y en el abordaje individual de la intervenciones de salud que no ubican como unidad de análisis a la familia como monitor central de las transformaciones culturales, asimismo se demuestra que la salud es un elemento, punto de encuentro en el cual las organizaciones comunitarias de diferentes signos políticos han logrado establecer un concenso para la b£squeda de solución a sus problemas. Concluye que los problemas de la salud no se resuelven con un enfoque unilateral e insuficiente de disciplinas específicas, en el que no se incluyen el análisis sociológico de elementos relacionados con las condiciones de vida de la población, los factores culturales, conducta, creencia, concepciones y valores sociales que son elementos que aportan a una concepción integral de intervención que permita reconocer y potenciar el nivel de respuesta social existente en la población frente a sus problemas de salud.

Cuchacovich T. M. et al. *Tratamiento de la enfermedad ocular inflamatoria con glucocorticoides y pulsos de ciclofosfamida*. Rev. méd. Chile. jul. 1995; 123(7) : 865-73.p Abstract: The effectiveness, toxicity and prognosis factors influencing responses to cyclophosphamide (CP) iv pulses plus oral glucocorticosteroids (GC) in patients with GC-resistant ocular inflammatory diseases (OID) was evaluated in a cohort of 15 consecutive patients suffering from active, non-infectious OID refractory to oral GC. All patients underwent monthly evaluations with clinical, hematological, hepatic, renal and ophthalmologic tests. These included checking visual acuity and both anterior chamber and posterior segment inflammation.

Cucurull E. et al. *Gonococcal arthritis.* Rheum Dis Clin North Am. 1998; 24(2) : 305-22.p Abstract: Disseminated gonococcal infection is the most common systemic complication of acute gonorrhea and occurs in 0.5% to 3.0% of patients with untreated mucosal infection. It is also the most common cause of septic arthritis in patients less than 30 years of age. Fortunately, the incidence of gonorrhea is decreasing dramatically in the United States and Western Europe, although it is still high in developing countries. Increasing resistance to antibiotics requires continuous surveillance of antimicrobial susceptibilities to determine the efficacy of current therapeutic measures.

Cummings M.C. et al. *Susceptibility of isolates of Neisseria gonorrhoeae to penicillin and tetracycline in Brooklyn, 1988-1992.* Sex Transm Dis. 1995; 22(2) : 110-3.p Abstract: BACKGROUND AND OBJECTIVES: The aim of this analysis was to determine the rate of resistance of Neisseria gonorrhoeae to penicillin and tetracycline over 5 years. STUDY DESIGN: The authors studied 500 isolates of N. gonorrhoeae. Minimum inhibitory concentrations of various antimicrobial agents, including penicillins, tetracyclines, quinolones, cephalosporins, spectinomycin, and trospectomycin, were determined using agar dilution. Organisms that produced beta-lactamase were classified as penicillinase-producing N. gonorrhoeae, and those with tetracycline minimum inhibitory concentrations > 16 micrograms/ml were considered presumptive high-level tetracycline resistant. Organisms with Minimum inhibitory concentrations > 2.0 micrograms/ml were presumptively considered to have chromosomally mediated resistance to penicillin or tetracycline. Isolates with none of these forms of resistance were considered susceptible to penicillin and tetracycline. RESULTS: Penicillinase-producing N. gonorrhoeae represented 34.7%, 40.7%, and 44.9% of gonococcal isolates in 1988, 1989, and 1990, respectively. Only 14.3% and 15.0% of the isolates in 1991 and 1992 were penicillinase-producing N. gonorrhoeae. In 1988, 1.0% of isolates were chromosomally mediated penicillin resistant. In contrast, chromosomally mediated penicillin resistant gonococci represented 7.5% to 22.4% of isolates from 1989 to 1992. In 1988, 26.0% of isolates were high-level tetracycline resistant. The prevalence of presumptive high-level tetracycline resistant organisms decreased after 1988. From 1989 to 1992, only 8.2% to 14.8% of gonococcal isolates were presumptive high-level tetracycline resistant. No chromosomally mediated tetracycline resistant isolates were identified in 1988. In 1989 and 1990, 11.6% and 10.2%, respectively, of isolates were chromosomally mediated tetracycline resistant. Chromosomally mediated tetracycline resistant N. gonorrhoeae represented 2.0% of isolates in 1991 and 25.0% of isolates in 1992. All isolates tested were susceptible to the other antibiotics. CONCLUSION: Continued surveillance of sensitivity of contemporary gonococci to antimicrobial agents is important.

Cunha B.A. *Antibiotic resistance. Control strategies.* Crit Care Clin. 1998; 14(2) : 309-27.p Abstract: Antibiotic resistance is a worldwide concern. Over the past several decades, antibiotic resistance has increased to many respiratory pathogens as well as aerobic gram-negative bacilli. Recently, methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus (VRE) have become important hospital pathogens. Antibiotic resistance is not related to a particular antibiotic structure and is not dependent upon mechanism of antibiotic action. The volume of use per se does not increase antimicrobial resistance. This article discusses control strategies and identifies which antibiotics are associated with the emergence of resistant organisms.

Cunha B.A. *Nosocomial diarrhea*. Crit Care Clin. 1998; 14(2) : 329-38.p Abstract: Nosocomial diarrheas are an important problem in hospitals, and in critical care units in particular. Hospital-acquired diarrhea may be on an infectious or noninfectious basis. Common noninfectious causes of nosocomial diarrhea include medication-induced changes in the fecal flora or changes secondary to enteral hyperalimenation. Infectious causes of nosocomial diarrhea are due to

enteric pathogens in outbreak situations and virtually all of the causes are due to Clostridium difficile. C. difficile is a resident of the human colon and does not cause disease if its toxins are not elaborated. Chemotherapeutic agents, and more commonly, antibiotics, induce the elaboration of toxin A and B from C. difficile in the distal gastrointestinal tract. The spectrum of disease of C. difficile in hospitalized patients includes asymptomatic carriage to mild watery diarrhea, fulminant and severe diarrhea, and pseudomembranous enterocolitis. The treatment of C. difficile diarrhea is usually with oral metronidazole or vancomycin, and C. difficile colitis is treated with intravenous metronidazole. Infection control measures are necessary to prevent the spread of this sporforming organism within the institution since it is capable of surviving in the hospital environment for prolonged periods.

Cunha B.A. et al. *Emergence of antimicrobial resistance in community-acquired pulmonary pathogens.* Semin Respir Infect. 1998; 13(1) : 43-53.p Abstract: Antibiotic resistance to the common respiratory tract pathogens is increasing worldwide. Penicillin-resistant pneumococci are of particular concern. Most strains of penicillin-resistant Streptococcus pneumoniae have intermediate resistance to penicillin, and highly resistant strains are rare at present. Careful selection of antibiotics with low resistance potential and excellent activity against highly penicillin-resistant pneumococci (ie, cefotaxime, ceftriaxone, cefepime, cefprozil, doxycycline, levofloxacin, sparfloxacin, and meropenem) is the best current strategy to delay or increase the emergence of highly penicillin-resistant strains of S pneumoniae.

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D'Agata E.M. et al. *Hospital-acquired infections among chronic hemodialysis patients.* Am J Kidney Dis. 2000; 35(6) : 1083-8.p Abstract: The epidemiological characteristics of nosocomial infections among patients requiring chronic hemodialysis, a high-risk and rapidly growing population, have not been fully elucidated. During a 30-month cohort study, rates of bloodstream infections (BSIs), urinary tract infections (UTIs), pneumonia, and diarrhea caused by Clostridium difficile and the distribution of pathogens among hospitalized chronic hemodialysis patients were compared with hospitalized patients not requiring chronic hemodialysis. To identify risk factors for developing a nosocomial infection among chronic hemodialysis patients, a matched case-control study was performed. A total of 1,557 nosocomial infections were detected during 1,317 of 68,361 admissions (2%). Of these, 47 nosocomial infections occurred in chronic hemodialysis patients during 31 of 578 admissions (5%). Nosocomial infections were significantly more frequent among the chronic hemodialysis group (9.1/1,000 patient-days) compared with the non-chronic hemodialysis group (3. 8/1,000 patient-days; relative risk [RR], 2.4; 95% confidence interval [CI], 1.8 to 3.2; $P < 0.001$). UTIs were the most common nosocomial infections among chronic hemodialysis patients, accounting for 47% of all infections in this population. UTIs were significantly more common among chronic hemodialysis patients (4.2/1, 000 patient-days) compared with non-chronic hemodialysis patients (0.7/1,000 patient-days; RR, 6.2; 95% CI, 3.8 to 9.5; $P < 0.001$). Among chronic hemodialysis patients, Candida spp and enterococci were the most common pathogens in contrast to coagulase-negative staphylococci and Staphylococcus aureus among patients not requiring hemodialysis. Using conditional logistic regression, a greater index of comorbidity was significantly associated with nosocomial infections among the chronic hemodialysis population (odds ratio, 3. 6; 95% CI, 1.2 to 10.7; $P = 0.02$). Chronic hemodialysis patients are at a substantially greater risk for developing a nosocomial infection compared with other hospitalized patients.

D'Angelo G. et al. *[Probiotics in childhood].* Minerva Pediatr. 1998; 50(5) : 163-73.p Abstract: The Probiotics (Lactic acid bacteria) represent a nutritional live microbial supplement that positively affects host by enhancing the microbial balance. A survey is made of the most relevant studies concerning the use of probiotics in the prevention and treatment of infantile acute diarrhoea (by rotavirus or other agents), pseudomembranous colitis, hospital-acquired and antibiotic-associated diarrhoeas. Although the probiotics mechanism of action is not yet completely understood, it has been hypothesized that they exert an inhibitory effect on the intestinal inflammation by immune response modulation. Due to this property, the use of probiotics has therefore been suggested in other severe diseases such as chronic inflammatory bowel diseases, rheumatoid arthritis, food allergy, atopic dermatitis and as immunoadjuvant for oral vaccines.

D'Arcangelo C. et al. *[Alpha-hemolytic streptococci and root canal irrigants. An evaluation of the bactericidal efficacy of sodium hypochlorite and chlorhexidine gluconate plus cetrimide].* Minerva Stomatol. 1998; 47(9) : 367-71.p Abstract: BACKGROUND AND AIMS: The main bacterial species present in pulpal and periapical microbic flora is alpha-hemolytic streptococci. They are regarded as facultative anaerobes which prefer to grow in anaerobiosis. Canal irrigation plays an important role in the success of endodontic treatment given that, on the one hand, it encourages the gradual elimination of the smear layer, and on the other it neutralises microbic flora in the root canal. The aim of this study was to test the microbiological efficacy of sodium hypochlorite 1% and s new generation irrigant based on chlorhexidine 0.2% and cetrimide 0.2%. METHODS: The test was performed on the following alpha-hemolytic streptococci bacteria (Dasit, Cornaredo, Italy): Streptococcus mitis ATCC 9811; Streptococcus mutans ATCC 35668; Streptococcus salivarius ATCC 13419; Streptococcus sanguis ATCC 10556. The working concentration (CFU/ml) was defined as 0.5 Mc Farland which corresponds to a concentration of microorganisms of approximately 1.5 x 10(8) bacteria. The following canal irrigants were used: 1) cetrimide 0.2% + chlorhexidine 0.2% (Cetrexidin Vebas, S. Giuliano Milanese, Italy); 2) NaOCl 1% (Ogna, Milan, Italy). Each individual substance remained in contact with the bacterial species used in the test for 10'-20'-30'. RESULTS: The results obtained show the bactericidal efficacy of both the irrigants used, even after a short period of contact. CONCLUSIONS: This does not mean that all irrigants are equal and/or promise the same results. This was a microbiological study, but it is nonetheless important to take other variables into account, such as contact time. Moreover, in order to increase the probabilities for the success of endodontic treatment, canal irrigants must also present other characteristics, namely: biocompatibility, scarce toxicity, high proteolytic power.

D'Orazio J.A. et al. *Human natural killer (NK) cells present staphylococcal enterotoxin B (SEB) to T lymphocytes.* Clin Exp Immunol. 1996; 104(2) : 366-73.p Abstract: Superantigen-mediated T cell activation requires the participation of antigen-presenting cells (APC). Once superantigen has bound class II MHC molecules on the surface of APC, it then can interact with the T cell receptor to induce T cell activation. Superantigen-mediated T lymphocyte activation, along with its consequent cytokine production is thought to be the basis for the pathophysiology of conditions such as toxic shock syndrome, Kawasaki's disease and possibly rheumatoid arthritis. We examined the role of CD56+ NK lymphocytes in the interaction between superantigens and T lymphocytes. First, we found that a subpopulation of CD56+ cells freshly isolated from human peripheral blood expressed class II MHC molecules. The amount of HLA-DR expression varied between individuals, ranging from 9.3% to 37.7%. CD56+ (NK) cells were purified from the peripheral blood by cell sorting and were tested for their ability to support SEB-mediated T cell activation as assessed by surface expression of IL-2 receptor alpha-chain (CD25) on CD3+ lymphocytes. We observed that when enriched T cells were incubated with SEB in the presence of NK cells, there was a significant up-regulation of CD25 expression of the T cells. When HLA-DR+ cells were removed from sort-

ed CD56+ populations, the remaining HLA-DR- NK cells were unable to support SEB-mediated T cell activation. Also, SEB up-regulated the expression of HLA-DR on CD56+ cells in peripheral blood mononuclear cell (PBMC) populations after 24 h of incubation, implying that the ability of NK cells to function as superantigen-presenting cells is up-regulated by superantigens themselves. Together, these data demonstrate for the first time that human CD56+ HLA-DR+ NK cells can function as superantigen-presenting cells, and imply that NK cells may be involved in the activation of non-specific T cell reactivity during early host defences against superantigen-elaborating microorganisms in vivo. Furthermore, the physical linkage of NK cells and T cells by the interaction of superantigen with HLA class II molecules and T cell receptors, respectively, may lead to NK cell activation and augmented lytic potential, helping to clear the body of superantigen-elaborating microorganisms.

Da Costa A. et al. *Role of the preaxillary flora in pacemaker infections: a prospective study.* Circulation. 1998; 97(18) : 1791-5.p Abstract: BACKGROUND: Infection remains a severe complication after pacemaker implantation. The purpose of our prospective study was to evaluate the role of the local bacteriologic flora in its occurrence. METHODS AND RESULTS: Specimens were collected at the site of implantation for culture from the skin and the pocket before and after insertion in a consecutive series of patients who underwent elective permanent pacemaker implantation. Microorganisms isolated both at the time of insertion and of any potentially infective complication were compared by using conventional speciation and ribotyping. There were 103 patients (67 men and 36 women) whose age ranged from 16 to 93 years (mean+/-SD, 67+/-15). At the time of pacemaker implantation, a total of 267 isolates were identified. The majority (85%) were staphylococci. During a mean follow-up of 16.5 months (range, 1 to 24), infection occurred in four patients (3.9%). In two of them, an isolate of Staphylococcus schleiferi was recognized by molecular method as identical to the one previously found in the pacemaker pocket. In one patient, Staphylococcus aureus, an organism that was absent at the time of pacemaker insertion, was isolated. In another patient, a Staphylococcus epidermidis was identified both at the time of pacemaker insertion and when erosion occurred; however, their antibiotic resistance profiles were different. CONCLUSIONS: This study strongly supports the hypothesis that pacemaker-related infections are mainly due to local contamination during implantation. S schleiferi appears to play an underestimated role in infectious colonization of implanted biomaterials and should be regarded as an important opportunistic pathogen.

Dabrowski P. et al. *[Chromosome sensitivity to bleomycin-induced damage in patients with laryngeal cancer as a marker of genetic risk].* Otolaryngol Pol. 1998; 52(3) : 245-50.p Abstract: An inter-individual variability in sensitivity to mutagen-induced genotoxicity was studied in respect to an estimation of larynx cancer risk. Bleomycin induced chromosome breaks were analysed in blood lymphocytes proliferating in vitro in a group of 35 larynx cancer subjects and in 18 healthy controls. A significantly higher index of chromosome breaks was found in larynx cancer subjects as compared with the controls. The distribution of individual results indicates that subjects oversensitive to bleomycine were identified only among laryngeal tumour patients. A potential usage of bleomycin test in tumour prognosis is discussed.

Daeihagh P. et al. *Efficacy of tissue plasminogen activator administration on patency of hemodialysis access catheters.* Am J Kidney Dis. 2000; 36(1) : 75-9.p Abstract : Patients with end-stage renal disease use hemodialysis catheters for either temporary or permanent blood access. Recurrent thrombosis and fibrin sheath formation are common causes of poor or inadequate blood flow rates that require intervention. We studied the effect of tissue plasminogen activator (tPA) in reestablishing adequate blood flow rates through nonfunctional vascular catheters in 22 consecutive chronic hemodialysis patients. From January 1, 1999, to May 20, 1999, there were 56 instances in which tPA was used in an attempt to improve blood flow rates. In all instances, 2 mg of tPA was infused into each port of a dual-lumen internal jugular catheter. Dwell time ranged between 2 and 96 hours (median, 24 hours), and patient follow-up ranged between 47 and 140 days (median, 133.5 days). tPA was effective in establishing adequate blood flow rates (>/=200 mL/min) during the next dialysis session in 49 of 56 cases (87.5%). Seven additional interventions were required because of early or late tPA failure (one fibrin sheath stripping, one catheter replacement for kinking, one catheter replacement for central venous stenosis, and four catheter replacements for persistently poor blood flow rates), and eight catheters were replaced for infection. Thus, further interventions to achieve adequate blood flow rates were required in 12.5% of the cases because of early or late tPA failure. tPA appears to be as effective as urokinase for reestablishing adequate blood flow rates through hemodialysis catheters that are thrombosed or have low blood flow rates.

Dagan R. *Clinical significance of resistant organisms in otitis media.* Pediatr Infect Dis J. 2000; 19(4) : 378-82.p Abstract: BACKGROUND: Otitis media is an important health care problem of childhood. The bacteriology of otitis media comprises three main pathogens: Streptococcus pneumoniae, nontypable Haemophilus influenzae and Moraxella catarrhalis. Although the prevalence of resistant strains varies geographically and temporally, antimicrobial resistance is widespread and increasing. RESISTANCE TO ANTIBIOTIC DRUGS: Among the risk factors for development of resistance in otitis media are antimicrobial use, young age, day-care attendance and prior hospitalization. The increasing rate of resistance to antibiotic drugs is associated with a decreased rate of successful eradication of pathogens from middle ear fluid, which is associated with clinical failure. A bacteriologic cure rate of 80 to 85% is observed for S. pneumoniae and nontypable H. influenzae when serum concentrations exceed the MIC for 40 to 50% of dosing interval. Comparative trials indicate that some of the beta-lactams can achieve bacteriologic eradication in acute otitis media, although major differences in outcome exist among agents based on pathogen, beta-lactamase status and MIC values. ANTIBIOTIC CHOICE: Overall the choice of antibiotics for treatment of otitis media should take into consideration their in vitro activity against the locally prevalent organisms, especially resistant organisms, and results obtained from studies in which bacteriologic outcome was used as the endpoint.

Dahlen G. et al. *Occurrence of enteric rods, staphylococci and Candida in subgingival samples.* Oral Microbiol Immunol. 1995; 10(1) : 42-6.p Abstract: The frequency and percentage of enteric rods, staphylococci and Candida were determined in 973 subgingival samples collected from 535 patients subjected to different periodontal treatment procedures. The analysis was performed with culture technique using selective and nonselective media. One or more organisms were detected in 65.5% of the samples and in 76.7% of the patients. In most samples enteric rods, staphylococci and/or Candida constituted a small amount of the total microbial viable count. Enteric rods exceeded 10% of the total viable count in 30 samples. Staphylococci occurred in more than 10% in only 3 samples. In these 3 samples, enterics constituted more than 10% of the total viable count. Candida was not found to exceed 10% of the total viable count in any of the samples. No statistically significant correlation was found between the presence of any of the target microorganisms and kind of periodontal treatment procedure received, antibiotic administration or sample transport time.

Dajani A.S. et al. *Prevention of bacterial endocarditis: recommendations by the American Heart Association.* Clin Infect Dis. 1997; 25(6) : 1448-58.p Abstract: OBJECTIVE: To update recommendations issued by the American Heart Association last published in 1990 for the prevention of bacterial endocarditis in individuals at risk for this disease. PARTICIPANTS: An ad hoc writing group appointed by the

American Heart Association for their expertise in endocarditis and treatment with liaison members representing the American Dental Association, the Infectious Diseases Society of America, the American Academy of Pediatrics, and the American Society for Gastrointestinal Endoscopy. EVIDENCE: The recommendations in this article reflect analyses of relevant literature regarding procedure-related endocarditis, in vitro susceptibility data of pathogens causing endocarditis, results of prophylactic studies in animal models of endocarditis, and retrospective analyses of human endocarditis cases in terms of antibiotic prophylaxis usage patterns and apparent prophylaxis failures. MEDLINE database searches from 1936 through 1996 were done using the root words endocarditis, bacteremia, and antibiotic prophylaxis. Recommendations in this document fall into evidence level III of the US Preventive Services Task Force categories of evidence. CONSENSUS PROCESS: The recommendations were formulated by the writing group after specific therapeutic regimens were discussed. The consensus statement was subsequently reviewed by outside experts not affiliated with the writing group and by the Science Advisory and Coordinating Committee of the American Heart Association. These guidelines are meant to aid practitioners but are not intended as the standard of care or as a substitute for clinical judgment. CONCLUSIONS: Major changes in the updated recommendations include the following: (1) emphasis that most cases of endocarditis are not attributable to an invasive procedure; (2) cardiac conditions are stratified into high-, moderate-, and negligible-risk categories based on potential outcome if endocarditis develops; (3) procedures that may cause bacteremia and for which prophylaxis is recommended are more clearly specified; (4) an algorithm was developed to more clearly define when prophylaxis is recommended for patients with mitral valve prolapse; (5) for oral or dental procedures the initial amoxicillin dose is reduced to 2 g, a follow-up antibiotic dose is no longer recommended, erythromycin is no longer recommended for penicillin-allergic individuals, but clindamycin and other alternatives are offered; and (6) for gastrointestinal or genitourinary procedures, the prophylactic regimens have been simplified. These changes were instituted to more clearly define when prophylaxis is or is not recommended, improve practitioner and patient compliance, reduce cost and potential gastrointestinal adverse effects, and approach more uniform worldwide recommendations.

Dallugge-Tamm H. et al. *[Nosocomial transmission of pneumococcus].* Immun Infekt. 1995; 23(5) : 185-6.p Abstract: Increasing resistance of pneumococci against antimicrobial agents in several parts of the world is reported. We observed a probably nosocomial transmission of a pneumococcal strain with reduced susceptibility to penicillin (capsular type 6A). Recommendations for diagnostic procedures in the laboratory and therapy are given.

Dalmau D. et al. *Clindamycin resistance in the Bacteroides fragilis group: association with hospital-acquired infections.* Clin Infect Dis. 1997; 24(5) : 874-7.p Abstract: A retrospective study was conducted to assess the relationships between clindamycin resistance in members of the Bacteroides fragilis group, previous antimicrobial therapy, and the context for the development of infection, whether in the community or during hospitalization. Eighty-five clindamycin-resistant clinical strains (one isolate per patient) isolated from January 1988 to October 1994 were matched (one to one) with clindamycin-susceptible isolates recovered during the same period, and the charts of the patients from whom the isolates were recovered were reviewed retrospectively. Of the clindamycin-resistant strains, 65% were recovered from patients with hospital-acquired infections compared with 40% of the clindamycin-susceptible strains (odds ratio [OR], 2.75; 95% confidence interval [CI], 1.41-5.38; P =.002). Prior antimicrobial therapy for > or = 48 hours was also associated with clindamycin resistance (OR, 2.33; 95% CI, 1.16-4.70; P =.02). However, clindamycin resistance remained associated with hospital-acquired infections independent of prior antimicrobial therapy (Mantel-Haenszel weighted average OR, 2.22; 95% CI, 1.03-4.89; P =.04). Clinicians should consider the risks for clindamycin resistance when treating hospital-acquired infections caused by members of the B. fragilis group.

Daly M. et al. *Molecular characterization of Irish Salmonella enterica serotype typhimurium: detection of class I integrons and assessment of genetic relationships by DNA amplification fingerprinting.* Appl Environ Microbiol. 2000; 66(2) : 614-9.p Abstract: Salmonella enterica is among the principal etiological agents of food-borne illness in humans. Increasing antimicrobial resistance in S. enterica is a cause for worldwide concern. There is concern at present in relation to the increasing incidence of human infection with antimicrobial agent-resistant strains of S. enterica serotype Typhimurium, in particular of phage type DT104. Integrons appear to play an important role in the dissemination of antimicrobial resistance genes in many Enterobacteriaceae including S. enterica. In this study the antimicrobial susceptibilities and phage types of 74 randomly collected strains of S. enterica serotype Typhimurium from the Cork region of southern Ireland, obtained from human, animal (clinical), and food sources, were determined. Each strain was examined for integrons and typed by DNA amplification fingerprinting (DAF). Phage type DT104 predominated (n = 48). Phage types DT104b (n = 3), -193 (n = 9), -195 (n = 6), -208 (n = 3), -204a (n = 2), PT U302 (n = 1), and two nontypeable strains accounted for the remainder. All S. enterica serotype Typhimurium DT104 strains were resistant to ampicillin, chloramphenicol, streptomycin, Sulfonamide Duplex, and tetracycline, and one strain was additionally resistant to trimethoprim. All DT104 strains but one were of a uniform DAF type (designated DAF-I) and showed a uniform pattern of integrons (designated IP-I). The DT104b and PT U302 strains also exhibited the same resistance phenotype, and both had the DAF-I and IP-I patterns. The DAF-I pattern was also observed in a single DT193 strain in which no integrons were detectable. Greater diversity of antibiograms and DAF and IP patterns among non-DT104 phage types was observed. These data indicate a remarkable degree of homogeneity at a molecular level among contemporary isolates of S. enterica serotype Typhimurium DT104 from animal, human, and food sources in this region.

Damaso D. et al. *[Relationship between antimicrobial susceptibility and virulence factors in Helicobacter pylori clinical isolates].* Rev Esp Quimioter. 1999; 12(4) : 340-5.p Abstract: The aim of this study was to determine the relationship between the antibiotic susceptibility and different virulence factors among Helicobacter pylori clinical isolates. One hundred and forty-five strains were isolated from biopsy cultures obtained from adult patients. Antimicrobial susceptibility to amoxicillin, clarithromycin, metronidazole and tetracycline were tested using an agar dilution method. cagA and iceA genes and s1 and s2 alleles of vacA were studied by polymerase chain reaction. A group of patients had been previously treated for H. pylori infection. We found a resistance rate of 28.7% and 16.5% to metronidazole and clarithromycin, respectively. We did not find any resistance to amoxicillin or tetracycline. The cagA gene and s1 allele were detected in 86.3% and 65.2% of the strains. One hundred and two (71.3%) strains were iceA+. cagA+ strains showed lower percentages of resistance to antibiotics, as did vacA s1 and iceA+ strains. The role of lower rates of resistance to clarithromycin and metronidazole in more virulent H. pylori strains may have favorable effects in their eradication in patients infected with these strains.

Dancer S.J. *Mopping up hospital infection.* J Hosp Infect. 1999; 43(2) : 85-100.p Abstract: Hospital cleaning is a neglected component of infection control. In the UK, financial constraints have forced managers to re-evaluate domestic services and general cleaning has been reduced to the bare minimum. Services have been contracted out in some hospitals, which has further lowered standards of hygiene. Control of infection personnel believe that cleaning is important in preventing hospital-acquired infections but they do not manage domestic budgets and have failed to stop their erosion. It is difficult

to defend high levels of hygiene when there is little scientific evidence to support cleaning practices. This review examines the common micro-organisms associated with hospital-acquired infection and their ability to survive in the hospital environment. It also describes studies which suggest that comprehensive cleaning disrupts the chain of infection between these organisms and patients. It is likely that restoring hygienic standards in hospitals would be a cost-effective method of controlling hospital-acquired infection. Furthermore, good cleaning is achievable whereas the enforcement of hand washing and good antibiotic prescribing are not.

Das A.C. et al. *Insecticides: their effect on microorganisms and persistence in rice soil.* Microbiol Res. 1995; 150(2) : 187-94.p Abstract: A field experiment was conducted to investigate the effect of four insecticides, HCH, phorate, carbofuran and fenvalerate, at recommended doses on the preponderance of bacteria, actinomycetes and fungi. We also measured the persistence of the insecticides in the rhizosphere soil of rice. HCH and fenvalerate stimulated the proliferation of all of the microorganisms significantly. Phorate increased the population of bacteria and actinomycetes. Carbofuran accentuated the preponderance of actinomycetes in soil. Insecticides, in general, did not have marked influence on the proliferation of Bacillus, Streptomyces, Aspergillus and Fusarium in soil. However, we observed a stimulation of growth of Staphylococcus, Proteus and Sarcina with HCH, Pseudomonas, Corynebacterium, Erysipelothrix and Rhizopus with phorate, Serratia, Corynebacterium, Klebsiella, Escherichia, Rhizopus and Humicola with carbofuran, and Staphylococcus, Sarcina, Klebsiella and Nocardia with fenvalerate. On the other hand, there was an inhibition in growth of Pseudomonas, Micrococcus, Nocardia and Penicillium with HCH, of Pseudomonas, Micrococcus and Penicillium with carbofuran, and of Pseudomonas, Micrococcus and Micromonospora with fenvalerate. Different types of insecticides exhibited differential patterns of dissipation in soil. HCH had the highest persistence followed by phorate, carbofuran and fenvalerate, respectively.

das Gracas Silva E. Souza W et al. *Resistance profile of Bacteroides fragilis isolated in Brazil. Do they shelter the cfiA gene?* J Antimicrob Chemother. 2000; 45(4) : 475-81.p Abstract: The epidemiology of antimicrobial resistance of clinical isolates and human intestinal strains of Bacteroides fragilis has assumed great importance in the last few years since this microorganism, like other members of the B. fragilis group, can be responsible for the spread of resistance determinants. It is possible that the presence of B. fragilis in polluted aquatic environments might contribute to the spread of resistance. The antimicrobial resistance profile of 44 clinical B. fragilis strains isolated from 1981-1988 and 1991-1998 from the University hospital of Rio de Janeiro, and of 17 faecal and 17 polluted aquatic environmental B. fragilis strains isolated between 1991 and 1998 was determined. The susceptibility tests against penicillin, cefoxitin, imipenem, meropenem, clindamycin, chloramphenicol and metronidazole were performed by Etest in Wilkins-Chalgren agar enriched with 5% sheep blood. Motivated by some high MIC values for cefoxitin and meropenem, the cfiA gene, which codes for a metallo-beta-lactamase, was investigated among all strains, using PCR amplification. The resistance to penicillin was high in the samples from 1981 to 1988 (92.9%) and also in those from 1991 to 1998 (100%), although the MIC90 decreased from 256 mg/L to 24 mg/L. An increase in the resistance level to clindamycin and cefoxitin was seen from one decade to the other, the MIC90 values changing from 4 mg/L to 12 mg/L and from 8 mg/L to 32 mg/L, respectively. The susceptibility profile for metronidazole, chloramphenicol, imipenem and meropenem remained stable, although two clinical strains showed MICs of 6 mg/L and 8 mg/L against meropenem. Almost all human intestinal strains were resistant to penicillin and all of them were susceptible to imipenem, meropenem, chloramphenicol and metronidazole. The MICs of meropenem against two strains isolated from a polluted aquatic environment were 6 mg/L and 32 mg/L. The cfiA gene was detected in five strains, two of which were isolated from clinical specimens against which the MIC values of cefoxitin were high and three from an aquatic environment, whose susceptibility to both cefoxitin and meropenem ranged from sensitive to resistant.

Das I. et al. *How useful are microbial filters in respiratory apparatus?* J Hosp Infect. 1997; 37(4) : 263-72.p Abstract: Following an outbreak of hepatitis C in surgical patients in Australia, it has been suggested that transmission can take place as a result of contaminated anaesthetic circuits. It has therefore been recommended that filters should be placed between patients and breathing systems with a new filter being used for each patient. Although nosocomial pneumonia is a major manifestation of hospital-acquired infection, it is unclear whether contamination of ventilator circuits is implicated in the aetiology of this condition. Some data suggest that bacteria cannot survive well in anaesthetic circuits and several studies have failed to demonstrate significant contamination of circuits in clinical situation. Several outbreaks of pneumonia related to contaminated anaesthetic equipment have been described, but many of these were controlled by appropriate decontamination of the respiratory equipment. Although ventilator filters are used by the majority of intensive care units and filters do have the ability to filter bacteria and viruses, there are few data suggesting that the use of filters reduce the rate of pulmonary infections in long-term ventilated patients. Furthermore, to change filters between operations would have significant financial implications, and there is no conclusive evidence that they would reduce cross infection. Until more data are available on the role of filters in both long-term ventilated patients and operations, standard hygienic measures such as appropriate disinfection protocols are still the most effective way of reducing ventilator-associated infections.

Daschner F.D. et al. *Glycopeptides in the treatment of staphylococcal infections.* Eur J Clin Microbiol Infect Dis. 1995; 14 Suppl 1 : S12-7.p Abstract: Gram-positive bacteria are rapidly becoming the most important pathogens in nosocomial infections. In recent years, attention and concern have been focused on the gram-positive bacteria, Staphylococcus aureus, Staphylococcus epidermidis and Enterococcus faecalis. These microorganisms are well equipped to exert their pathogenic effects and to display virulence. Treatment of severe infections caused by gram-positive bacteria remains difficult because of the increase in infections caused by methicillin-resistant staphylococci, and this has renewed interest in the glycopeptide antibiotics, vancomycin and teicoplanin. According to National Nosocomial Infection Surveillance Study data, in 1989, 60% of coagulase-negative staphylococci and 22% of Staphylococcus aureus strains showed methicillin resistance. Among other factors, successful antimicrobial therapy depends on rapid and reliable antibiotic delivery to the infection site at a concentration adequate to inhibit the majority of infecting organisms. Glycopeptides may be important in the therapy of catheter-related infections, which are mainly caused by coagulase-negative staphylococci and Staphylococcus aureus.

David E. et al. *[The sensitivity of Salmonella strains in diarrheal disease to new quinolones compared with other antimicrobial substances].* BacteriolVirusol Parazitol Epidemiol. 1996; 41(1-2) : 43-6.p Abstract: The sensitivity of 59 Salmonella strains isolated in children with acute diarrhoea was tested against the new quinolones like: Ciproflaxicin (CIP), Norfloxacin (NOR) and Ofloxacin (OFX), as compared to the sensitivity against same aminosides: Gentamicin (GM), Amikacin (AN) against cephalosporins: Ceftazidime (CAZ), Cefalotine (CF) and other currently used antimicrobial agents: Tetraciclin (T), Ampicilin (A), Cloramfenicol (C), Furazolidon (FU). The majority of the studied Salmonella strains, 43 out of 59 strains, belonged to the serotype typhimurium, the most frequently serotype isolated in our geographical area. A very high percentage of Salmonella strains were sensitive against the three quinolones: 98,30% sensitive against NOR, 91,5% sensitive against OFX, 91,50% sensitive against CIP and 96,6% sensitive against AN. In contrast, the Salmonella strains

sensitivity was lower in the other tested antimicrobial substances: C (32,2% sensitive strains), GM (8,5%), A (16,9%), CF (11,9%), T (3,4%), FU (1,7%). Out of 59 strains, 45 where resistant to more than four antibiotics, the most often observed pattern was: A, CAZ, CF, GM, T, C, FU.

David T.S. et al. *Perioperative lower urinary tract infections and deep sepsis in patients undergoing total joint arthroplasty.* J Am Acad Orthop Surg. 2000; 8(1) : 66-74.p Abstract: Deep sepsis in the involved joint after hip or knee arthroplasty may be the result of hematogenous seeding from a remote infectious source. This mechanism has been used to explain the well-documented association between postoperative urinary tract infections and subsequent joint infection after hip or knee arthroplasty. However, it is unclear whether there is an association between preoperative bacteriuria and deep prosthetic infection. The purpose of this review is to identify perioperative risk factors associated with bacteriuria that have a positive correlation with deep joint sepsis following total hip or knee arthroplasty. The classic symptoms of dysuria, urgency, and frequency seen with urinary tract infections are often absent in the elderly despite the presence of urine coliforms; in these patients, pyuria (as indicated by the presence of more than 1x10(3) white blood cells per milliliter of noncentrifuged urine) may be used as a preliminary screening criterion. If there are irritative symptoms, the presence of more than 1x10(3) bacteria per milliliter of urine should be regarded as indicative of a urinary tract infection. If there is bacteriuria without symptoms of urinary irritation or obstruction, the current literature supports proceeding with total joint arthroplasty and treating those patients with urine colony counts greater than 1x10(3)/mL with an 8- to 10-day postoperative course of an appropriate oral antibiotic. Postponement of total joint surgery should be considered if preoperative evaluation reveals symptoms related to obstruction of the urinary pathway. Irritative symptoms in combination with a bacterial count greater than 1x10(3)/mL should also serve as an indication to postpone surgery. To diminish postoperative urinary tract infection, a bladder catheter should be inserted immediately preoperatively and removed within 24 hours of surgery to diminish the risk of urinary retention, which has been shown to increase the likelihood of a postoperative urinary tract infection.

Davies B.I. et al. *Clinical effectiveness of levofloxacin in patients with acute purulent exacerbations of chronic bronchitis: the relationship with in-vitro activity.* J Antimicrob Chemother. 1999; 43 Suppl C : 83-90.p Abstract: The objective of this randomized, double-blind study was to compare the clinical efficacy of levofloxacin at two different dosages with that of cefuroxime axetil in patients with acute purulent exacerbations of chronic bronchitis and, in particular, to assess the impact of the susceptibility to levofloxacin on the clinical findings. In total, 124 evaluable patients were treated for 7 days with oral levofloxacin 250 mg or 500 mg od, or cefuroxime axetil 250 mg bd. Sputum cultures were monitored pre-treatment, and at 1 and 7 days after the end of treatment. The susceptibility of Streptococcus pneumoniae isolates was tested by agar dilution in Columbia blood agar and by disc diffusion, but all other isolates were tested solely by the disc diffusion method. A greater number of infections were eradicated by levofloxacin than by cefuroxime axetil: infections were eradicated in 68% of patients receiving the 500 mg dosage and in 63% of those taking 250 mg levofloxacin, whereas the eradication rate with the comparator drug was much lower (48%). Against all pre-treatment S. pneumoniae isolates (n = 39), the MICs of levofloxacin were between 0.25 and 2 mg/L (geometric mean 0.95 mg/L), similar to those of the post-treatment strains (n = 32; mean 1.11 mg/L). All except one of the S. pneumoniae isolates were susceptible to penicillin G (MIC < or = 0.06 mg/L), and the remaining isolate was inhibited by 0.5 mg/L of penicillin G, but was fully susceptible to levofloxacin. Some pretreatment strains of Pseudomonas aeruginosa were resistant to levofloxacin, but many more resistant strains were encountered afterwards. All strains of Moraxella catarrhalis and Haemophilus influenzae were highly susceptible to levofloxacin in the disc diffusion tests. All the antimicrobial agents used in the study were well tolerated: only two patients discontinued treatment because of adverse drug effects. The results of this study indicated that, although there were some failures in patients with S. pneumoniae and P. aeruginosa infections, resistance to levofloxacin did not emerge rapidly among strains of S. pneumoniae during therapy with levofloxacin, and that natural resistance among pneumococci, H. influenzae and M. catarrhalis was rare.

Davies J. et al. *Bacterial resistance to aminoglycoside antibiotics.* Trends Microbiol. 1997; 5(6) : 234-40.p Abstract: The aminoglycoside antibiotics are broad-spectrum antibacterial compounds that are used extensively for the treatment of many bacterial infections. In view of the current concerns over the global rise in antibiotic-resistant microorganisms, there has been renewed interest in the mechanisms of resistance to the aminoglycosides, including the superfamily of aminoglycoside-modifying enzymes.

Davis M.A. et al. *Changes in antimicrobial resistance among Salmonella enterica Serovar typhimurium isolates from humans and cattle in the Northwestern United States, 1982-1997.* Emerg Infect Dis. 1999; 5(6) : 802-6.p Abstract: We compared antimicrobial resistance patterns of Salmonella enterica serovar Typhimurium (ST) of isolates from humans (n = 715) and cattle (n = 378) in the Pacific Northwest from 1982 through 1997. The major changes in antimicrobial resistance can be attributed to the widespread clonal dissemination of multidrug-resistant definitive phage type 104 ST.

Davis S.N. et al. *Activity and dosage of alteplase dilution for clearing occlusions of venous-access devices.* Am J Health Syst Pharm. 2000; 57(11) : 1039-45.p Abstract: The activity and sterility of reconstituted alteplase solution and the effectiveness of an alteplase dose-escalation protocol for the clearance of midline-catheter and central-venous-access device occlusions were studied. Reconstituted alteplase solution was stored at -70, -25, or 2 degrees C at concentrations of 0.5, 1, or 2 mg/mL. Durations of storage in the freezer were 0, 7, and 14 days, and durations of storage in the refrigerator were 0, 48, and 72 hours and 7 and 14 days. Samples were also assayed and cultured without prior freezing after refrigeration at 2 degrees C for 0, 48, and 72 hours and 7, 14, and 28 days. Fifty-eight pediatric and adult patients were enrolled in a separate study in which catheter clearance was initiated with alteplase 0.5 mg, and the dose was escalated to 1 and 2 mg sequentially until the catheter was cleared. The primary endpoint was restoration of catheter patency, and the secondary endpoint was the occurrence of bleeding episodes within 24 hours of alteplase administration. Catheter removal due to failure to restore patency was also documented. The activity and sterility of alteplase were maintained under all conditions studied. Fifty catheters (86.2%) were cleared with alteplase 0.5 mg, 5 (8.6%) after dose escalation to 1 mg, and 1 (1.7%) after escalation to 2 mg. The alteplase solution did not clear the occlusion in 2 catheters (3.4%): 1 had a mechanical obstruction and 1 cleared two hours after the 1-mg dose was deemed a failure. None of the six catheter removals was due to recalcitrant clots. Bleeding observed was not considered to be the result of alteplase administration. For use in clearing occlusions of venous-access devices, alteplase 0.5, 1, and 2 mg/mL retained sufficient fibrinolytic activity when stored for up to 14 days at 2 degrees C (28 days for the 0.5-mg/mL dilution) and when stored for 14 days at -70 or -25 degrees C followed by up to 14 days at 2 degrees C. The dose-escalation protocol was effective.

Daw N.C. et al. *Nasopharyngeal carriage of penicillin-resistant Streptococcus pneumoniae in children with sickle cell disease.* Pediatrics. 1997; 99(4) : E7.p Abstract: OBJECTIVE: We studied the prevalence of nasopharyngeal (NP) carriage, antimicrobial susceptibilities, and serotypes of Streptococcus pneumoniae (SP) in children with sickle cell disease (SCD) in the Mid-South. In addition, we examined risk factors for NP carriage of penicillin-resistant SP (PRSP). STUDY DESIGN: Between July 1994 and December 1995, we obtained NP

cultures from 312 children with SCD followed at the Mid-South Sickle Cell Center, 208 (67%) of whom were receiving penicillin prophylaxis. RESULTS: Among the 312 patients, colonization with SP occurred in 42 (13%), 30 (71%) of whom were receiving penicillin prophylaxis. Twenty-three of the 42 SP isolates (55%) were resistant to penicillin; 5 of the 23 (22%) were highly resistant. PRSP organisms were also resistant to cefotaxime (43%), trimethoprim-sulfamethoxazole (57%), and erythromycin (22%). Serotypes 6A, 6B, 14, 19A, and 23F accounted for 19 (90%) of 21 resistant strains. Children who were treated with antibiotics during the preceding month were more likely to carry PRSP than children who were not treated. CONCLUSIONS: There is a high prevalence of NP carriage of PRSP in children with SCD in the Mid-South, which raises concerns regarding the continued effectiveness of penicillin prophylaxis in these children. Further studies on the antimicrobial susceptibilities of resistant organisms and the relationship between NP carriage of SP and invasive disease are needed before developing new recommendations for prophylaxis and treatment.

Dayan P.S. et al. *A comparison of the initial to the later stream urine in children catheterized to evaluate for a urinary tract infection*. Pediatr Emerg Care. 2000; 16(2) : 88-90.p Abstract: BACKGROUND: To avoid potential contamination, it is recommended that the first few drops of urine be discarded when obtaining a catheterized urine sample from a child being evaluated for a urinary tract infection (UTI). The existing evidence to make such a recommendation is scant. Our goal, therefore, was to determine whether the urinalysis, Gram stain, and culture results were significantly different from the initial and later urine samples collected from catheterized children. METHODS: A prospective diagnostic discrimination between early and later urine samples was conducted on a convenience sample of pediatric patients being evaluated for a UTI in an urban emergency department. Results of the urinalysis, Gram stain, and quantitative culture were compared between the early and later stream urine samples. RESULTS: Data from 86 children were analyzed. Four of 80 patients had a false identification of low colony count bacteruria from the early but not from the later stream. For patients with negative cultures, the early stream was also more likely to falsely identify > or =5 wbc/hpf ($P<0.01$) or bacteruria ($P<0.05$) on urinalysis than the later stream. CONCLUSIONS: There is a small but potentially meaningful contamination of the early stream urine compared with the later stream in young children catheterized to evaluate for a urinary tract infection.

de Andrade D. et al. *A bacteriological study of hospital beds before and after disinfection with phenolic disinfectant*. Rev Panam Salud Publica. 2000; 7(3) : 179-84.p Abstract: In hospitals, one of the ways to control microbial contamination is by disinfecting the furniture used by patients. This study's main objective was to evaluate the microbiological condition of hospital mattresses before and after such disinfection, in order to identify bacteria that are epidemiologically important in nosocomial infection, such as Staphylococcus aureus and Pseudomonas aeruginosa. RODAC plates with two different culture media were used to collect specimens. Patient beds were selected according to previously established criteria, and surface areas on the mattresses were chosen at random. From the total of 1,040 plate cultures from 52 mattresses, positive results were obtained from 500 of them (48.1%), 263 before disinfection and 237 after disinfection. Considering the selectivity of the culture media, the positivity rate was high. There were high prevalences of S. aureus both before and after mattress disinfection. The study results suggest that the usual disinfection procedures, instead of diminishing the number of microbes, merely displace them from one part of the mattress to another, and the number of microorganisms remains the same.

de Boer W.A. et al. *Optimal treatment of Helicobacter pylori with ranitidine bismuth citrate (RBC): a randomized comparison between two 7-day triple therapies and a 14-day dual therapy*. Am J Gastroenterol. 1998; 93(7) : 1101-7.p Abstract: OBJECTIVE: We investigated two promising 1-wk RBC-triple therapies in comparison to the already well investigated 2-wk RBC dual therapy. METHODS: We conducted two randomized, open, parallel group studies in 13 hospitals in the Netherlands. H. pylori-positive patients without active ulceration were randomized to 14-day RBC 400 mg b.i.d. plus clarithromycin 500 mg b.i.d. (n = 56) or to either 7-day RBC 400 mg b.i.d. plus tetracycline 500 mg q.i.d. plus metronidazole 500 mg t.i.d. (n = 63) in study 1, or to 7-day RBC 400 mg b.i.d. plus amoxycillin 1000 mg b.i.d. plus clarithromycin 500 mg b.i.d. (n = 49) in study 2. At least 6 wk later patients were reendoscoped with antral and corpus biopsies for CLOtest, culture, and histology, and cure was assumed if all tests were negative. RESULTS: Results from the studies were pooled. All regimens were well tolerated with only 1 drop-out because of side effects. Cure rates per protocol/intention to treat were 96%/95% for RBC-CLA dual therapy, 89%/86% for RBC-TET-MET triple therapy, and 93%/92% for RBC-AMO-CLA triple therapy. From 126 patients, a pretreatment antibiogram was available. Metronidazole resistance did not affect the performance of RBC-CLA or RBC-AMO-CLA. In the RBC-TET-MET group, 97% (32/33) with a metronidazole sensitive strain were cured vs 57% (four of seven) with a resistant strain. Of three patients with a pretreatment clarithromycin resistant strain; one failed RBC-CLA dual therapy and two failed RBC-AMO-CLA triple therapy. CONCLUSIONS: All regimens were well tolerated and achieved comparable and very high cure rates. Statistical or clinical relevant differences were not detected. All three regimens can be used as initial anti-Helicobacter therapy and can compete with 7-day PPI-triple therapies. More data are needed on the influence of antimicrobial resistance on the performance of individual triple therapies. The local prevalence of antimicrobial resistance will determine which regimen should be chosen for a certain geographical area.

de Carvalho C.B. et al. *Epidemiology and antimicrobial resistance of B. fragilis group organisms isolated from clinical specimen and human intestinal microbiota*. Rev Inst Med Trop Sao Paulo. 1996; 38(5) : 329-35.p Abstract: Epidemiological aspects and the antimicrobial susceptibility profile of the Bacteroides fragilis group isolated from clinical and human intestinal specimens were examined in this study. B. fragilis group strains were isolated from 46 (37%) of 124 clinical specimens and the source of the samples was: Blood culture (3), intraabdominal infection (27), brain abscess (2), soft tissue infection (17), respiratory sinus (3), pleural aspirate (9), breast abscess (3), surgical infected wound (22), pelvic inflammatory disease (22), chronic otitis media (9) and miscellaneous (7). Intraabdominal and soft tissue infections were responsible for more than half of the clinical isolates. Susceptibility to penicillin, cefoxitin, tetracycline, metronidazole, chloramphenicol and clindamycin was examined. All isolates were susceptible to metronidazole and chloramphenicol. For clindamycin and cefoxitin the resistance rates observed were 21.7% and 10.9% respectively. Susceptibility profiles varied among the different species tested. A total of 37 species of B. fragilis group isolated from intestinal microbiota of individuals who had no antimicrobial therapy for at least 1 month before the sampling was also examined. All strains were also susceptible to chloramphenicol and metronidazole and the resistance rates to clindamycin and cefoxitin were 19.4% and 5.4% respectively. A few institutions, in Brazil, have monitored the antimicrobial susceptibility of B. fragilis group strains isolated from anaerobic infections. The resistance rates to cefoxitin and clindamycin and the variation in susceptibility patterns among the species isolated in this study emphasize the need for monitoring of susceptibility patterns of B. fragilis group organisms isolated, especially at our University Hospitals.

De Cicco M. et al. *Time-dependent efficacy of bacterial filters and infection risk in long-term epidural catheterization*. Anesthesiology. 1995; 82(3) : 765-71.p Abstract: BACKGROUND: Epidural infection represents a serious albeit infrequent complication of long-term epidural catheterization. The catheter hub is regarded as the main point of entry for microorganisms among the three possible routes (hematogenous, insertion site, hub) of microbial colonization of the

inserted catheter. The current study was aimed at evaluating whether frequent changing of antimicrobial filters carries an increased risk of catheter hub contamination and the time-dependent efficacy of commonly used antimicrobial filters after prolonged use. METHODS: In the first part of the study, a microbiologic survey (skin, filter, hub, and catheter tip) was performed weekly in a group of 47 patients with cancer bearing subcutaneously tunneled catheters managed at home. Subsequently, the time-dependent efficacy of 96 micropore filters (32 Portex, 32 Sterifix-Braun, 32 Encapsulon TFX-Medical) differing in surface areas and/or composition of the filtering membrane was evaluated in a laboratory study. Filters were perfused, under the usual conditions of clinical use (flow resistance, injection pressure, temperature), every 8 h up to 60 days, with 5 ml of two different analgesic solutions, either sterile or containing 1.5 x 10(5)/ml of Streptococcus milleri I. Eight filters of each type subsequently were flushed with a S. milleri suspension (0.5 McFarland) after 7, 14, 28, and 60 days of continuous perfusion, and the resulting filtrates were cultured. RESULTS: In 16 of 19 positive hub cultures, the same microorganisms (species, biotype, antibiotype) were cultured from skin and filters. A statistically significant positive trend was found between the number of filter changes and the rate of positive hub cultures (chi 1(2) trend 5.11; P = 0.02). A high correlation coefficient was found between number of positive skin cultures and number of positive filtrates (r = 0.88; P = 0.01) and between number of positive filtrates and number of positive hub cultures (r = 0.93; P = 0.003). Cultures obtained from Portex and Sterifix-Braun filters yielded no bacterial growth (64/64) throughout the study period. Cultures from Encapsulon TFX-Medical filters showed bacterial growth 2/8 at seventh day, 7/8 at the 14th day, and 16/16 from the 28th day onward. CONCLUSIONS: Our data indicate significant correlation between the incidence of catheter hub colonization and the filter-change frequency, when the skin close to the filter-hub connection is contaminated. Our results also show that Portex and Sterifix-Braun bacterial filters, when perfused with reduced volumes at low injection pressures, maintain an unmodified antimicrobial function for at least 60 days. Based on these data, it appears clinically feasible to reduce the frequency of filter changes during long-term epidural catheterization, with a consequent possible decrease of epidural catheter colonization.

De Gaspari E.N. *Detection of Neisseria meningitidis in cerebrospinal fluid samples from suspicious cases of meningococcal meningitis using polymerase chain reaction and counterimmunoelectrophoresis.* Rev Argent Microbiol. 2000; 32(2) : 97-103.p Abstract: Rapid diagnosis of meningococcal disease followed by an early treatment is essential. However, blood or cerebrospinal fluid cultures may not be successful because antibiotic treatment is often started before proper specimens are collected and because bacteria may die during transportation to the laboratory. Improvements in antibiotic therapy for specific microorganisms will require the use of more than one method for immunodiagnosis. In this study a collection of cerebrospinal fluid samples from Brazilian patients was analyzed. Gram stains, culture, counterimmunoelectrophoresis and clinical evaluations for meningococcal diseases were available. The sensitivity of nested PCR (nPCR) was 73% for cerebrospinal fluid of clinically suspected cases, whereas both sensitivity and specificity were 100% when subtypes of Brazilian epidemic strains (P1.7, P1.9 and P1.15) isolated from the samples were used.

De Giusti M. et al. *Phenotypic detection of nosocomial mecA-positive coagulase-negative staphylococci from neonates.* J Antimicrob Chemother. 1999; 44(3) : 351-8.p Abstract: Over a 3-year period, we screened antimicrobial resistance genotype (mecA-positive or -negative) in clinically significant coagulase-negative staphylococci isolated from patients residing in our neonatal intensive care unit. For the 152 study strains, the accuracy of standard methods (agar dilution MIC, disc diffusion and agar screen tests) in detecting oxacillin resistance during 48 h of incubation was evaluated. Using mecA gene PCR and Southern blot hybridization as the gold standard, the differential in MICs of additional antibiotics selected for their relevant clinical use in our setting was also compared with mecA status of the isolates. The frequency of mecA was 48.6% among study strains. When applying the previous (1998) and most current (1999) NCCLS interpretive criteria, the specificities of oxacillin agar dilution MICs in detecting the 78 mecA-negative isolates were 100 and 89.7%, respectively, at 24 h, and 100 and 80.7%, respectively, at 48 h. In this respect, the sensitivities of oxacillin agar dilution MICs in detecting the 74 mecA-positive strains were 75.6 and 97.2%, respectively, at 24 h, and 86.4 and 100%, respectively, at 48 h. When applying the previous and most current NCCLS zone size interpretive criteria, oxacillin zone diameters were in false-susceptible error for 13.5 and 8.1%, respectively, of the 74 mecA-positive strains tested at 24 h, and for 6.7 and 2.7%, respectively, at 48 h. Accordingly, when the 78 mecA-negative strains were considered, oxacillin zone diameters were in false-resistant error for 2.5 and 8.9%, respectively, at 24 h, and for 8.9 and 15.3%, respectively, at 48 h. The oxacillin salt agar screen assay accurately identified all mecA-negative strains at both 24 and 48 h. However, 26 (35.1%) and 7 (9.4%) of the mecA-positive strains were misinterpreted as susceptible by the agar screen test at 24 and 48 h, respectively. Using the presence of mecA as the reference standard for interpreting oxacillin susceptibility results, strains lacking mecA were more likely to be susceptible to ampicillin, ceftazidime, gentamicin, netilmicin and rifampicin than were mecA-positive strains. Vancomycin was the only antibiotic tested for which all strains, regardless of mecA status, remained susceptible.

De Lencastre H. et al. *Carriage of respiratory tract pathogens and molecular epidemiology of Streptococcus pneumoniae colonization in healthy children attending day care centers in Lisbon, Portugal.* Microb Drug Resist. 1999; 5(1) : 19-29.p Abstract: In an effort to establish the rate of carriage of antibiotic resistant respiratory pathogens in children attending urban day care centers (DCC) in Portugal, seven DCC in Lisbon were selected for determining the rate of nasopharyngeal colonization of children between the ages of 6 months to 6 years by Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis. Of the 586 children studied between January and March 1996, 47% carried S. pneumoniae, 72% H. influenzae, and 54% M. catarrhalis. Twenty-four percent of the pneumococci had reduced susceptibility to penicillin, and most of these belonged to serogroups 19, 23, 14, and 6. An additional 19% were fully susceptible to penicillin but showed decreased susceptibility to other antimicrobials. These isolates expressed serogroups 6, 11, 14, 18, 19, and 34. The majority (96%) of M. catarrhalis and 20% of H. influenzae were penicillin resistant due to the production of beta-lactamases. Recent antimicrobial use was associated with carriage of penicillin non-susceptible pneumococci and beta-lactamase producing H. influenzae ($p < 0.05$). Individual DCC differed substantially from one another in their rates of carriage of antibiotic resistant H. influenzae and S. pneumoniae. Characterization of antibiotic resistant S. pneumoniae isolates by molecular fingerprinting techniques showed that each DCC had a unique microbiological profile, suggesting little, if any, exchange of the resistant microbial flora among them. An exception to this was the presence of isolates belonging to two internationally spread epidemic clones: the multiresistant Spanish/USA clone expressing serotype 23F, and the penicillin and sulfamethoxazole-trimethoprim resistant French/Spanish clone (serotype 14) which were detected in four and three DCC, respectively.

de Lucas C. et al. *Transpyloric enteral nutrition reduces the complication rate and cost in the critically ill child.* J Pediatr Gastroenterol Nutr. 2000; 30(2) : 175-80.p Abstract: BACKGROUND: Studies in adults have shown that transpyloric enteral nutrition (TEN) is useful in certain patients who cannot tolerate oral or gastric feeding. This study was conducted to compare TEN with parenteral nutrition (PN) in critically ill pediatric patients. METHODS: A retrospective descriptive study conducted in the pediatric intensive care unit of a tertiary pediatric referral center. All patients in the pediatric intensive care unit (PICU) receiving PN and/or TEN from January 1993 through December 1996 were included in the study. RESULTS:

Two hundred forty patients (14.6% of all patients admitted to the PICU) received PN and/or TEN (168 exclusively PN, 21 exclusively TEN, and 51 a combined regimen). The number of patients receiving PN and duration of PN declined significantly from 1993 (65 patients, 703 days) through 1996 (48 patients, 395 days). This was mirrored by the increase in the number of patients receiving TEN and duration of TEN. The incidence of complications (hyperglycemia, hypertriglyceridemia, and cholestasis) was higher in the PN group. There was no difference in the incidence of hospital-acquired infection or mortality between the two groups. The cost of TEN was lower than that of PN, with an estimated annual saving of $5,422. CONCLUSIONS: Transpyloric enteral nutrition is a suitable method of nutritional support for critically ill pediatric patients. It has fewer complications and a lower cost than PN.

de Man P. et al. *An antibiotic policy to prevent emergence of resistant bacilli.* Lancet. 2000; 355(9208) : 973-8.p Abstract: BACKGROUND: Fear of infection in neonatal intensive care units (NICUs) often leads to early use of empiric broad-spectrum antibiotics, a strategy that selects for resistant bacteria. We investigated whether the emergence of resistant strains could be halted by modifying the empiric antibiotic regimens to remove the selective pressure that favours resistant bacteria. METHODS: Two identical NICUs were assigned to different empiric antibiotic regimens. On unit A, penicillin G and tobramycin were used for early-onset septicaemia, flucloxacillin and tobramycin were used for late-onset septicaemia, and no broad-spectrum beta-lactam antibiotics, such as amoxicillin and cefotaxime were used. In unit B, intravenous amoxicillin with cefotaxime was the empiric therapy. After 6 months of the study the units exchanged regimens. Rectal and respiratory cultures were taken on a weekly basis. FINDINGS: There were 436 admissions, divided equally between the two regimens (218 in each). Three neonates treated with the penicillin-tobramycin regimen became colonised with bacilli resistant to the empirical therapy used versus 41 neonates on the amoxicillin-cefotaxime regimen (p<.0001). The relative risk for colonisation with strains resistant to the empirical therapy per 1000 patient days at risk was 18 times higher for the amoxicillin-cefotaxime regimen compared with the penicillin-tobramycin regimen (95% CI 5.6-58.0). Enterobacter cloacae was the predominant bacillus in neonates on the amoxicillin-cefotaxime regimen, whereas Escherichia coli predominated in neonates on the penicillin-tobramycin regimen. These colonisation patterns were also seen when the units exchanged regimens. INTERPRETATION: Policies regarding the empiric use of antibiotics do matter in the control of antimicrobial resistance. A regimen avoiding amoxicillin and cefotaxime restricts the resistance problem.

De Miguel Martinez I. et al. *[Antimicrobial therapy in chronic suppurative otitis media].* Acta Otorrinolaringol Esp. 1999; 50(1) : 15-9.p Abstract: A randomized study was made of 125 patients with chronic middle ear infection. The most frequently isolated microorganisms were: Pseudomonas aeruginosa, Staphylococcus aureus and Enterobacteriaceae. Ciprofloxacin is very active against the microorganisms usually isolated and it has been shown to provide effective therapy in ear infections. In order to study the effectiveness of ciprofloxacin in chronic otitis media, we selected four different treatment groups: oral ciprofloxacin (500 mg/12 h); 0.5 and 0.2% topical solutions of ciprofloxacin (3 drops/8 h), and oral ciprofloxacin plus 0.2% topical solution. Topical polymyxin and neomycin were used as controls. Topical ciprofloxacin (0.2%) was the most effective regimen of those tested for the treatment of chronic otitis media.

de Miranda C.M. et al. *The effect of areca nut on salivary and selected oral microorganisms.* Int Dent J. 1996; 46(4) : 350-6.p Abstract: The aim of this study was to investigate the effect on the growth of salivary and selected oral microorganisms of areca nut, aqueous extracts of the nut, its major alkaloid arecoline and the components tannic acid and catechin of its tannin fraction. The antibacterial properties of the above were tested on Streptococcus mutans, Streptococcus salivarius, Candida albicans and Fusobacterium nucleatum and, as a control, Staphylococcus aureus. This was followed by investigating its effect on salivary organisms cultured from the saliva after chewing boiled areca nut. Extracts inhibited the growth of the selected organisms in a concentration dependent manner, baked and boiled nuts being significantly more potent than raw nut. Growth of C. albicans was the least affected by the nut extracts. Tannic acid was strongly antibacterial but not catechin or arecoline. No antibacterial effect could be demonstrated on salivary organisms after chewing the nut for 5 minutes but exposure of saliva to the cud for 1 hour caused a significant depression of bacterial growth. It is concluded that the hydrolysable tannins in the tannin fraction, which include tannic acid, are responsible for the antibacterial properties of the nut and that prolonged intraoral exposure to the nut can suppress bacteria in the mouth.

de Vera M.E. et al. *Antibiotic-resistant enterococci and the changing face of surgical infections.* Arch Surg. 1996; 131(3) : 338-42.p Abstract: BACKGROUND: Enterococci have not been thought to play an important role in intra-abdominal infections because of their relatively low virulence. However, this notion is changing because of the recent emergence of these microbes as significant nosocomial pathogens. OBJECTIVES: To review the mechanisms of antibiotic resistance of enterococci and to discuss the significance of multidrug-resistant enterococci in surgical infections. DATA SOURCES: Medical and basic science literature relating to enterococci. DATA SYNTHESIS: In addition to having intrinsic resistance to a number of antibiotics, enterococci have the ability to acquire resistant genes through the exchange of plasmids or transposons from other bacterial species. Moreover, enterococci have been shown to transmit these genes to other bacterial species in turn. The extensive resistance of these microorganisms has led to their emergence as significant nosocomial pathogens, ranking second only to Escherichia coli in the number of pathogenic isolates recovered from patients in intensive care units. There has also been a marked increase in vancomycin-resistant enterococcal infections in surgical patients in the last 5 years. Some studies associate the prior use of vancomycin or third-generation cephalosporins with the emergence of these strains. Overall, enterococcal infections are associated with increased morbidity and mortality. CONCLUSIONS: In view of the marked resistance of enterococci to antibiotics and their ability to disseminate resistance genes, these microbes have become important pathogens. Enterococci pose a threat to surgical patients, often causing significant therapeutic dilemmas.

Debbia E.A. et al. *Epidemiology of resistance to antimicrobial drugs in the major respiratory pathogens circulating in Europe.* Infection. 1999; 27 Suppl 2 : S9-12.p Abstract: There is an overwhelming consensus on the fact that Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis represent the prevailing bacterial pathogens of community-acquired lower respiratory tract infections. Their specific incidence as causative agents of the more common syndromes is known to vary even profoundly depending on geographic location, and the same holds true for the rates of resistance to antimicrobial drugs. Europe does not escape the threat posed by the present pandemic spread of penicillin resistance in S. pneumoniae although, as expected, countries like Spain and France are greatly affected, while others including Germany, Italy, The Netherlands and the Scandinavian region are comparatively spared. In several sites multiple resistance has been described in S. pneumoniae and the most affected drugs include penicillin, the macrolides, co-trimoxazole and tetracycline. In H. influenzae synthesis of beta-lactamases the main trait of resistance is expressed. Lack of susceptibility to beta-lactams dictated by a different mechanism remains extremely rare. Considerable variations in the incidence of this characteristic are apparent when European countries are considered. France and Spain are again widely affected, while Germany, The Netherlands and Italy display rates of beta-lactamase-positive H. influenzae of about 10%. M. catarrhalis must be considered generally resistant to non-protected aminopenicillins since over 90% of these organisms produce beta-lactamases.

Debelian G.J. et al. *Bacteremia in conjunction with endodontic therapy.* Endod Dent Traumatol. 1995; 11(3) : 142-9.p Abstract: This study characterizes oral microorganisms believed to have spread from the root canal into the blood stream during and after endodontic therapy of teeth with Asymptomatic apical periodontitis. Microbiological samples were taken under aseptic conditions from the root canal of 26 single-rooted teeth in 26 patients. In the endodontic treatment of 13 of the patients (Group 1), the first 3 reamers, sizes 15, 20 and 25, were used to a level 2 mm beyond the apical foramen. In the other 13 patients (Group 2), the instrumentation ended inside the root canal 1 mm short of the apical foramen. Blood samples were taken from the patients during the instrumentation and 10 min after the treatment was completed. Anaerobic microorganisms were isolated from all root canals. In 7 patients of Group 1, Propionibacterium acnes, Peptostreptococcus prevotii, Fusobacterium nucleatum, Prevotella intermedia and Saccharomyces cerevisiae were recovered from the blood. In 4 patients of Group 2, P. intermedia, Actinomyces israelii, Streptococcus intermedius and Streptococcus sanguis were isolated from the blood. Biochemical tests and antibiograms revealed that the isolates from the root canal and blood had identical profiles within the patients, strongly suggesting that the microorganisms isolated from the blood had the root canal as their source.

Debelian G.J. et al. *Electrophoresis of whole-cell soluble proteins of microorganisms isolated from bacteremias in endodontic therapy.* Eur J Oral Sci. 1996; 104(5-6) : 540-6.p Abstract: We have previously demonstrated that anaerobic bacteria are the microorganisms most frequently isolated from blood following endodontic therapy of teeth with apical periodontitis. Phenotypic characterisation of the isolates suggested that the bacteria in the blood originated from the root canal. The present experiment using sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) was carried out in an effort to verify these findings, and to further study the microorganisms involved in endodontic bacteremias. Soluble cellular proteins were extracted from 11 reference strains and 26 bacterial isolates recovered from the root canal and blood. These included Propionibacterium acnes, Peptostreptococcus prevotii, Fusobacterium nucleatum, Prevotella intermedia. Actinomyces israelii, Streptococcus intermedius, Streptococcus sanguis. The electrophoretic patterns mostly confirmed the identity of the isolates as determined by the biochemical and antimicrobial resistance tests. Furthermore, with this typing method the species Prevotella intermedia and Prevotella nigrescens could be differentiated. These species had been recovered from both root canal and blood. Also, differences between subspecies of Fusobacterium nucleatum became evident with SDS-PAGE, and the results indicated that the organism recovered from the root canal and blood was Fusobacterium nucleatum subsp. vincentii. The electrophoretic patterns of the different organisms isolated from the root canal and the blood were similar, providing further evidence that the bacteria found in the blood originated from the root canal.

Dedkov V.S. et al. *Actinobacillus and Streptococcus: producers of isoschizomers of the restriction endonucleases R.HphI, R.SauI, R.NheI, R.MboI and R.SwaI.* Biol Chem. 1998; 379(4-5) : 573-4.p Abstract: New restriction endonucleases have been found in microorganisms isolated from the microflora of human teeth. The strain-producers are Actinobacillus suis and Streptococcus milleri. The new enzymes are isoschizomers of the prototypes as follows: AsuHPI - HphI; AsuSAI - SauI; AsuNHI - NheI; AsuMBI and SmiMBI - MboI; SmiI - rare-cutter SwaI.

Dega H. et al. *Infections associated with totally implantable venous access devices (TIVAD) in human immunodeficiency virus-infected patients.* J Acquir Immune Defic Syndr Hum Retrovirol. 1996; 13(2) : 146-54.p Abstract: We report on a retrospective study evaluating infectious morbidity associated with totally implantable venous access devices (TIVAD) (Port-A-Cath) in HIV-infected patients. This study of 84 consecutive HIV-infected patients requiring 89 TIVAD between January 1990 and October 1993 was performed in the Department of Infectious Diseases Hopital de l'Institut Pasteur, Paris, France. The total number of catheter days was 11,595. Eighteen of 89 patients with TIVAD (20%) were infected, causing 25 infectious events (25/89: 28%) among 17 different patients (17/84: 20%). The infection rate was 0.22 per 100 catheter days. Mean onset of infection was 82 days. Twenty microorganisms were isolated: Staphylococcus aureus in eight cases (40%), coagulase-negative Staphylococcus in six cases (30%), Streptococcus D faecalis in one case; Gram-negative bacilli were found in five cases (25%). All patients received an intravenous antibiotherapy combined with a local lock treatment in eight cases. Nine TIVAD removals were performed. One death was related to the TIVAD infection. No additional predisposing factor for infection was identified other than the implied condition of the HIV infection. The population and material in this study were homogeneous. The TIVAD infection rate was comparable to other published reports. Prospective evaluation comparing tunneled catheter and TIVAD in HIV-infected patients is needed.

Deguchi K. et al. *[Antimicrobial activities of meropenem against clinically isolated strains. The result against strains isolated from blood and cerebrospinal fluid].* Jpn J Antibiot. 1996; 49(4) : 377-85.p Abstract: In order to evaluate the antimicrobial activity of meropenem (MEPM), minimum inhibitory concentrations (MICs) of MEPM and control drugs were determined against clinical isolates from blood and cerebrospinal fluid that were obtained from January, 1993 to December, 1994. The results are summarized as follows; 1. The MIC-range, 50% MIC (MIC50) and 90% MIC (MIC90) of MEPM were equal to those of imipenem (IPM) and panipenem (PAPM) against Streptococcus pneumoniae including benzylpenicillin (PCG)-insensitive or -resistant S. pneumoniae, Streptococcus agalactiae and Listeria monocytogenes which are Gram-positive strains, and were stronger than those of ampicillin (ABPC) and cefotaxime (CTX). 2. The MIC-range, MIC50 and MIC90 of these 3 drugs of carbapenems (MEPM, IPM and PAPM) were different against Escherichia coli and Haemophilus influenzae which are Gram-negative strains. The MIC90 of MEPM was < or = 0.025 microgram/ml and those of IPM and PAPM were 0.2 microgram/ml against E. coli. The MIC90 of MEPM was 0.1 microgram/ml, that of IPM was 25 micrograms/ml and that of PAPM was 6.25 micrograms/ml against H. influenzae. Thus, the antimicrobial activity of MEPM was stronger than those of IPM and PAPM. The MIC90's of IPM and PAPM against H. influenzae were high with the MIC of IPM at 12.5 approximately 25 micrograms/ml and the MIC of PAPM at 3.13 approximately 12.5 micrograms/ml against 3 IPM-resistant strains among 17 isolates. 3. The MIC90 of ABPC was 0.39 microgram/ml and that of CTX was 0.1 microgram/ml against 20 strains of S. pneumoniae including 6 strains of PCG-insensitive or resistant S. pneumoniae. The MIC90 of ABPC and CTX were higher than those of 3 carbapenem drugs. There were E. coli of 8 strains with ABPC-high resistance (the MIC of ABPC was > 100 micrograms/ml) and 2 strains for which MIC of CTX were 0.39 microgram/ml and 3.13 micrograms/ml. It was found that 29.4% of H. influenzae were beta-lactamase producing strains. 4. It appeared that antimicrobial activities of carbapenems, particularly MEPM were strong against clinical isolates from blood and cerebrospinal fluid. MEPM will be first choice drug by empiric therapy in infections including sepsis and purulent meningitis.

Deguchi K. et al. *[Antimicrobial activities of cefozopran against Streptococcus pneumoniae from children].* Jpn J Antibiot. 1996; 49(7) : 703-9.p Abstract: In order to evaluate antimicrobial activity of cefozopran (CZOP), minimum inhibitory concentrations (MICs) of CZOP and control drugs were determined against Streptococcus pneumoniae from children that were isolated from October of 1995 to January of 1996. Determinations were made for the detection frequency of penicillin-insensitive or resistant strains in biovar utilizing hydrolysis products, and for the correlation of antibacterial susceptibility and macrolides (MLs)-resistant patterns. The results are summarized as

follows; 1. MIC90 of CZOP was < or = 0.025 micrograms/ml against benzylpenicillin (PCG)-susceptible S. pneumoniae (PSSP, 50 strains). MIC distribution of CZOP against these strains was approximately equal to that of PCG, and showed stronger activities of CZOP than those of ceftazidime (CAZ), flomoxef (FMOX) and erythromycin (EM). 2. MIC90 of CZOP was 0.39 micrograms/ml against 50 strains of PCG-insensitive S. pneumoniae (PISP) and PCG-resistant S. pneumoniae (PRSP). Antimicrobial activities of CZOP against these strains were stronger than those of CAZ, FMOX, PCG and EM. 3. These isolated strains of PISP and PRSP did not show type III biovar, but showed types I and II. The detection frequency of MLs-constitutive resistant strains were high among type III PSSP and those of MLs-inductive resistant strains were high among types I and II PISP and PRSP. These data suggested that CZOP had strong antimicrobial activities against multiple drug resistant S. pneumoniae including penicillin-resistant strains. CZOP will be effective against S. pneumoniae which often are causative organisms in infections of children.

Deguchi K. et al. *[The drug susceptibility pattern of the presumed etiologic agents of infectious enteritis including verotoxin-producing Escherichia coli O-157].* Jpn J Antibiot. 1997; 50(10) : 829-43.p Abstract: The drug susceptibility patterns were investigated for verotoxin-producing Escherichia coli (VTEC) including O-157, Salmonella spp., Vibrio parahaemolyticus and Campylobacter jejuni subsp. jejuni that were obtained in and after July 1996. The results are summarized as follows; 1. We found highly resistant strains of VTEC to tetracycline (TC) and ampicillin (ABPC). Minimum inhibitory concentrations (MIC) of some of the drugs against VTEC in an aerobic condition were significantly different from those in an anaerobic condition. For example, aerobic.anaerobic MIC ranges of the drugs tested were as follows: chroramphenicol (CP): 1.56-3.13 micrograms/ml.0.78-1.56 micrograms/ml, TC: 1.56-> 100 micrograms/ml.0.78-> 100 micrograms/ml, minocycline (MINO): 1.56-12.5 micrograms/ml.0.78-3.13 micrograms/ml, kanamycin (KM): 3.13-6.25 micrograms/ml.25-100 micrograms/ml, fosfomycin (FOM): 3.13-25 micrograms/ml.0.78-6.25 micrograms/ml, norfloxacin (NFLX): < or = 0.025-0.2 microgram/ml.< or = 0.025-0.2 microgram/ml, ABPC: 1.56-> 100 micrograms/ml.0.78-> 100 micrograms/ml and cefaclor (CCL): 1.56-25 micrograms/ml.56-12.5 micrograms/ml. MICs of CP and tetracyclines (TCs) in an anaerobic condition were lower by twofold and the MIC of FOM was lower by fourfold, but the variabilities of MIC-ranges of NFLX, ABPC and CCL were small. The MIC of KM was high. 2. We observed that some of Salmonella spp. were highly resistant to CP, TCs and MINO, and some were moderately resistant to NFLX. 3. The detection frequency of TC-resistant strains and NFLX-insensitive or resistant strains were high among C. jejuni subsp. jejuni. 4. Strains of V. parahaemolyticus and C. jejuni subsp. jejuni were mostly resistant to ABPC and CCL, MICs of which were in high ranges. 5. Fecal concentrations in MINO, KM, FOM and NFLX reported in literatures are high enough to have some antimicrobial activities, leed dose of ABPC and CCL are quite low.

Deguchi K. et al. *[Antimicrobial activities of arbekacin against methicillin-resistant Staphylococcus aureus].* Jpn J Antibiot. 1997; 50(1) : 1-11.p Abstract: In order to evaluate antimicrobial activity of arbekacin (ABK), coagulase-type and minimum inhibitory concentrations (MICs) of ABK and other drugs were determined against 700 strains of methicillin-resistant Staphylococcus aureus (MRSA) that were obtained in our laboratory from 1990 to 1996, 7 years. The results are summarized as follows; 1. The MIC-distributions of ABK against 100 strains of MRSA obtained yearly did not show stochastically significant differences. 2. The coagulase-type distributions showed differences over the years. Coagulase-type II strains increased and type IV strains decreased, and MIC-distributions of ABK and other drugs were different according to coagulase-types. 3. The detection frequencies of ABK-resistant strains (MIC of ABK: > or = 12.5 micrograms/ml) were 2.0 approximately 8.0% through the years. The frequency reported in 1980 was equal to the frequency obtained in 1992 approximately 1993 in a nationwide survey. Coagulase-types II, IV and VII that were ABK-resistant strains were frequently obtained, and most of ABK-resistant strains were also highly resistant to gentamicin.

Deguchi K. et al. *[Antimicrobial activities of sulbactam/ampicillin against clinically isolated microbial strains].* Jpn J Antibiot. 1995; 48(4) : 529-47.p Abstract: Antimicrobial activities were examined for sulbactam/ampicillin (SBT/ABPC) against clinically isolated microbial strains in 1987, 1990, 1994. Besides, the beta-lactamase productivity and MICs of these strains were measured, and the following conclusions were obtained. 1. The ratio of beta-lactamase producing strains were 90% of methicillin (DMPPC)-susceptible Staphylococcus aureus subsp. aureus (MSSA), about 80% of DMPPC-resistant S. aureus (MRSA), 100% of Escherichia coli, Klebsiella pneumoniae subsp. pneumoniae and Proteus mirabilis, 95% of Moraxella subgenus Branhamella catarrhalis and 15-20% of Haemophilus influenzae. Several kinds of beta-lactamase productivity were observed. 2. Antimicrobial activities of SBT/ABPC against beta-lactamase producing strains of MSSA, M. (B.) catarrhalis, H. influenzae, and almost all of Enterobacteriaceae were stronger than those of ampicillin (ABPC) and piperacillin (PIPC), but antimicrobial activities of SBT/ABPC were weak against MRSA and cephems (CEPs)-resistant strains detected in some of Enterobacteriaceae. 3. It appeared that benzylpenicillin (PCG)-insensitive Streptococcus pneumoniae (PISP) or PCG-resistant S. pneumoniae (PRSP) and CEPs-resistant Escherichia coli increased year by year. 4. Antimicrobial activities of SBT/ABPC were strong against Streptococcus pyogenes, S. pneumoniae, M. (B.) catarrhalis and H. influenzae including beta-lactamase producing strains. Additionally, beta-lactamase inhibiting effect of SBT was observed against beta-lactamase produced by S. aureus and K. pneumoniae which demonstrate indirect pathogenicity. Thus, SBT/ABPC is an injectable antibiotic that is expected to demonstrate clinical usefulness, especially as the first line drug for the respiratory tract infections that are community-acquired.

Deguchi T. et al. *Fluoroquinolone treatment failure in gonorrhea. Emergence of a Neisseria gonorrhoeae strain with enhanced resistance to fluoroquinolones.* Sex Transm Dis. 1997; 24(5) : 247-50.p Abstract: BACKGROUND AND OBJECTIVES: Although emergence of clinical isolates of Neisseria gonorrhoeae with decreased susceptibilities to fluoroquinolones and treatment failures in gonorrhea have been reported, there have been no clinical reports that fluoroquinolone treatments actually select quinolone-resistant strains, nor have isolates that exhibited clinically significant resistance been analyzed for resistance mechanisms. GOALS: To report a case of fluoroquinolone treatment failure in gonorrhea and emergence of a posttreatment isolate with enhanced resistance to fluoroquinolones; and to study mechanisms of quinolone resistance in the isolates from this patient. STUDY DESIGN: A patient with gonococcal urethritis treated with ofloxacin, 200 mg, three times daily for 5 days is described. Pretreatment and posttreatment isolates were tested for minimum inhibitory concentrations (MICs) of antimicrobial agents and analyzed for alterations in DNA gyrase and topoisomerase IV. They were also examined for ofloxacin uptake. RESULTS: Treatment failure with multiple doses of ofloxacin was observed in this case of gonorrhea. The pretreatment isolate showed decreased susceptibilities to fluoroquinolones (MIC of ofloxacin, 1.0 mg/l; MIC of ciprofloxacin, 0.25 mg/l), and had amino acid changes of Ser-91—>Phe in GyrA and Ser-87—>Ile in ParC. The posttreatment isolate exhibited an increase in resistance to fluoroquinolones (MIC of ofloxacin, 8.0 mg/l; MIC of ciprofloxacin, 1.0 mg/l). This isolate had identical alterations in GyrA and ParC, but exhibited significantly reduced uptake of ofloxacin. This isolate also showed a small decrease in susceptibilities to cephalosporins. CONCLUSIONS: Alterations in DNA gyrase and topoisomerase IV confer clinically significant resistance to fluoroquinolones in N. gonorrhoeae strains. Treatment

with multiple doses of fluoroquinolones is likely to bring about selection of more fluoroquinolone-resistant strains of N. gonorrhoeae and to influence susceptibilities to cephalosporins.

Deguchi T. et al. *In-vitro antimicrobial activity of HSR-903, a new fluoroquinolone, against clinical isolates of Neisseria gonorrhoeae with quinolone resistance-associated alterations in GyrA and ParC.* J Antimicrob Chemother. 1997; 40(3) : 437-9.p Abstract: The in-vitro antimicrobial activity of HSR-903, a new fluoroquinolone, was tested against 51 clinical Neisseria gonorrhoeae isolates in comparison with ciprofloxacin, levofloxacin and sparfloxacin. The MICs of HSR-903 for 11 isolates with alterations in both GyrA and ParC, for 19 isolates with alterations only in GyrA and for 21 isolates without alterations in either GyrA or ParC ranged from 0.03 mg/L to 1.0 mg/L (MIC90 = 0.25 mg/L), from 0.03 mg/L to 0.5 mg/L (MIC90 = 0.125 mg/L) and from < or = 0.001 mg/L to 0.008 mg/L (MIC90 = 0.004 mg/L), respectively. Levofloxacin and ciprofloxacin were the least active of the four quinolones tested, particularly against the mutant strains. Sparfloxacin was more active, but HSR-903 exhibited the most potent in-vitro activity against the clinical N. gonorrhoeae isolates, including those harbouring quinolone-resistance-associated alterations in GyrA and ParC.

Deiwick J. et al. *Mutations in Salmonella pathogenicity island 2 (SPI2) genes affecting transcription of SPI1 genes and resistance to antimicrobial agents.* J Bacteriol. 1998; 180(18) : 4775-80.p Abstract: The Salmonella typhimurium genome contains two pathogenicity islands (SPI) with genes encoding type III secretion systems for virulence proteins. SPI1 is required for the penetration of the epithelial layer of the intestine. SPI2 is important for the subsequent proliferation of bacteria in the spleens of infected hosts. Although most mutations in SPI2 lead to a strong reduction of virulence, they have different effects in vitro, with some mutants having significantly increased sensitivity to gentamicin and the antibacterial peptide polymyxin B. Previously we showed that certain mutations in SPI2 affect the ability of S. typhimurium to secrete SPI1 effector proteins and to invade cultured eukaryotic cells. In this study, we show that these SPI2 mutations affect the expression of the SPI1 invasion genes. Analysis of reporter fusions to various SPI1 genes reveals highly reduced expression of sipC, prgK, and hilA, the transcriptional activator of SPI1 genes. These observations indicate that the expression of one type III secretion system can be influenced dramatically by mutations in genes encoding a second type III secretion system in the same cell.

Del' Alamo L. et al. *Antimicrobial susceptibility of coagulase-negative staphylococci and characterization of isolates with reduced susceptibility to glycopeptides.* Diagn Microbiol Infect Dis. 1999; 34(3) : 185-91.p Abstract: The antimicrobial susceptibility of 239 coagulase-negative staphylococci (CNS) isolates consecutively collected from blood culture in patients admitted in a 600-bed teaching hospital was evaluated. The isolates were identified to the species level by conventional methods and the MicroScan Positive Combo Panel type 6 system, and their susceptibility to vancomycin, teicoplanin, and oxacillin were tested by agar dilution, disk diffusion, and MicroScan-WalkAway system. The species distribution was as follows: Staphylococcus epidermidis 120 (50.2%), S. hominis 29 (12.1%), S. haemolyticus 24 (10.0%), S. cohnii 14 (5.9%), and isolates from other CNS species 52 (21.8%). The percentage of resistance to oxacillin was 74.5% by agar dilution. The highest percentages of oxacillin resistance were found among S. haemolyticus (95.8%) and S. epidermidis (80.8%). Teicoplanin resistance (MIC > or = 32 micrograms/mL) was detected in five S. haemolyticus isolates, whereas intermediate resistance (MIC = 16 micrograms/mL) was detected in nine strains. These isolates with reduced susceptibility to teicoplanin were resistant to oxacillin, but remained susceptible to vancomycin (MIC < or = 4 micrograms/mL). Two isolates, one S. haemolyticus and one S. epidermidis, showed a vancomycin MIC of 8 micrograms/mL, and both MicroScan and disk diffusion methods classified these isolates as susceptible. Our results showed that glycopeptide resistance is emerging among CNS isolates in our institution and the disk diffusion method may not detect isolates with decreased susceptibility to these antimicrobial agents.

Del Campo J. et al. *Antimicrobial effect of rosemary extracts.* J Food Prot. 2000; 63(10) : 1359-68.p Abstract: A rosemary extract commercially exploited (Oxy'less) as an antioxidant of lipids in foods was dissolved in ethanol (100 mg/ml), and the solution was tested against foodborne microorganisms. For gram-positive bacteria, the MIC of the ethanolic solution was 1% for Leuconostoc mesenteroides, 0.5% for Listeria monocytogenes, 0.5% for Staphylococcus aureus, 0.13% for Streptococcus mutans, and 0.06% for Bacillus cereus. It slowed the growth of Penicillium roquefortii and Botrytis cinerea. Up to 1% of the ethanolic solution had no activity on the gram-negative bacteria Escherichia coli, Salmonella Enteritidis, and Erwinia carotovora and on the yeasts Rhodotorula glutinis and Cryptococcus laurentii. Antibacterial activity of the rosemary extract was strongly influenced by the composition of the media. The MIC was reduced by low pH, high NaCl contents, and low temperatures. Low pH and high NaCl concentration had a synergistic effect on the MIC of the rosemary extract for S. aureus. Lipids, surface-active agents, and some proteins decreased its antibacterial activity, whereas pectin had no effect. The inhibitory effect was little modified by heat treatment (100 degrees C). The natural microflora of pasteurized zucchini broth was inhibited by 0.5% of the rosemary extract. The antibacterial activity was linked to the compounds extracted with hexane, which are presumably phenolic diterpenoids.

del Castillo F. et al. *Influence of recent antibiotic therapy on antimicrobial resistance of Streptococcus pneumoniae in children with acute otitis media in Spain.* Pediatr Infect Dis J. 1998; 17(2) : 94-7.p Abstract: BACKGROUND: Despite the high prevalence of penicillin resistance among Streptococcus pneumoniae strains in Spain (40 to 60% with MIC > or = 0.1 microg/ml), the data on acute otitis media (AOM) isolates are scarce. We conducted a prospective, longitudinal study to determine the rates of antimicrobial resistance of S. pneumoniae isolates from children with AOM in our country and to analyze the effect of previous antibiotic therapy on these rates. METHODS: Tympanocentesis was performed on 169 children diagnosed with AOM (age range, 1 month to 14 years). Two groups were considered: Group A, 113 patients with non-antibiotic-treated AOM, subdivided into Group A1 (collected from 1989 to 1992) and Group A2 (1992 to 1996); Group B, 56 patients from the period 1992 to 1996, with AOM clinical failure, defined as worsening or persistent symptoms after at least 2 days of appropriate antibiotic therapy. Amoxicillin-clavulanate was the most frequent antibiotic used (68%), followed by azithromycin (21%), cefaclor and cefixime (11%). RESULTS: A total of 63 S. pneumoniae isolates were recovered, 42 in Group A and 21 in Group B. Resistance to penicillin (MIC > or = 0.1 microg/ml) was found in 38% of strains in Group A (32% in A1 and 50% in A2), but in Group B the rate of resistance reached 90% (P = 0.0002). Erythromycin resistance was also increased from 35% (Group A2) to 62% (Group B), and trimethoprim-sulfamethoxazole resistance rose from 64% to 81%. CONCLUSIONS: Resistance to penicillin among S. pneumoniae AOM isolates is frequent and is increasing in Spain. After failure of standard antibiotic therapy, the rates of penicillin resistance reached 90% of the isolates.

Del Pont J.M. et al. *Infective endocarditis in children: clinical analyses and evaluation of two diagnostic criteria.* Pediatr Infect Dis J. 1995; 14(12) : 1079-86.p Abstract: A new diagnostic schema for infective endocarditis (IE), the Duke criteria, has been compared with the previously published criteria of von Reyn in adult patients. This study was designed to analyze the clinical characteristics of a group of pediatric patients with IE and to compare the diagnostic efficiency of both sets of criteria. We reviewed retrospectively the clinical records of 38 patients, 22 with predisposing heart disease (Subgroup A) and 16 with no known cardiologic abnormality (Subgroup B). Ventricular

septal defect was the most frequent preexisting heart disease (31.8%) and central venous catheters were the most frequent predisposing factor (68.7%). Comparison of the clinical features between subgroups (A vs. B) showed differences only for the presence of a new regurgitant murmur (9% vs. 44%, P < 0.05) and a hemoglobin value < or = 10 g/dl (50% vs. 94%, P < 0.05). The most frequent microorganisms isolated were viridans streptococci (36%) in Subgroup A and Staphylococcus aureus (50%) in Subgroup B. Of the 6 pathologically confirmed cases all would have been classified as clinically definite by the Duke criteria, as compared with 2 of 6 being defined as probable and one being rejected by von Reyn criteria. Of the 32 cases clinically defined 19 (59%) were classified as definite by the Duke criteria, and 11 (34%) were probable by the von Reyn criteria (difference 25%, P < 0.01). Although no case of IE was rejected by Duke criteria, 8 (25%) were rejected by von Reyn criteria (difference 25%, P < 0.01), with all 8 classified as possible by Duke criteria. We conclude that the Duke criteria were superior to the von Reyn criteria for the diagnosis of pediatric IE, including more cases as definite and significantly fewer cases as rejected.

del Rey Calero J. *[Infectious disease trends].* An R Acad Nac Med (Madr). 1999; 116(1) : 41-68; discussion 69-72.p Abstract: Infectious disease mortality has increased during the last decades: from a rate of 38.10(5) inhabitants in 1980-95 to 41, 5.10(5) in 1998. Demographic changes have modified susceptibility to infections, due to the increment of elderly people—who have less immunity—, and the increase in drug-abusers and HIV-infected subjects. Social and technological environmental factors have had some influence on emergent and re-emergent diseases. Key issues to be considered are problems with antimicrobial resistance, infectious related- to chronic diseases, infections in immunodeficient subjects, and new vaccines to use. Among the challenges to public health is the need for incorporating new and rapidly technologies as microarrays, strategies of planning, multisectorial approaches to detecting preventing and controlling emerging and re-emerging infectious diseases.

Del Solar V. E. et al. *Mecanismos enzimáticos de resistencia a antibióticos aminoglicósidos en bacilos gram negativos de hospitales chilenos.* Rev. med. Chile. mar. 1995; 123(3) : 293-7.p Abstract: The presence of aminoglycoside modifying enzyme (AMEs) has been investigated by an agar diffusion method, in 344 strains of aminoglycoside-resistant Gram negative bacilli isolated in different Chilean hospitals. Most of the strains exhibited a combination of enzymatic mechanism of resistance, but 2 acetylatting (AAC(3)II and AAC(6')I) and one phosphorylating (APH(3')I) enzymes were mechanism detected in the strains. A significant increase in the frequency of strains producing AAC(6')I), possibly due to wide use of amikacin, has been found when results were compared with those of a report published in 1985 (AU).

del Valle O. et al. *[The prevalence of methicillin-resistant Staphylococcus aureus phagotype 95 in the Hospitales Vall d'Hebron of Barcelona].* Enferm Infecc Microbiol Clin. 1999; 17(10) : 498-505.p Abstract: BACKGROUND: In our hospital endemic methicillin resistant Staphylococcus aureus (MRSA) has been documented since 1971, with epidemic and interepidemic periods. During these years phage groups I, I-III, and non-typable were found by the international set of phages Phage group 95 (F95) was unusual between 1986 (when phage typing was first available) and 1991, with prevalence of 5.2% (mean), and 100% of sensibility to methicillin. In November 1991 appeared the first MRSA F95 strain, and its prevalence has been increasing until 1997. MATERIAL AND METHODS: We have studied 133 strains of MRSA F95 isolated from 87 patients, 39 of them hospitalized in the General Hospital (HG), 38 in Traumatology Hospital (HT) and 8 in the Children's Hospital (HI). Two of these patients had successive stancies in HG and HT. Antimicrobial susceptibility was determined by the disk diffusion method and microdilution to check oxacillin resistance. Moreover these method we have maked: detection of mecA, phage typing with the international set of phages and study of the PGFE patterns by digestion of chromosomic DNA with SmaI. RESULTS: The percentage of methicillin resistance in F95 strains was increased since the appear of the first strain between 8.3% in 1991 to a maximum of 76.9% in 1995, we had a descens to 13.7% in 1996 but 1997 can back to augment it to 72.5%. MICs for oxacillin of these strains were low (< or = 64 mg/l to 87.4% of strains), and all of them were mecA positive, 78.1% of them were resistant to macrolides, 96.5% to tobramycin and 84.9% to quinolones, but only 10.5% to gentamicin, 4.7% were resistant to cotrimoxazol, 1.2% to fosfomycin and 2.5% to rifampin. All of them were sensible to doxycycline, and vancomycin. The pulse field gel electrophoresis showed 7 restriction patterns in MRSA F95, 73.8% of strains correspond to one of them (B), spreading from the spinal cord injury unit and prevalent in HT; and 10.8% to another (C), the first that appear, spreading from the neurosurgical unit and with high prevalence in HG. 6.9% has pattern J a B subtype that appear in broth HG and HT. Pattern E is prevalent in HI it was spread from neonatology unit. CONCLUSIONS: The emergence in a Center with endemic resistance of new strains of MRSA, not all of them of the same clone, with characteristic resistance pattern to antibiotics and in convivence with other phage groups is one demonstration of genetic variability of SAMR in our entorn.

DeLeo F.R. et al. *NADPH oxidase activation and assembly during phagocytosis.* J Immunol. 1999; 163(12) : 6732-40.p Abstract: Generation of superoxide (O2-) by the NADPH-dependent oxidase of polymorphonuclear leukocytes is an essential component of the innate immune response to invading microorganisms. To examine NADPH oxidase function during phagocytosis, we evaluated its activation and assembly following ingestion of serum-opsonized Neisseria meningitidis, serogroup B (NMB), and compared it with that elicited by serum-opsonized zymosan (OPZ). Opsonized N. meningitidis- and OPZ-dependent generation of reactive oxygen species by polymorphonuclear leukocytes peaked early and then terminated. Phosphorylation of p47phox coincided with peak generation of reactive oxygen species by either stimulus, consistent with a role for p47phox phosphorylation during NADPH oxidase activation, and correlated with phagosomal colocalization of flavocytochrome b558 (flavocytochrome b) and p47phox and p67phox (p47/67phox). Termination of respiratory burst activity did not reflect dephosphorylation of plasma membrane- and/or phagosome-associated p47phox; in contrast, the specific activity of phosphorylated p47phox at the phagosomal membrane increased. Most significantly, termination of oxidase activity paralleled the loss of p47/67phox from both NMB and OPZ phagosomes despite the continued presence of flavocytochrome b. These data suggest that 1) the onset of respiratory burst activity during phagocytosis is linked to the phosphorylation of p47phox and its translocation to the phagosome; and 2) termination of oxidase activity correlates with loss of p47/67phox from flavocytochrome b-enriched phagosomes and additional phosphorylation of membrane-associated p47phox.

Deliere E. et al. *Epidemiological investigation of Ochrobactrum anthropi strains isolated from a haematology unit.* J Hosp Infect. 2000; 44(3) : 173-8.p Abstract: Ochrobactrum anthropi is an oxidase-producing gram-negative bacillus preferring aqueous environments. It is an opportunist of low pathogenicity with a wide and unpredictable antibiotic resistance. We observed bacteraemia caused by this organism in two immunocompromized patients hospitalized in the same haematology unit and catheter-associated sepsis was recognized within two days. Another isolate was obtained from the stools of a third patient of the same unit. Environmental investigations recovered an isolate from a tap-water sample of the unit. Pulsed-field gel electrophoresis analysis of these four isolates and two others isolates previously found in the same ward, showed identical restriction patterns for the two blood isolates and confirmed that the two bacteraemia were epidemiologically related. Copyright 2000 The Hospital Infection Society.

Delpassand E.S. et al. *Rapid identification of common human pathogens by high-resolution proton magnetic resonance spectroscopy.* J Clin Microbiol. 1995; 33(5) : 1258-62.p Abstract: Routine procedures for recovery of bacteria from clinical specimens involve culturing the latter on various nonselective and selective agar media. The bacteria are then identified by means of biochemical and immunological test procedures. Reduction of the time required to identify the bacteria is highly desirable for rapid clinical diagnosis. Towards this end the potential of proton nuclear magnetic resonance (NMR) spectroscopy for providing a "fingerprint" within the proton spectrum of five bacterial genera, reflecting their characteristic cell wall constituents, has been investigated. Establishing a database of high-resolution proton NMR spectra of a large number of bacterial species is a prerequisite for attaining this objective. A database has been established for five common human pathogens: Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, and Enterococcus faecalis. On the basis of the presence of characteristic resonances in their spectra, a simple algorithm has been developed to differentiate and identify these microorganisms. The NMR spectra of E. coli and S. aureus showed no dependency on the type of growth medium, growth density, or incubation time.

DeMarais P.L. et al. *Nosocomial infections in human immunodeficiency virus-infected patients in a long-term-care setting.* Clin Infect Dis. 1997; 25(5) : 1230-2.p Abstract: To our knowledge, the epidemiology of hospital-acquired infections in human immunodeficiency virus (HIV)-infected patients during long-term care has not been reported. For 13 months, we observed HIV-infected patients (50 men and 15 women) in a dedicated 21-bed unit in a long-term-care facility to determine the rate of nosocomial infections. The mean age of the patients was 39 years (range, 22-78 years); 74% of the patients had CD4 cell counts of < 200/mm3. There was a total of 152 infections (24 infections per 1,000 long-term-care days). The factors associated with the occurrence of a nosocomial infection were low CD4 cell counts, poor functional status, and longer duration of stays at the facility. The three most common infections were Clostridium difficile-associated diarrhea, primary bacteremia, and urinary tract infection. Eighteen hospital-manifested opportunistic infections occurred. More than 50% of the cases of bacteremia were due to multidrug-resistant organisms. Nosocomial infections occur commonly in HIV-infected patients in long-term care and thus are important considerations in patient management.

Dembele T. et al. *[Antibacterial activity of lactobacilli].* Epidemiol Mikrobiol Imunol. 1998; 47(2) : 43-6.p Abstract: The antagonistic action of lactobacilli is an important factor in the protection of the vagina of fertile women from infection by other microorganisms. In the present study the authors investigated 17 strains of lactobacilli, incl. 11 of vaginal origin. The objective was to investigate in more detail the antibacterial activity of lactobacilli and to attempt to assess substances responsible for inhibition. The investigated lactobacilli inhibited some strains of Escherichia coli, Serratia marcescens, Shigella boydii, Staphylococcus aureus, Listeria monocytogenes, Listeria innocua and Listeria ivanovii with different intensity. The authors provided evidence that inhibition is due mainly to organic acids and to a lesser extent to bacteriocins. The authors assessed also the effect of enterobacteria on lactobacilli but did not observe any inhibition of lactobacilli.

Demetriou C.A. et al. *Serratia marcescens bacteremia after carotid endarterectomy and coronary artery bypass grafting.* Heart Lung. 1999; 28(4) : 293-4.p Abstract: Serratia Marcescens is a common, water-borne hospital colonizer. Respiratory secretions, wounds, and urine are frequently recognized areas of Serratia colonization. Serratia bacteremias usually occur nosocomially and are associated with high mortality and morbidity rates. Serratia bacteremias may be primary or secondary from an identifiable source. Hospital-acquired S marcescens bacteremias have no known source in half of the cases. We present a case of nosocomial primary S marcescens bacteremia in a surgical patient successfully treated with levofloxacin.

Denecke J. et al. *[Arthrogryposis, renal tubular dysfunction, cholestasis (ARC) syndrome: case report and review of the literature].* Klin Padiatr. 2000; 212(2) : 77-80.p Abstract: The ARC-syndrome is a rare disease with the obligatory symptoms arthrogryposis, renal tubular dysfunction and cholestasis. Optional further symptoms like ichthyosis, diarrhea, central nervous system defects and recurrent infections have been reported. The ARC-syndrome was first reported by Lutz-Richner and Landolt in 1973. The pathophysiology is still unknown, an autosomal recessive inheritance is postulated. Patients rarely exceed an age of six month. We report a boy of consanguineous Turkish parents who suffered from congenital deformities of the lower extremities, a metabolic acidosis and failure to thrive. In the sequel he developed a renal Fanconi syndrome and cholestasis. Histology of liver and muscle biopsy specimen showed the typical findings of the disease with giant cell hepatitis and neurogenous muscle atrophy. His condition could be stabilized and he increased in weight by substituting fluid, electrolytes, buffer and parenteral nutrition. Total enteral nutrition of the 280 ml/kg/d he required failed even by nasogastric tube and percutaneous endoscopic gastrostomy. Additional fluid substitution by central venous catheter remained necessary. At the age of 7 month he died.

Denning G.M. et al. *Pseudomonas pyocyanin increases interleukin-8 expression by human airway epithelial cells.* Infect Immun. 1998; 66(12) : 5777-84.p Abstract: Pseudomonas aeruginosa, an opportunistic human pathogen, causes acute pneumonia in patients with hospital-acquired infections and is commonly associated with chronic lung disease in individuals with cystic fibrosis (CF). Evidence suggests that the pathophysiological effects of P. aeruginosa are mediated in part by virulence factors secreted by the bacterium. Among these factors is pyocyanin, a redox active compound that increases intracellular oxidant stress. We find that pyocyanin increases release of interleukin-8 (IL-8) by both normal and CF airway epithelial cell lines and by primary airway epithelial cells. Moreover, pyocyanin synergizes with the inflammatory cytokines tumor necrosis factor alpha and IL-1alpha. RNase protection assays indicate that increased IL-8 release is accompanied by increased levels of IL-8 mRNA. The antioxidant n-acetyl cysteine, general inhibitors of protein tyrosine kinases, and specific inhibitors of mitogen-activated protein kinases diminish pyocyanin-dependent increases in IL-8 release. Conversely, inhibitors of protein kinases C (PKC) and PKA have no effect. In contrast to its effects on IL-8 expression, pyocyanin inhibits cytokine-dependent expression of the monocyte/macrophage/T-cell chemokine RANTES. Increased release of IL-8, a potent neutrophil chemoattractant, in response to pyocyanin could contribute to the marked infiltration of neutrophils and subsequent neutrophil-mediated tissue damage that are observed in Pseudomonas-associated lung disease.

Dens F. et al. *Caries-related salivary microorganisms and salivary flow rate in bone marrow recipients.* Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1996; 81(1) : 38-43.p Abstract: Cancer treatments often induce oral complications. In this study we investigate longitudinally the salivary gland function, the salivary caries-related microorganisms, and buffer capacity in bone marrow recipients. Stimulated saliva samples were taken midmorning. The salivary factors were studied in 42 patients from before transplant until 4 months after transplant. A dramatic reduction (66%) of salivary flow rate is noticed in all patients at 1 month after transplant, and only a partial recovery (42% reduction) is seen after 4 months. A clear shift toward a lower buffer capacity and a higher amount of cariogenic microorganisms is seen posttransplant. This shift is more pronounced when total body irradiation was included in the pretransplant conditioning therapy. These findings indicate that the studied parameters in transplant recipients can contribute to a higher caries risk and oral complications during the early posttransplant period.

Denys A. *[Theoretical basis for the antibiotic therapy of the upper part of the respiratory system].* Otolaryngol Pol. 1997; 51 Suppl 25 : 155-60.p Abstract: The paper presents the views on the etiology of infections in the respiratory system. Beside the so called "old pathogens" such as Streptococcus pneumoniae, Haenophilus influenzae, Moraxella catarrhalis, "atypic" microorganisms are becoming more and more important, i.e. Mycoplasma pneumoniae, Legionella pneumophila, Chlamydia pneumoniae. Mixed flora with aerobic and anaerobic bacteria is observed in chronic infections. Viral infections facilitate bacterial infections. Antibiotic used first should be active against the "old" and "new" pathogens. Future prospects are set on macrolides such as clarythromycin.

Descheemaeker P. et al. *Evaluation of arbitrarily primed PCR analysis and pulsed-field gel electrophoresis of large genomic DNA fragments for identification of enterococci important in human medicine.* Int J Syst Bacteriol. 1997; 47(2) : 555-61.p Abstract: The increasing problems encountered with enterococcal nosocomial infections and the intrinsic and acquired resistance of the enterococci to different antimicrobial compounds highlight the need for a rapid identification technique. Enterococcus faecalis is readily identified by biochemical tests, but species differentiation within the Enterococcus faecium and Enterococcus gallinarum species groups is less well established. In the present study, 66 strains representing the most prevalent human enterococci were used to develop a PCR-based species-specific identification protocol. Whole-cell protein analysis by sodium dodecyl sulfate-polyacrylamide gel electrophoresis was used as a reference method for species identification. In addition, the genomic SmaI macro-restriction fragment distribution of all of the strains was examined by pulsed-field gel electrophoresis (PFGE). Oligonucleotide D11344-primed PCR was as discriminative as whole-cell protein analysis and resulted in more easily interpreted band patterns. This PCR-based technique allowed identification of clinical isolates by visual examination of the DNA profiles obtained. The inability of both methods to discriminate between Enterococcus casseliflavus and Enterococcus flavescens brought into question the species status of E. flavescens. PFGE did not result in species-discriminative DNA bands or band patterns, but proved to be superior for interpretation of interstrain relationships.

Deshmukh S.R. et al. *Norfloxacin induced resistance to fluoroquinolones & structurally unrelated antimicrobial agents in coagulase negative staphylococci.* Indian J Med Res. 1997; 106 : 461-4.p Abstract: Nine clinical isolates of coagulase negative staphylococci (CONS) susceptible to norfloxacin (MIC 1.8-2 micrograms/ml) were manipulated in vitro to induce norfloxacin resistance by means of serial passage in brain heart infusion broth containing increasing concentrations of norfloxacin. Exposure of CONS to norfloxacin resulted in 18 to 20 times increase in MIC of norfloxacin and change in in vitro susceptibility to ciprofloxacin, pefloxacin, ofloxacin, kanamycin, neomycin and tobramycin, indicating development of cross resistance to fluoroquinolones and aminoglycosides. These results show that exposure to increasing concentrations of norfloxacin can induce the development of resistance to various antimicrobial agents, suggesting its mutagenic role.

Deshpande L.M. et al. *Antimicrobial activity of advanced-spectrum fluoroquinolones tested against more than 2000 contemporary bacterial isolates of species causing community-acquired respiratory tract infections in the United States (1999).* Diagn Microbiol Infect Dis. 2000; 37(2) : 139-42.p Abstract: In vitro activity of four newer fluoroquinolones (clinafloxacin, gemifloxacin, moxifloxacin, sitafloxacin) and an equal number control drugs in the same class (ciprofloxacin, grepafloxacin, levofloxacin, trovafloxacin) was determined by reference dilution tests against 2156 recent United States clinical isolates of Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis. All the fluoroquinolones demonstrated excellent in vitro activity against these pathogens. Streptococcus pneumoniae isolates were fully susceptible to clinafloxacin, sitafloxacin, and gemifloxacin at 0.5 microg/ml, and over 98% of sampled strains had MICs of </=1 microg/ml for grepafloxacin, moxifloxacin and trovafloxacin. Penicillin resistance did not influence the potency of the tested fluoroquinolones. All the isolates of H. influenzae and M. catarrhalis were inhibited by the investigational, as well as comparator fluoroquinolones at </=0.5 microg/ml, irrespective of their beta-lactamase producing abilities. In conclusion, the investigational fluoroquinolones demonstrated excellent activity against these major respiratory tract pathogens isolated in 1999, and some remain safe candidates for empiric therapy of community-acquired respiratory tract infections and selected infections in hospitalized patients.

DeSimone N.A. et al. *Bactericidal effect of 0.95-mW helium-neon and 5-mW indium-gallium-aluminum-phosphate laser irradiation at exposure times of 30, 60, and 120 seconds on photosensitized Staphylococcus aureus and Pseudomonas aeruginosa in vitro.* Phys Ther. 1999; 79(9) : 839-46.p Abstract: BACKGROUND AND PURPOSE: Studies have demonstrated a bactericidal effect of laser irradiation when lasers with power outputs of (6 mW are directed toward pathogenic or opportunistic bacteria previously treated with a photosensitizing agent. The purpose of this study was to determine the bactericidal capabilities of irradiation from lasers with power outputs of less than 6 mW on photosensitized microorganisms. METHODS: Two bacteria that commonly infect skin lesions, Staphylococcus aureus and Pseudomonas aeruginosa, were used. The 2 lasers used, the 0.95-mW helium -neon laser and the 5-mW indium-gallium-aluminum-phosphate laser, emit light at a wavelength close to the absorption maxima of the sensitizing agent chosen, toluidine blue O. This agent was used because of its proven effectiveness in sensitizing bacteria. For each bacterial strain, toluidine blue O was added to a 108 cells/mL solution until a 0.01% weight/volume ratio was obtained. These mixtures were spread on agar-coated petri dishes, which were then exposed to 1 of the 2 lasers for 30, 60, and 120 seconds. The cultures were then grown overnight and examined for one or more visible zones of inhibition. The areas surrounding the irradiated zone provided a control for the effects of toluidine blue O alone. To determine the effects of laser irradiation without prior toluidine blue O sensitization, separate plates were established using unsensitized bacteria. RESULTS: Although inconsistencies between plates were noted, both lasers produced at least one zone of inhibition in both bacterial species at all 3 time periods. The 5-mW laser, however, produced a greater number of these zones. CONCLUSION AND DISCUSSION: Laser-induced microbial killing of photosensitized organisms could have clinical applications in the treatment of infected skin lesions, pending in vivo studies.

Dettenkofer M. et al. *Infection control and changes in management of hospitals: the European experience.* J Hosp Infect. 1999; 43 Suppl : S161-4.p Abstract: The general setting for the management of many European hospitals has undergone enormous changes during the last five to 10 years, especially with respect to economic, personnel and technical resources. This change has had a serious influence on the practice of infection control. To get an insight of the problems infection control practitioners in Europe today have to face, hospital epidemiologists representing nine European countries were asked to answer a questionnaire. In most countries, new laws on communicable disease prevention and infection control in hospitals have been implemented during the last few years. In conjunction with the widespread introduction of quality assurance and the accreditation of hospitals, organizational aspects of infection control have gained importance. However, budget restrictions and the growing competition between institutions are major challenges. In general, there has been a remarkable influence of the documented changes on the practice of infection control in European hospitals. Facing this situation, infection control practitioners should abandon unproven measures and implement those that are evidence-based, to prevent hospital acquired infection (HAI). Cost reducing initiatives, like the use of well designed multi-use devices and the reuse of disposables should be considered and scientifically assessed.

Deva A.K. et al. *Detection of persistent vegetative bacteria and amplified viral nucleic acid from in-use testing of gastrointestinal endoscopes.* J Hosp Infect. 1998; 39(2) : 149-57.p Abstract: Hospital-acquired infection attributed to inadequate decontamination of gastrointestinal endoscopes prompted an in use evaluation of recommended procedures. Specimens were obtained from the internal channels of 123 endoscopes before, during and after decontamination by flushing with saline and brushing with a sterile brush, and examined for vegetative bacteria by broth and plate culture. Four endoscopy units were tested; the chemical disinfectants used were: 2% glutaraldehyde in Centres 1 and 2 (automated) and Centre 3 (manual); peracetic acid in Centre 4 (automated). Samples from patients in Centre 1 with known chronic hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV-1) infection were also examined for viral nucleic acid by ultracentrifugation, nucleic acid extraction, reverse transcription (for RNA) and polymerase chain reaction (PCR). No persistent vegetative bacteria were found following standard manual cleaning and disinfection for 20 min in 2% glutaraldehyde in Centres 2 and 3 (N = 37). At Centre 1, while plate culture yielded no growth, 34% of samples (10/29) grew vegetative bacteria in broth culture after cleaning and disinfection for 20 min in 2% glutaraldehyde. Investigation revealed an error in manual cleaning; no bacteria were detected in 37 samples taken after this was corrected. At Centre 4, despite the use of peracetic acid as a sterilant, three out of 20 (15%) of post decontamination samples grew bacteria; one contained persistent bacteria. HBV and HCV PCR analysis detected viral nucleic acid in three out of four and four out of six samples from viraemic patients undergoing endoscopy in Centre 1 during the period of improper manual washing. After proper cleaning was instituted, samples from nine out of nine HCV viraemic patients were negative. HIV RNA was detected in five of 14 samples taken from endoscopes after use on HIV positive patients but all post decontamination samples were negative. Detection of bacteria in washes from endoscope channels is a useful warning of a breakdown in decontamination practice. Inadequate brushing of internal channels may result in persistent HCV and HBV viral nucleic acid, the significance of which is not clear. These results reinforce the importance of adequate manual cleaning of endoscopes before chemical disinfection.

Dever L.L. et al. *Vancomycin-resistant Enterococcus faecium in a Veterans Affairs Medical Center: association with antibiotic usage.* Am J Infect Control. 1998; 26(1) : 40-6.p Abstract: BACKGROUND: Colonization and infection with vancomycin-resistant Enterococcus faecium (VREF) has been associated with the use of vancomycin and other antibiotics in individual patients. The objective of this study was to determine the association of VREF with the aggregate usage of antibiotics on nursing units in a hospital. METHODS: This was a retrospective correlation study. A usage ratio was calculated for each parenteral antibiotic on each nursing unit as the per-bed usage by weight of that antibiotic divided by its average usage throughout the hospital. An average usage ratio (AUR) for each nursing unit was calculated as the mean of usage ratios of individual antibiotics. The AUR was used to compare the usage of antibiotics among nursing units in the hospital. The incidence of VREF infections on individual nursing units in a Veterans Affairs Medical Center was correlated with the usage of parenteral antibiotics separately and in aggregate in univariate and multivariate regression analyses. RESULTS: The AUR was strongly and positively correlated with the recovery of VREF on individual nursing units. By univariate analyses, increasing use of each antibiotic tested was associated with isolation of VREF but only clindamycin remained significant in the multivariate model. However, usage of various antibiotics was highly interrelated, and only clindamycin usage was significantly correlated with usage of all other antibiotics studied. Intensive care and acute care units and units with fewer patient beds were more likely to have patients with VREF infection than were subacute care units ($p < 0.003$) or larger units ($p < 0.01$). CONCLUSIONS: VREF infections were associated with greater aggregate antibiotic use on nursing units. Determination of antibiotic usage ratios may provide a convenient and useful tool for examining the association of antibiotic usage with other nosocomial infections.

Devlin H.R. *Bacteria for the nineties.* Ostomy Wound Manage. 1998; 44(8) : 32-40; discussion 34-8; quiz 41-2.p Abstract: Staphylococcus aureus and Enterococci have gained prominence as the causes of wound infections during this decade. Methicillin-resistant Staphylococcus aureus (MRSA) became commonplace in the United States during the 1980s. In Canada, infections with MRSA have been increasing in frequency since 1995. MRSA develops resistance by producing an altered penicillin-binding protein, PBP 2a, coded for by the mecA gene. Vancomycin is the usual drug of choice. Recently, strains with intermediate resistance to vancomycin (VISA) have been isolated from patients in Japan and the United States. Interim guidelines for their control have been developed by the Centers for Disease Control. Enterococci have developed a resistance to a variety of antimicrobials during the past three decades, including beta-lactams and aminoglycosides. Recently, strains resistant to vancomycin (VRE) have been found in the United States and Canada. They are particularly difficult to treat, although some success has been achieved with experimental drugs. These microorganisms have the ability to escape control by antimicrobials almost as soon as they are developed. Thus, we must practice good infection control and reserve antimicrobials only for clear cases of infection if we are to prevent or delay the emergence of resistance.

Devyatyarova-Johnson M. et al. *The lipopolysaccharide structures of Salmonella enterica serovar Typhimurium and Neisseria gonorrhoeae determine the attachment of human mannose-binding lectin to intact organisms.* Infect Immun. 2000; 68(7) : 3894-9.p Abstract: Mannose-binding lectin (MBL) is an important component of the innate immune system. It binds to the arrays of sugars commonly presented by microorganisms and activates the complement system independently of antibody. Despite detailed knowledge of the stereochemical basis of MBL binding, relatively little is known about how bacterial surface structures influence binding of the lectin. Using flow cytometry, we have measured the binding of MBL to a range of mutants of Salmonella enterica serovar Typhimurium and Neisseria gonorrhoeae which differ in the structure of expressed lipopolysaccharide (LPS). For both organisms, the possession of core LPS structures led to avid binding of MBL, which was abrogated by the addition of O antigen (Salmonella serovar Typhimurium) or sialic acid (N. gonorrhoeae). Truncation of the LPS within the core led to lower levels of MBL binding. It was not possible to predict the magnitude of MBL binding from the identity of the LPS terminal sugar alone, indicating that the three-dimensional disposition of LPS molecules is probably also of importance in determining MBL attachment. These results further support the hypothesis that LPS structure is a major determinant of MBL binding.

Dezateux C. et al. *Oral non-steroidal anti-inflammatory drug therapy for cystic fibrosis.* Cochrane Database Syst Rev. 2000; (2) : CD001505.p Abstract: BACKGROUND: Maintenance of optimal lung function is an important therapeutic goal in cystic fibrosis as it is lung damage that, in the long term, is responsible for most premature death among affected people. It has been hypothesised that lung damage results from inflammation and that prolonged use of non-steroidal anti-inflammatory drugs may prevent progressive pulmonary deterioration and respiratory morbidity in cystic fibrosis. It is thus important to establish the current level of evidence about the potential benefits and harms of treatment with non-steroidal anti-inflammatory drugs. OBJECTIVES: The aim of this systematic review is to assess the effectiveness of treatment with non-steroidal anti-inflammatory agents in cystic fibrosis. SEARCH STRATEGY: Trials were ascertained from the Cochrane Cystic Fibrosis and Genetic Disorders Specialised Register of Controlled Trials which includes published and unpublished trials identified through electronic data-

bases such as Medline and Embase as well as those identified from handsearching of journals and conference proceedings. Pharmaceutical companies manufacturing non-steroidal anti-inflammatory drugs were also contacted to identify any trials of non-steroidal anti-inflammatory drugs in cystic fibrosis. Date of the most recent search of the Group's specialised register: November 1999. SELECTION CRITERIA: All randomised or pseudorandomised controlled trials, published and unpublished, comparing non-steroidal anti-inflammatory drugs, administered orally at any dose for a period of at least two months, to placebo in patients with cystic fibrosis. DATA COLLECTION AND ANALYSIS: The following outcomes were assessed: objective measures of lung function, nutritional status, radiological assessment of pulmonary involvement, use of intravenous antibiotics, hospital admissions, survival, frequency of major and minor adverse effects and compliance with therapy. MAIN RESULTS: Three trials involving 145 patients aged from five to 39 years with a maximum follow up of four years met the inclusion criteria. Methodological quality was deemed good or adequate in two. Two trials, both reporting effectiveness of ibuprofen in subjects with mild lung disease, were from the same centre and included some patients in common, while the third assessed piroxicam in subjects with more severe impairment of respiratory function. Variation in outcomes reported and their summary measures precluded calculation of pooled treatment estimates. Only one trial reported within-subject changes in pulmonary function and the findings of this trial suggested that there was a greater absolute annual decline in percentage predicted forced expiratory volume in one second among controls than among those treated with ibuprofen. In a post-hoc sub-group analysis this effect was confined to children aged five to 13 years. In addition, in this one trial long term use of high dose ibuprofen was associated with reduced intravenous antibiotic usage, improved nutritional and radiological pulmonary status. No major adverse effects were reported but the power of the trials to identify clinically important differences in the incidence of adverse effects was low. REVIEWER'S CONCLUSIONS: While there is preliminary evidence to suggest that non-steroidal anti-inflammatory drugs may prevent pulmonary deterioration in subjects with mild lung disease due to cystic fibrosis, currently their routine use cannot be recommended. Further trials are required to confirm that their use prevents pulmonary deterioration and is associated with improved nutritional status. Such trials should also address the age group of subjects most likely to benefit, the prevalence of important adverse effects and the optimal dosage schedule as well as any reduction in concomitant therapy. Multi-centre trials will add to the validity of findings by enhancing their generalisability. The question of whether anti-inflammatory treatment prevents lung damage in pre-symptomatic.

Dhar U. et al. *Clinical features, antimicrobial susceptibility and toxin production in Vibrio cholerae O139 infection: comparison with V. cholerae O1 infection*. Trans R Soc Trop Med Hyg. 1996; 90(4) : 402-5.p Abstract: We prospectively compared the clinical features of cholera due to Vibrio cholerae O1 and V. cholerae O139 in 242 men 18-60 years of age, with a history of diarrhoea of 24 h or less, and moderate or severe dehydration. The antimicrobial susceptibility of all of the V. cholerae strains isolated from these patients was determined, and in vitro cholera toxin production determined for 68 isolates. On admission, the 110 patients infected with V. cholerae O1 significantly more often had body temperature < 36 degrees C (85% vs. 66%, P < or = 0.05), faecal leucocyte count > 50/high power microscope field (40% vs. 12%), and lower mean faecal chloride content (94 vs. 103 mmol/L) than did the 132 patients infected with V. cholerae O139. Patients infected with V. cholerae O1 also initially had significantly higher median volumes of stool (13 vs. 11 mL per kg body weight per h), vomitus (1 mL/kg/h vs. nil), and intravenous fluid requirements (23 vs. 21 mL/kg/h). All V. cholerae O1 and O139 isolates were susceptible to ciprofloxacin, all but one were susceptible to doxycycline and erythromycin, and the majority of both serogroups were resistant to co-trimoxazole (95% and 97%, respectively). V. cholerae O1 and O139 susceptibilities differed for tetracycline (58% vs. 100%) and furazolidone (27% vs. 93%) (P < 0.001 in both cases). The amount of cholera toxin produced in vitro by strains of V. cholerae O1 and O139 was similar, and did not correlate with stool volume. The results demonstrated that V. cholerae O139 does not cause more severe, or more invasive, disease than V. cholerae O1, as had been previously suggested, but that clinically important differences in antimicrobial susceptibility do exist among strains isolated in Bangladesh.

Dhawan B. et al. *Incidence of Clostridium difficile infection: a prospective study in an Indian hospital*. J Hosp Infect. 1999; 43(4) : 275-80.p Abstract: Clostridium difficile is the commonest cause of hospital-acquired diarrhoea. A prospective study comprising of 156 patients and 54 healthy controls was undertaken to assess C. difficile associated diarrhoea (CDAD) incidence in an Indian hospital. Methods used included C. difficile culture and enzyme linked immunosorbent assay (ELISA) for Toxin A. Attempts were made to type isolates by antibiogram and SDS-PAGE. Of the 210 stool samples tested, 12 gave positive results in at least one assay. Of these, 11 were positive by the ELISA method, eight by culture, and seven by both methods. Neither the organisms nor the toxin was found in healthy controls or neonates. The average disease incidence of CDAD estimated by using both methods was 15%. Two antibiotypes of the isolates were obtained and of the isolates characterized by SDS-PAGE, two had identical patterns. This study shows that CDAD is an emerging problem in Indian hospitals. Monitoring should enable the development and implementation of policies and procedures that minimize the risk of this nosocomial pathogen.

Dhillon S.S. et al. *Pneumococcal bacteremia associated with an infected central venous catheter.* Chest. 2000; 117(5) : 1515-6.p Abstract: Pneumococcus (Streptococcus pneumoniae) bacteremia is a serious infection. Pneumococcus has never been implicated as a cause of a central venous catheter-related bacteremia. It has been isolated from the catheter tip only twice before, and in one case caused the infection of an infusion port device. We report case of a 41-year-old woman who developed pneumococcal bacteremia after 6 days of an indwelling central venous catheter. The catheter tip grew > 300 cfu of S pneumoniae by the roll-plate method described by Maki and colleagues. No other focus of infection could be found in this patient. To the best of our knowledge, this is the first reported case of pneumococcal bacteremia associated with an infected central venous catheter.

di Carlo I. et al. *Catheter fracture and cardiac migration: a rare complication of totally implantable venous devices.* J Surg Oncol. 2000; 73(3) : 172-3.p Abstract: Totally implantable venous device (TIVD) are widely used for the treatment of patients requiring long-term chemotherapy, total parenteral nutrition and fluid replacement. Until today, many kinds of complications have been reported in the literature. We report an unusual case of catheter fracture as a consequence of pinchoff syndrome, and discuss the potential methods to avoid this complication and its evolution.

Dias A.P. et al. *Clinical, microbiological and ultrastructural features of angular cheilitis lesions in Southern Chinese.* Oral Dis. 1995; 1(1) : 43-8.p Abstract: OBJECTIVE: To obtain baseline data on angular cheilitis in Southern Chinese. DESIGN: A cross-sectional investigation of the clinical, microbiological and ultrastructural features of the condition. SUBJECTS AND METHOD: Thirty six Chinese adults with angular cheilitis; 28 controls matched for age and sex, with no inflammation. Clinical examination, swabs of lesions for microbiology, impressions of lesions for ultrastructure, using replica technique. MAIN OUTCOME MEASURES: Severity of lesions, associated signs and symptoms, incidence and type of microorganisms, ultrastructural features. RESULTS: Of a total 68 lesions 32 were bilateral and four unilateral. Forty four (65%) were mild (Type I) and the remaining 24 (35%) moderate (Type II). Infective agents were isolated from 37

(54%) lesions; pure growth of Candida spp and Staph. aureus was noted in nine lesions each; a mixed growth of the two in II, beta-haemolytic streptococci in three and a mixed flora including coliforms in the other five. Candida spp were present in one control, beta-haemolytic streptococci in two and coliforms in four others. Scanning electron microscopy revealed natural topography of the angular skin with sparse colonisation by bacteria and yeasts. CONCLUSIONS: Angular cheilitis in Southern Chinese seems to be characterised by a milder clinical presentation and classic infective agents of the disease: Candida spp and Staph. aureus.

Dias E.P. et al. *Congenital papillomas and papillomatoses associated with the human papilloma virus (HPV): report on 5 cases.* São Paulo med. j. 1995; 113(4) : 957-63.p Abstract: Introduçao: Os autores apresentam um estudo de cinco casos de papilomas e papilomatoses vulvares congênitas em neo e nati-mortos. Material e Métodos: O material utilizado foi proveniente de cinco necrópsias. A avaliaçao histopatológica mostrou aspectos sugestivos de infecçao pelo Pailomavirus humano (HPV). A microscopia eletrônica de três dos casos identificou partículas viróticas nucleares e citoplasmáticas variando de 40 a 60 nm, compatíveis com HPV. Resultados: O estudo imunohistoquímico destas lesoes demonstrou imunopositividade citoplasmática e nuclear. Conclusao: Os autores concluíram que a presença de partículas viróticas somada a imunopositividade em células escamosas, sao evidências do provável envolvimento etiológico do HPV nestas lesoes. (Au).

Dias J.C.d.A.R. et al. *Antimicrobial and mercury chloride resistance in vibrio isolates from marine fish of the southeastern brazilian region.* Rev. microbiol. 1995; 26(4) : 253-9.p Abstract: Foram analisadas 199 amostras de víbrios isolados de trato intestinal de peixes marinhos, representados pela tainha (Mugil sp.) e corvina (Micropogon sp.) capturados em águas de baía e da orla litor*f*nea da cidade do Rio de Janeiro, compreendendo V. anguillarum (52), V.haveyi (41), V. proteolyticus (39), V. campbelli (13) V. alginlyticus (10), V. splendidus (8), V. marinus (2), V.logei (1), V. parahaemolyticus (1) e Vibrio sp. - halofílico (32). O antibiograma, para oito drogas e o resistograma ao cloreto de merc£rio apontaram a taxa de 96,4 por cento para a presença de marcadores, congregando os percentuais de 77,0 por cento para a resistência antimicrobiana e de 21,8 por cento, para aquela associada ao Hg. A multirresistência (>ou = 3 marcos) foi significativa ($p<0,05$) na ordem de 71,0 por cento, bem como a incidência de fenótipo Hgr nas cepas multirresistentes (64,2 por cento), englobando apenas aquelas advindas do pescado corvina. Os marcos Su e Ap, além de Sm mostraram-se em destaque no cömputo gera e tambem no conjunto de amostras resistentes ao Hg. Indistintamente de espécie, a totalidade das culturas revelou a presença de pelo menos um marcador, excetuando V.parahaemolyticus. A conjugação de 28 amostras de víbrios com cepas de Escherichia coli K12 revelou a transferência de marcadores em 71,4 por cento dos experimentos. Transconjugantes para Su, Sm, Km e Ap foram observados a partir das culturas doadoras de V.anguillarum e V.harveyi. Não foram isoladas colânias transconjugantes para o marco Hg. Os resultados indicam a associação entre esses dois marcadores nas amostras de víbrios, possivelmente, em consequência do processo de evolução dos marcadores de resistência no bioma marinho.

Dickerson L.M. et al. *The pharmacist's role in promoting optimal antimicrobial use.* Pharmacotherapy. 2000; 20(6) : 711-23.p Abstract: Optimal use of antimicrobials is essential in the face of escalating antibiotic resistance, and requires cooperation from all sectors of the health care system. Although antibiotic-restriction policies in the hospital setting are important in altering microbial susceptibility patterns, an overall reduction in antibiotic prescriptions in the outpatient setting is more likely to significantly impact antibiotic resistance. Education of providers, application of clinical practice guidelines, audit and feedback activities, and multifaceted interventions all have had an effect in altering antibiotic prescribing in a research setting. Clinicians must alter antibiotic prescribing for the treatment of infectious diseases, and patients must change their perception of the need for these drugs. Pharmacists can play a major role through clinician education and focused clinical services. With cooperation of health care teams, the effectiveness of available antibiotics may be sustained and the threat of resistance minimized.

Didier M.E. et al. *Total nutrient admixtures appear safer than lipid emulsion alone as regards microbial contamination: growth properties of microbial pathogens at room temperature.* JPEN J Parenter Enteral Nutr. 1998; 22(5) : 291-6.p Abstract: BACKGROUND: The extraordinary growth properties of most microorganisms in 10% and 20% lipid emulsions has led to the Centers for Disease Control and Prevention recommendation that if lipids are given through an i.v. line, the administration set should be replaced every 24 hours rather than the usual 72-hour interval used for crystalloid solutions, including those used for conventional total parenteral nutrition. For nearly 15 years, parenteral alimentation has been given as a total nutrient admixture (TNA), with the glucose, amino acids, and lipid mixed within the same bag and infused continuously over 24 hours. METHODS: We prospectively studied in a representative TNA (17.6% glucose, 5% amino acids, 4% lipid; pH 5.6, osmolality 1778) and in a control solution, 5% dextrose-in-water (D5%/W), the growth properties at 4, 25, and 35 degrees C of three isolates each of Staphylococcus epidermidis, Staphylococcus aureus, Enterobacter cloacae, Klebsiella oxytoca, Serratia marcescens, Acinetobacter calcoaceticus, Stenotrophomonas maltophilia, Pseudomonas aeruginosa, Burkholderia cepacia, Flavobacterium spp, and Candida albicans, and two isolates of Staphylococcus saprophyticus, the species that are most likely to contaminate TNA during preparation or administration and that have been implicated in >95% of all outbreaks and sporadic cases of nosocomial bloodstream infections traced to contaminated parenteral admixtures reported in the world literature. RESULTS: Growth in TNA at 25 and 35 degrees C occurred with only two species, C. albicans and S. saprophyticus, and only after 24 to 48 hours; D5%/W allowed growth at 25 degrees C of two gram-negative species, S. marcescens and B. cepacia. CONCLUSIONS: We conclude that TNA is a poor growth medium for most nosocomial pathogens and is no better than D5%/W. The need to replace administration sets every 24 hours with TNA should be reconsidered and ideally be studied in a prospective randomized trial.

Dieckhaus K.D. et al. *Infection control concepts in critical care.* Crit Care Clin. 1998; 14(1) : 55-70.p Abstract: Patients with critical illnesses requiring aggressive medical intervention are at risk of acquiring serious nosocomial infection that may lead to increases in medical expenditures, morbidity, and mortality. Infection control in this population entails continuous surveillance for hospital-acquired infection, with investigation of outbreaks. Policies for effective antibiotic utilization, disinfection of medical devices and hospital environment, and patient isolation may limit nosocomial infection in this population. Finally, an effective infection control program should protect the health care worker from hospital-acquired infections through educational programs, routine health surveillance, vaccinations, and post-exposure care.

Diekema D.J. et al. *Antimicrobial activity of gatifloxacin compared to seven other compounds tested against gram-positive organisms isolated at 10 cancer-treatment centers.* Diagn Microbiol Infect Dis. 1999; 34(1) : 37-43.p Abstract: Gram-positive bacterial pathogens are important causes of disease in cancer patients and are becoming increasingly resistant to available antimicrobial agents. We examined the in vitro activity of gatifloxacin, a new fluoroquinolone, compared with other quinolones, ceftazidime, and traditional Gram-positive-active agents tested against pathogens isolated from patients at 10 cancer treatment hospitals in the United States. A total of 1,128 Gram-positive isolates were tested by the E-test method (AB BIODISK, Solna, Sweden) with results validated by concurrent quality control strain analysis. Gatifloxacin was more potent than either ciprofloxacin or levofloxacin against all Gram-positive species. Vancomycin was the most

active agent tested against all species except Bacillus spp., which were more susceptible to the fluoroquinolones. When tested against these Gram-positive pathogens from patients with cancer, the spectrum of gatifloxacin was also greater than that of levofloxacin and ciprofloxacin. Gatifloxacin may have a role as part of prophylactic or therapeutic antimicrobial regimens for selected cancer patients with Gram-positive infections.

Diekema D.J. et al. *Trends in antimicrobial susceptibility of bacterial pathogens isolated from patients with bloodstream infections in the USA, Canada and Latin America. SENTRY Participants Group.* Int J Antimicrob Agents. 2000; 13(4) : 257-71.p Abstract: From January through June of 1998, 4579 bloodstream infections (BSI) due to bacterial pathogens were reported from SENTRY hospitals in Canada, the USA and Latin America. Staphylococcus aureus, Escherichia coli, and coagulase-negative staphylococcus (CoNS) were the most common pathogens, together accounting for 55.2% of all BSI during this time period. Compared with the 5794 BSI reported from SENTRY from January through June of 1997, no major change was seen in the frequencies of occurrence of the most common bacterial causes of BSI. Between 1997 and 1998, the major change in antimicrobial resistance was an increase in oxacillin-resistance in both S. aureus and CoNS in all regions. These data demonstrate widespread antimicrobial resistance in Canada, Latin America and the USA, with a notable increase in oxacillin-resistance among staphylococci. Ongoing surveillance remains essential, and will enhance efforts to limit the scope of this worldwide problem.

Diekema D.J. et al. *Survey of bloodstream infections due to gram-negative bacilli: frequency of occurrence and antimicrobial susceptibility of isolates collected in the United States, Canada, and Latin America for the SENTRY Antimicrobial Surveillance Program, 1997.* Clin Infect Dis. 1999; 29(3) : 595-607.p Abstract: During 1997, a total of 4,267 nosocomial and community-acquired bloodstream infections due to gram-negative organisms were reported from SENTRY hospitals in Canada (8 sites), the United States (30 sites), and Latin America (10 sites). Escherichia coli was the most common isolate (41% of all gram-negative isolates), followed by Klebsiella species (17.9%), Pseudomonas aeruginosa (10.6%), and Enterobacter species (9.4%). For all gram-negative isolates combined, the most active antimicrobials tested were meropenem, imipenem, and cefepime. The quinolones levofloxacin (MIC90, 2 microg/mL), ciprofloxacin (MIC90, 1 microg/mL), gatifloxacin (MIC90, 2 microg/mL), sparfloxacin (MIC90, 2 microg/mL), and trovafloxacin (MIC90, 2 microg/mL) were also active against most isolates. Bloodstream infection isolates from Latin America were uniformly more resistant to all classes of antimicrobial agents tested than were isolates from Canada or the United States. Resistance phenotypes consistent with extended-spectrum beta-lactamase production were also most common among E. coli and Klebsiella species from Latin America. Further investigation of the reasons for regional differences in resistance patterns is needed, as is ongoing surveillance to detect resistance trends and to guide antimicrobial use.

Digrak M. et al. *Antimicrobial activities of several parts of Pinus brutia, Juniperus oxycedrus, Abies cilicia, Cedrus libani and Pinus nigra.* Phytother Res. 1999; 13(7) : 584-7.p Abstract: In this study, the antimicrobial activities of several parts of various trees grown in the Kahramanmaras region of Turkey were investigated by the disc diffusion method. Chloroform, acetone and methanol extracts of leaves, resins, barks, cones and fruits of Pinus brutia Ten., Juniperus oxycedrus L., Abies cilicia Ant. & Kotschy Carr., Cedrus libani A. Rich. and Pinus nigra Arn. were prepared and tested against Bacillus megaterium DSM 32, Bacillus subtilis IMG 22, Bacillus cereus FMC 19, Escherichia coli DM, Klebsiella pneumoniae FMC 3, Enterobacter aerogenes CCM 2531, Staphylococcus aureus Cowan 1, Mycobacterium smegmatis RUT, Proteus vulgaris FMC 1, Listeria monocytogenes Scoot A, Pseudomonas aeruginosa DSM 5007, Candida albicans CCM 314, Candida tropicalis MDC 86 and Penicillium italicum K. The results showed that antifungal effects were not observed for the whole extracts, E. coli was not inhibited by any of the plant extracts except by the chloroform and acetone extracts of the leaves of A. cilicia, which showed inhibition zones of 16-18 mm, respectively. All the plant extracts used in this study inhibited the development of the other bacteria studied. When the results of this study were compared with an ampicillin standard, it was found that the microorganisms studied were generally susceptible, intermediate or resistant to the extracts of species when compared with the ampicillin standard. On the other hand, the acetone and methanol extracts of Juniperus fruits were found to be quite resistant. Copyright 1999 John Wiley & Sons, Ltd.

Dinc L. et al. *The effectiveness of an educational intervention in changing nursing practice and preventing catheter-related infection for patients receiving total parenteral nutrition.* Int J Nurs Stud. 2000; 37(5) : 371-9.p Abstract: Catheter-related infections are one of the most serious complications of TPN therapy. Nurses have important responsibilities in the care of patients who are receiving TPN. This quasi-experimental study was conducted for the purpose of investigating the effectiveness of an educational intervention on changing nursing practice and preventing catheter-related infections in patients receiving total parenteral nutrition. The nurses' practice and the colonisation rate of control and comparative group patients in the surgical clinics of Hacettepe University Hospital (Turkey), and related variables were examined before and after an educational intervention. The findings of the study indicate that the intervention was successful in improving appropriate nursing practice, mean scores of nurses' practices were 45.7 before and 66.5 after the intervention ($p<0.05$). The rate of microorganism colonisation was also decreased but statistical analysis demonstrated no association between nursing practices and microorganism colonisation of catheter cultures.

Diniz C.G. et al. *Effect of metronidazole on the pathogenicity of resistant Bacteroides strains in gnotobiotic mice.* Antimicrob Agents Chemother. 2000; 44(9) : 2419-23.p Abstract: Metronidazole is widely used to treat protozoan and fungal infections. As an antibacterial drug, it is used mainly against anaerobes. Among anaerobes, the Bacteroides fragilis group is the most relevant in terms of frequency of recovery and antimicrobial resistance patterns. The use of metronidazole and other antimicrobial drugs induces morphological changes in this bacterial group. The present study investigated in vivo if these morphological modifications were accompanied by changes in virulence patterns by using germfree mice experimentally challenged with metronidazole-resistant Bacteroides strains before and after exposure to metronidazole. It was observed that metronidazole-resistant strains were more virulent after contact with the drug, as demonstrated by anatomicopathologic data for spleen, liver, and small intestine samples. These results suggest that long-term therapy and high metronidazole concentrations could interfere with microbial pathogenicity, resulting in changes to host-bacterium relationships.

Diouf M.L. et al. *[Hepatic tuberculosis of the pseudotumoral form].* Dakar Med. 1999; 44(1) : 123-5.p Abstract: The authors report a case of a 30 years old immunocompetent woman with liver tuberculosis with an unusual pseudotumoral presentation and secondary occurrence of abcedation with cutaneous fistulization. The diagnosis was based on the bacteriological positivity for acido-alcoolo resistant bacillus in pus of the abscess obtained by ponction guided by ultrasonographic examination. The authors emphasize in the differential diagnosis with the other causes of liver abscess (amibiasis and pyogenic microorganisms) and liver carcinoma. They also note the importance of the function guided by ultrasonographic examination permitting histologic and bacte+eriologic study in the diagnosis of this unusual presentation of liver tuberculosis. The patient was treated by antibacillary antibiotics and evacuation function. The prognostic was good with 6 months of follow-up.

DiPersio J.R. et al. *Fluoroquinolone-resistant Moraxella catarrhalis in a patient*

with pneumonia: report from the SENTRY Antimicrobial Surveillance Program (1998). Diagn Microbiol Infect Dis. 1998; 32(2) : 131-5.p Abstract: Fluoroquinolone resistance in Moraxella catarrhalis isolates has been quite rare. This report presents a case history of a 22-year-old man with compromised immune status and severe pneumonia caused by M. catarrhalis. The organism was markedly resistant (MICs, 1.5- > 32 micrograms/mL) to several marketed fluoroquinolones including the agent (levofloxacin) used for concurrent and prior therapy. The emergence of this problematic strain seems related to chronic exposure of the patient to compounds in the class and poor patient compliance to prescribed medications. The strain was not clonally related to other M. catarrhalis strains isolated in the same hospital during early 1998. This second documented case of a fluoroquinolone-resistant M. catarrhalis clinical isolate presents a warning that resistances can emerge in at-risk patients, and that surveillance systems (SENTRY) will be necessary to monitor for unusual organisms and spread of resistance phenotypes among commonly isolated respiratory tract pathogens.

DiPiro J.T. *Short-term prophylaxis in clean-contaminated surgery.* J Chemother. 1999; 11(6) : 551-5.p Abstract: Postoperative infections are not consistently controlled by current practice measures. From a recent study of 12,384 patients, postoperative infection occurred in 22% of colorectal procedures and 25% of upper gastrointestinal procedures. Infections were associated with a higher death rate, longer hospitalization, and more intense post-discharge care. Control of infections for clean-contaminated procedures requires effective bowel cleansing when appropriate, meticulous surgical technique, and timely antimicrobial administration. Many patients undergoing clean-contaminated surgery do not receive properly timed antimicrobials. Although the comparative value of oral (neomycin and erythromycin) or parenteral antimicrobials for colon surgery remains an unresolved issue, the combination can be beneficial for many colorectal operations. Third generation cephalosporins are not consistently more effective than older agents such as cefoxitin and increase bacterial resistance. Improper antimicrobial timing is one of the most common problems with surgical prophylaxis and is fully under the control of the surgeon. To maximize benefits of antimicrobial prophylaxis, systems should be devised to assure timely administration.

Diz J.C. et al. *Reciprocating tachycardia during central venous cannulation in a patient with Wolff-Parkinson-White syndrome.* Acta Anaesthesiol Scand. 2000; 44(5) : 630-2.p Abstract: Wolff-Parkinson-White syndrome is important for the anesthesiologist because the sudden development of tachyarrhythmias may result in deleterious hemodynamic changes. We describe an episode of reciprocating tachycardia triggered by the insertion of the guide wire during central venous cannulation in a patient with this syndrome.

Djajakusumah T. et al. *Plasmid patterns and antimicrobial susceptibilities of Neisseria gonorrhoeae in Bandung, Indonesia.* Trans R Soc Trop Med Hyg. 1998; 92(1) : 105-7.p Abstract: Antimicrobial susceptibilities of Neisseria gonorrhoeae isolates from female sex workers and from men with urethritis in Bandung, Indonesia, were determined by an agar dilution technique. Typing of the Tet M plasmid in tetracycline-resistant isolates (TRNG) was performed using a polymerase chain reaction (PCR) technique and plasmid profiles of penicillinase-producing isolates (PPNG) were determined. All PPNG possessed the 4.4 MDa beta-lactamase plasmid and all TRNG showed a PCR fragment characteristic of the 'Dutch' type Tet M plasmid. Of the 50 gonococci isolates tested, all were resistant to tetracycline; 47 were TRNG, 26 were PPNG, and 6 were resistant to thiamphenicol. Chromosomal resistance to penicillin was not detected. All isolates were susceptible to ceftriaxone, ciprofloxacin, norfloxacin, ofloxacin, kanamycin, spectinomycin, and trimethoprim/sulfamethoxazole. Spectinomycin and fluoroquinolones are useful primary drugs for treatment of gonococcal infection in Bandung. Continued surveillance of antimicrobial resistance should be part of gonorrhoea control in Indonesia.

Dmitrieva N.V. et al. *[The microbiological aspects of infectious complications in the oncology clinic].* Antibiot Khimioter. 1999; 44(10) : 16-9.p Abstract: At present 10 to 30 per cent of the microbial strains from cancer patients are problem ones: oxacillin resistant strains of Staphylococcus aureus, coagulase negative strains of Staphylococcus spp., aminoglycoside resistant strains of Escherichia coli, 3rd generation cephalosporin resistant strains of Klebsiella spp. and fungi of Candida which requires development of more rational approaches to antibacterial chemotherapy and prophylaxis of infectious complications. The infectious processes in the cancer patients proved to be highly polyetiological. Therefore, the study is significant for epidemiologic and therapeutic measures. Such an analysis in oncological clinic should be regular.

Dmitrieva N.V. et al. *[A trial of the use of mupirocin in the nasal carriage of Staphylococcus aureus in medical personnel].* Antibiot Khimioter. 2000; 45(3) : 35-8.p Abstract: Many hospital-acquired purulent diseases and wound infections are due to multiresistant hospital strains of Staphylococcus aureus. The role of S. aureus nasal carriage in development of wound infections due to autoinfection is confirmed. Not only inpatients but also hospital staff can be highly colonized with coagulase positive staphylococci. The S. aureus persistence in hospital personnel results in distribution of the microorganisms in the environment. Therefore, detection of S. aureus carriers without signs of the infection among the hospital personnel and eradication of the pathogen make it possible to control outbreaks of S. aureus infection in hospitals. Clinical efficacy of nasal ointment of mupirocin in the treatment of S. aureus carriers among the intensive care personnel of the N. N.Blokhin Cancer Research Center was evaluated. S. aureus nasal carriage was diagnosed in 17 (26 per cent) out of 65 persons. All the isolates were susceptible to oxacillin. 5-7 days after discontinuation of the mupirocin nasal ointment use eradication of S. aureus was stated in 100 per cent of the cases. The effect was still observed in 94 per cent of the cases in 1 month, in 76 per cent of the cases in 5-6 months and in 60 per cent of the cases in 8-9 months. It is believed that mupirocin nasal ointment (Bactroban) is convenient to use, low toxic and highly active in the treatment of persons with S. aureus nasal carriage.

Dobardzic R. et al. *The minimum inhibitory concentration of seventeen antimicrobials for Salmonella isolates from septic patients.* J Chemother. 1996; 8(5) : 369-74.p Abstract: Herein we are reporting, for the first time in Kuwait, the minimum inhibitory concentrations (MICs) of Salmonella blood culture isolates vs. 17 clinically relevant antimicrobial agents. The screening of blood culture specimens was performed with the most advanced Bactec 9240 (Becton Dickinson). From over 20,000 blood cultures, 112 Salmonella isolates were obtained from 67 patients. Their MICs were determined using the automated Vitek microdilution technique (Biomerieux Vitek Inc.). During the whole 1991-1995 study period, the MICs for cefotaxime, ceftazidime, aztreonam, amikacin, gentamicin, ciprofloxacin and imipenem were below their respective susceptibility breakpoints. Resistance to chloramphenicol, ampicillin and cotrimoxazole varied from year to year, from 18% to 50%, except in 1991 when it was nil (1991 was the first year after the Gulf War, with very few newcomers from the Indian subcontinent). All ampicillin-susceptible S. typhi isolates had extremely low MIC values (< or = 0.25 microgram/ml).

Doebbeling B.N. *The epidemiology of methicillin-resistant Staphylococcus aureus colonisation and infection.* J Chemother. 1995; 7 Suppl 3 : 99-103.p Abstract: Methicillin-resistant Staphylococcus aureus (MRSA) is an increasingly common nosocomial pathogen in health care facilities throughout the world. Overall, approximately two-thirds of nosocomial cases and outbreaks have occurred in critical care units. Major risk factors for colonisation and infection in nursing homes include age, underlying conditions, nasal colonisation and the presence of indwelling devices such as catheters, tracheostomies and nasogastric tubes. In general, patients with MRSA infections in

an acute care facility are more likely to have had a prolonged hospital stay, to have received prior antibiotics and to have severe underlying disease, than patients infected with methicillin-susceptible S. aureus. Risk factors for MRSA bacteraemia include: a higher frequency of severe underlying disease, poorer underlying prognosis, prior antibiotic therapy, prolonged hospitalisation, intravascular catheterisation, and intensive care unit location. Risk factors for developing MRSA postoperative wound infections include: prior antimicrobial therapy, prolonged hospitalisation and severity of underlying disease. Little data are available to identify specific risk factors for colonisation or infection of burn wounds by MRSA.

Doern G.V. *Antimicrobial resistance among lower respiratory tract isolates of Haemophilus influenzae: results of a 1992-93 western Europe and USA collaborative surveillance study. The Alexander Project Collaborative Group.* J Antimicrob Chemother. 1996; 38 Suppl A : 59-69.p Abstract: During 1992 and 1993, 2718 respiratory tract isolates of Haemophilus influenzae were obtained from two study centres in each of five West European countries and five study centres in the USA. beta-Lactamase production was assessed and MICs of 14 antimicrobial agents determined in a single co-ordinating laboratory using a broth microdilution method in Mueller-Hinton-lysed horse blood medium. The prevalence of strains producing beta-lactamase varied between 0 and 37.9%. In general, the highest prevalence was in study centres from Spain and the USA with slightly lower rates observed in France and the UK. Only a single confirmed beta-lactamase-negative, ampicillin resistant strain was recovered during the entire study. Erythromycin resistance, defined as an MIC of > or = 4.0 mg/L, was noted in 57.5% of isolates. Among the other antimicrobials tested, resistance rates > or = 1.0% were observed only with cefaclor (3.7%), chloramphenicol (1.4%) and co-trimoxazole (2.5%). In no case, was the prevalence of resistance or beta-lactamase production significantly greater in 1993 than in 1992.

Doern G.V. *Trends in antimicrobial susceptibility of bacterial pathogens of the respiratory tract*. Am J Med. 1995; 99(6B) : 3S-7S.p Abstract: Rates of antimicrobial resistance have been increasing in bacteria responsible for community-acquired lower respiratory tract infections in the United States. Nearly 100% of clinical isolates of Moraxella catarrhalis now produce beta-lactamase, an enzyme that renders this pathogen resistant to such agents as penicillin, ampicillin, and amoxicillin. However, this organism remains nearly uniformly susceptible to alternative oral antimicrobials, such as cephalosporins, macrolides, tetracyclines, beta-lactamase inhibitor combinations, and the combination of trimethoprim/sulfamethoxazole. The susceptibility of M. catarrhalis to these agents is not expected to change markedly in the next few years. A linear increase in the prevalence of beta-lactamase-mediated ampicillin resistance has been evident among isolates of nontypeable Haemophilus influenzae during the past decade in the United States. By the year 2000, 45-50% of isolates are likely to produce beta-lactamase. Although the susceptibility of this organism to alternative oral antimicrobials varies, rates of resistance to cefuroxime axetil, cefpodoxime, cefixime, azithromycin, and perhaps clarithromycin remain < 1%. The rate of penicillin resistance among isolates of Streptococcus pneumoniae, which has increased steadily in recent years, currently stands at approximately 25% in the United States and will likely reach 40-50% during the next 5-10 years. Because of cross-resistance, in general all beta-lactam antimicrobials have reduced activity against penicillin-resistant strains of S. pneumoniae. A 1994-1995 survey found that 3.4% of S. pneumoniae isolates were highly resistant to cefotaxime, and 4-8% were resistant to chloramphenicol, tetracycline, and the macrolides. Resistance to these antimicrobials has usually followed the emergence of penicillin resistance in other countries. Therefore, S. pneumoniae resistance to these drugs is expected to increase markedly during the next few years in the United States.

Doern G.V. et al. *Antimicrobial resistance of Streptococcus pneumoniae recovered from outpatients in the United States during the winter months of 1994 to 1995: results of a 30-center national surveillance study.* Antimicrob Agents Chemother. 1996; 40(5) : 1208-13.p Abstract: A total of 1,527 clinically significant outpatient isolates of Streptococcus pneumoniae were prospectively collected in 30 different U.S. medical centers between November 1994 and April 1995. Overall, 23.6% of strains were not susceptible to penicillin, with 14.1% intermediate and 9.5% high-level resistant. The frequencies of recovery of intermediate and high-level resistant strains varied considerably between different medical centers and in different geographic areas. In general, intermediate and high-level penicillin resistance was most common with isolates of S. pneumoniae recovered from pediatric patients. The in vitro activities of 22 other antimicrobial agents were assessed against this collection of isolates. Ampicillin was consistently 1 twofold dilution less active than penicillin. Amoxicillin and amoxicillin-clavulanate were essentially equivalent to penicillin in activity. The rank order of activity for cephalosporins was cefotaxime = ceftriaxone > or = cefpodoxime > or = cefuroxime > cefprozil > or = cefixime > cefaclor = loracarbef > cefadroxil = cephalexin. The National Committee for Clinical Laboratory Standards [Performance Standards for Antimicrobial Susceptibility Testing, Sixth Information Supplement (M100-S6), 1995] has established MIC breakpoints for resistance (i.e., > or = 2 micrograms/ml) with three cephalosporins versus S. pneumoniae, namely, cefotaxime, ceftriaxone, and cefuroxime. The overall percentages of strains resistant to these three antimicrobial agents were 3, 5, and 12, respectively. The overall frequency of resistance was 10% with all three macrolides examined in this study, clarithromycin, erythromycin, and azithromycin. The overall percentages of chloramphenicol, tetracycline, and trimethoprim-sulfamethoxazole resistance were 4.3, 7.5, and 18, respectively. The resistance percentages among the cephalosporins, macrolides, chloramphenicol, tetracycline, and trimethoprim-sulfamethoxazole were consistently higher among penicillin-intermediate strains than among susceptible isolates and even higher still among organisms expressing high-level penicillin resistance. Multiply resistant strains represented 9.1% of the organisms examined in this study. Finally, rifampin resistance was uncommon (i.e., 0.5%), and vancomycin resistance was not detected. The quinopristin-dalfopristin combination was consistently active at concentrations of 0.25 to 4 micrograms/ml, but rates of resistance could not be determined in the absence of established interpretive criteria for MIC results.

Doern G.V. et al. *Antimicrobial resistance with Streptococcus pneumoniae in the United States, 1997 98*. Emerg Infect Dis. 1999; 5(6) : 757-65.p Abstract: From November 1997 to April 1998, 1,601 clinical isolates of Streptococcus pneumoniae were obtained from 34 U.S. medical centers. The overall rate of strains showing resistance to penicillin was 29. 5%, with 17.4% having intermediate resistance. Multidrug resistance, defined as lack of susceptibility to penicillin and at least two other non-ss-lactam classes of antimicrobial drugs, was observed in 16.0% of isolates. Resistance to all 10 ss-lactam drugs examined in this study was directly related to the level of penicillin resistance. Penicillin resistance rates were highest in isolates from middle ear fluid and sinus aspirates of children ambulatory-care settings. Twenty-four of the 34 medical centers in this study had participated in a similar study 3 years before. In 19 of these 24 centers, penicillin resistance rates increased 2.9% to 39.2%. Similar increases were observed with rates of resistance to other antimicrobial drugs.

Doern G.V. et al. *Multicenter laboratory evaluation of the bioMerieux Vitek antimicrobial susceptibility testing system with 11 antimicrobial agents versus members of the family Enterobacteriaceae and Pseudomonas aeruginosa.* J Clin Microbiol. 1997; 35(8) : 2115-9.p Abstract: A four-center study in which a total of 1,082 recent clinical isolates of members of the family Enterobacteriaceae and Pseudomonas aeruginosa were examined versus 11 antimicrobial agents with the bioMerieux Vitek susceptibility test system (Hazelwood, Mo.) and the GNS-F6 card was conducted. In addition, a challenge set consisting of the same 200 organisms was examined in each of the four participating labo-

ratories. Results obtained with the Vitek system were compared to MICs determined by a standardized broth microdilution method. For purposes of comparison, susceptibility categories (susceptible, intermediate, or resistant) were assigned on the basis of the results of both methods. The result of the broth microdilution test was considered definitive. The total category error rate with the Vitek system and the recent clinical isolates (11,902 organism-antimicrobial comparisons) was 4.5%, i.e., 1.7% very major errors, 0.9% major errors, and 1.9% minor errors. The total category error rate calculated from tests performed with the challenge set (i.e., 8,800 organism-antimicrobial comparisons) was 5.9%, i.e., 2.2% very major errors, 1.1% major errors, and 2.6% minor errors. Very major error rates higher than the totals were noted with Enterobacter cloacae versus ampicillin-sulbactam, aztreonam, ticarcillin, and ticarcillin-clavulanate and with P. aeruginosa versus mezlocillin, ticarcillin, and ticarcillin-clavulanate. Major error rates higher than the averages were observed with Proteus mirabilis versus imipenem and with Klebsiella pneumoniae versus ofloxacin. Excellent overall interlaboratory reproducibility was observed with the Vitek system. The importance of inoculum size as a primary determinant in the accuracy of susceptibility test results with the Vitek system was clearly demonstrated in this study. Specifically, when an inoculum density fourfold higher than that recommended by the manufacturer was used, high rates of false resistance results were obtained with cell wall-active antimicrobial agents versus both the Enterobacteriaceae and P. aeruginosa.

Doern G.V. et al. *Prevalence of antimicrobial resistance among 723 outpatient clinical isolates of Moraxella catarrhalis in the United States in 1994 and 1995: results of a 30-center national surveillance study.* Antimicrob Agents Chemother. 1996; 40(12) : 2884-6.p Abstract: Seven hundred twenty-three isolates of Moraxella catarrhalis obtained from outpatients with a variety of infections in 30 medical centers in the United States between 1 November 1994 and 30 April 1995 were characterized in a central laboratory. The overall rate of beta-lactamase production was 95.3%. When the National Committee for Clinical Laboratory Standards MIC interpretive breakpoints for Haemophilus influenzae were applied, percentages of strains found to be susceptible to selected oral antimicrobial agents were as follows: azithromycin, clarithromycin, and erythromycin, 100%; tetracycline and chloramphenicol, 100%; amoxicillin-clavulanate, 100%; cefixime, 99.3%; cefpodoxime, 99.0%; cefaclor, 99.4%; loracarbef, 99.0%; cefuroxime, 98.5%; cefprozil, 94.3%; and trimethoprim-sulfamethoxazole, 93.5%.

Doern G.V. et al. *Emergence of high rates of antimicrobial resistance among viridans group streptococci in the United States.* Antimicrob Agents Chemother. 1996; 40(4) : 891-4.p Abstract: Three hundred fifty-two blood culture isolates of viridans group streptococci obtained from 43 U.S. medical centers during 1993 and 1994 were characterized. Included were 48 isolates of "Streptococcus milleri," 219 S. mitis isolates, 29 S. salivarius isolates, and 56 S. sanguis isolates. High-level penicillin resistance (MIC, > or = 4.0 micrograms/ml) was noted among 13.4% of the strains; for 42.9% of the strains, penicillin MICs were 0.25 to 2.0 micrograms/ml (i.e., intermediate resistance). In general, amoxicillin was slightly more active than penicillin. The rank order of activity for five cephalosporins versus viridans group streptococci was cefpodoxime = ceftriaxone > cefprozil = cefuroxime >> cephalexin. The percentages of isolates resistant (MIC, > or = 2 micrograms/ml) to these agents were 15, 17, 18, 20, and 96, respectively. The rates of resistance to erythromycin, tetracycline, and trimethoprim-sulfamethoxazole were 12 to 38%. Resistance to either chloramphenicol or ofloxacin was uncommon (i.e., < 1%). In general, among the four species, S. mitis was the most resistant and "S. milleri" was the most susceptible.

Doern G.V. et al. *Multicenter evaluation of the in vitro activity of six broad-spectrum beta-lactam antimicrobial agents in Puerto Rico. The Puerto Rico Antimicrobial Resistance Study Group.* Diagn Microbiol Infect Dis. 1998; 30(2) : 113-9.p Abstract: The minimum inhibitory concentrations of 6 broad-spectrum beta-lactam antimicrobial agents were determined by use of the Etest versus a total of 569 bacteria in 7 Puerto Rican hospital laboratories. These included 342 recent clinical isolates of Enterobacteriaceae, 63 Pseudomonas aeruginosa, 54 Acinetobacter species, and 110 oxacillin-susceptible staphylococci. Extended spectrum beta-lactamase production was noted among 11% of Klebsiella pneumoniae isolates. Hyperproduction of Amp C cephalosporinase was observed with > 20% of isolates of Enterobacter spp., Serratia spp., and Citrobacter freundii. The overall rank order of activity of the six beta-lactams examined in this study versus all clinical isolates was imipenem (95.8% susceptible) > cefepime (91.1%) > piperacillin/ tazobactam (82.3%) > cefotaxime (77.6%) > piperacillin (72.5%) > ceftazidime (67.0%).

Doern G.V. et al. *Haemophilus influenzae and Moraxella catarrhalis from patients with community-acquired respiratory tract infections: antimicrobial susceptibility patterns from the SENTRY antimicrobial Surveillance Program (United States and Canada, 1997).* Antimicrob Agents Chemother. 1999; 43(2) : 385-9.p Abstract: Between February and June of 1997, a large number of community-acquired respiratory tract isolates of Haemophilus influenzae (n = 1,077) and Moraxella catarrhalis (n = 503) from 27 U.S. and 7 Canadian medical centers were characterized as part of the SENTRY Antimicrobial Surveillance Program. Overall prevalences of beta-lactamase production were 33.5% in H. influenzae and 92.2% in M. catarrhalis with no differences noted between isolates recovered in the United States and those from Canada. Among a total of 21 different antimicrobial agents tested, including six cephalosporins, a beta-lactamase inhibitor combination, three macrolides, tetracycline, trimethoprim-sulfamethoxazole (TMP-SMX), rifampin, chloramphenicol, five fluoroquinolones, and quinupristin-dalfopristin, resistance rates of > 5% with H. influenzae were observed only with cefaclor (12.8%) and TMP-SMX (16.2%).

Doern G.V. et al. *Bacterial pathogens isolated from patients with skin and soft tissue infections: frequency of occurrence and antimicrobial susceptibility patterns from the SENTRY Antimicrobial Surveillance Program (United States and Canada, 1997). SENTRY Study Group (North America).* Diagn Microbiol Infect Dis. 1999; 34(1) : 65-72.p Abstract: As part of the SENTRY Antimicrobial Surveillance Program, 1562 bacterial isolates were recovered from hospitalized patients with skin and soft tissue infections (SSTIs) in 30 United States (U.S.) and 8 Canadian medical centers between October and December, 1997. The overall rank order of recovery of the six most common pathogens was Staphylococcus aureus (42.6%) > Pseudomonas aeruginosa (11.3%) > Enterococcus spp. (8.1%) > Escherichia coli (7.2%) > Enterobacter spp. (5.2%) > beta-hemolytic streptocci (5.1%). With one exception, essentially the same order was observed in both the U.S. and Canada. The single exception was the Enterococcus group, which were the third most common isolate in the U.S. (9.6%), but the seventh most common isolate in Canada (3.7). Of note, 24.0% of S. aureus isolates were oxacillin resistant; vancomycin was uniformly active. Vancomycin resistance among Enterococcus spp. (16.5%) was observed only in the U.S. Several antimicrobial agents remained broadly active for SSTI isolates of P. aeruginosa, including meropenem, amikacin, tobramycin, and piperacillin with or without tazobactam. Imipenem resistance (MICs, > or = 8 micrograms/mL) was observed in 11.9% of isolates of P. aeruginosa and ceftazidime, and cefepime had equivalent activity (85.2% and 85.8% susceptible, respectively). Numerous beta-lactams, aminoglycosides and fluoroquinolones were broadly active against E. coli SSTI isolates (i.e. < 5% resistance). Extended-spectrum beta-lactamase production was uncommon both with E. coli and Klebsiella spp. in both nations. Cefepime, imipenem, and meropenem; the aminoglycosides; and fluoroquinolones were conspicuously more active against Enterobacter spp. than other agents tested. High-level, stably derepressed Amp C beta-lactamase production was commonly observed in this group (26.8%), but cefepime generally retained activity against these ceftazidime-resistant organisms. The results of this study

serve to define the most common bacterial causes of SSTIs in North America, elucidate patterns of antimicrobial resistance and can be used as a basis for making initial empiric antimicrobial management decisions in hospitalized patients with such infections.

Doern G.V. et al. *The prevalence of fluoroquinolone resistance among clinically significant respiratory tract isolates of Streptococcus pneumoniae in the United States and Canada—1997 results from the SENTRY Antimicrobial Surveillance Program*. Diagn Microbiol Infect Dis. 1998; 32(4) : 313-6.p Abstract: As part of the SENTRY antimicrobial resistance surveillance program, a total of 1100 clinically significant respiratory tract isolates of Streptococcus pneumoniae were tested for susceptibility to six fluoroquinolone antimicrobial agents: ciprofloxacin, levofloxacin, gatifloxacin, grepafloxacin, sparfloxacin, and trovafloxacin. Isolates were obtained during the 5-month period, February to June, 1997 from 27 United States medical center laboratories and seven laboratories in Canadian health care institutions. All testing was performed in a single center. Of 1100 test strains, 3 (0.3%), all from different U.S. centers, were fluoroquinolone resistant. Among the remaining 1097 fluoroquinolone-susceptible isolates, the rank order of activity among the six agents tested in this study was grepafloxacin (modal MIC = 0.25 microgram/mL) = trovafloxacin (modal MIC = 0.25 microgram/mL) = sparfloxacin (0.25 microgram/mL) > gatifloxacin (0.5 microgram/mL) > levofloxacin (1 microgram/mL) = ciprofloxacin (1 microgram/mL). Fluoroquinolone resistance is currently uncommon among respiratory tract isolates of S. pneumoniae in North America, but there exist clear differences between the in vitro activities of different fluoroquinolones for this organism.

Doern G.V. et al. *Prevalence of antimicrobial resistance among respiratory tract isolates of Streptococcus pneumoniae in North America: 1997 results from the SENTRY antimicrobial surveillance program*. Clin Infect Dis. 1998; 27(4) : 764-70.p Abstract: As part of the ongoing multinational SENTRY antimicrobial resistance surveillance program, a total of 1,047 respiratory tract isolates of Streptococcus pneumoniae, 845 from 27 United States medical centers and 202 from seven Canadian institutions, were collected between February and June 1997 and characterized in a central laboratory. In the United States, the overall percentages of penicillin-intermediate strains and strains with high-level resistance to penicillin were 27.8% and 16.0%, respectively. In Canada, these values were 21.8% and 8.4%, respectively. Among the 31 centers in the United States and Canada that contributed at least 19 isolates, the combined rate of intermediate plus resistant strains varied between 24.0% and 67.8%. The in vitro activity of 19 other antimicrobials was assessed against all study isolates. Overall rates of resistance among selected agents in the United States and Canada, respectively, were as follows: amoxicillin, 18.1% and 10.5%; cefaclor, 38.3% and 26.2%; cefuroxime, 19.5% and 12.9%; cefpodoxime, 18.6% and 11.4%; cefepime, 8.2% and 4.5%; cefotaxime, 4.0% and 3.0%; macrolides (i.e., erythromycin, azithromycin, and clarithromycin), 11.7%-14.3% and 5.0%-7.4%; clindamycin, 3.5% and 3.5%; chloramphenicol, 3.9% and 4.0%; tetracycline, 10.2% and 10.9%; and trimethoprim-sulfamethoxazole, 19.8% and 15.8%.

Dohar J.E. et al. *In vitro susceptibility of aural isolates of Pseudomonas aeruginosa to commonly used ototopical antibiotics.* Am J Otol. 1996; 17(2) : 207-9.p Abstract: The choice of antimicrobial agents used to treat Pseudomonas aeruginosa infections of the ear is quite empiric. Yet in spite of this, very little has been published examining susceptibility patterns of aural isolates of P. aeruginosa. Recently, increasing concern has emerged over the development of resistance to many of the commonly used ototopical preparations with activity against P. aeruginosa. This concern stems from the fact that these preparations have been in use for a long time, and P. aeruginosa is known to develop resistance fairly readily. We prospectively studied the susceptibilities of aural isolates of P. aeruginosa in 231 consecutive children who were seen in the outpatient Pediatric Otolaryngology Department at Children's Hospital of Pittsburgh during the years 1992 and 1993. The agents tested included neomycin, polymyxin B, colistin, and norfloxacin. We found that only 17.8% of the isolates were sensitive to neomycin, as opposed to > 95% for each of the other agents tested (polymyxin B, 99.6%; colistin, 97.4%; and norfloxacin, 98.3%). This difference proved to be statistically significant ($p < 0.05$). Given the concern of aminoglycoside-induced ototoxicity and the high rate of neomycin resistance, we believe that further investigation of other alternative ototopic agents with activity against P. aeruginosa is warranted.

Dollman A. et al. *Consenso Latino-Americano sobre infecções em bronquite crônica*. Rev. bras. clin. ter. 1997; 23(4) : 132-44.p Abstract: Infecções bacterianas crônicas ou de repetição dão início e perpetuam o ciclo vicioso de lesão das vias aéreas através da estimulação dos mecanismos inflamatórios, desencadeada pelos produtos bacterianos e pela invasão bacteriana recorrente. As exacerbações agudas de bronquite crônica(EABC) são caracterizadas por quadro abrupto de tosse,aumento da dispnéia e aumento no volume de escarro produzido. Em dois terços ou mais dos casos típicos de EABC são isolados patógenos bacterianos. O patógeno predominante é o H. influenzae, o qual se encontra nitidamente associado ao círculo vicioso de inflamação e infecção de repetição. Entre outros patógenos comumente encontrados se incluem Moraxella catarrhalis, muitas das quais resistentes s aminopenicilinas devido à produção de á-lactamase e, também, Streptococcus pneumoniae, em relação aos quais se tem observado aumento no número de cepas resistentes à penicilina e macrolídeos, em ƒmbito mundial...(AU).

Domin M.A. *Highly virulent pathogens—a post antibiotic era?* Br J Theatre Nurs. 1998; 8(2) : 14-8.p Abstract: The spectrum of infectious diseases is changing rapidly. Emerging infectious agents present an intriguing constellation of nosocomial challenges. Antimicrobial resistance results in increased morbidity, mortality and costs of health care. Resistance to antimicrobial agents has been recorded since 1940 with penicillin resistant Escherichia coli (E coli) (Abraham and Chain 1940). A similar pencillin resistance was reported in 1944 in Staphylococus aureus (S. aureus) (Kirby 1944) Even before the widespread global use of penicillin, resistance had already been detected in both gram-positive and gram-negative organisms. The 1990s herald the era of multiple drug resistance. To grasp further the enormity and complexity of our modern antimicrobial resistance problem, one only needs to think about how many—how fast—and in how many settings (hospitals, clinics, outpatients nursing and long term facilities, etc), these pathogens have developed antimicrobial resistance: Multiple drug-resistant Mycobacterium tuberculosis, penicillin-resistant Streptococcus pneumonia, fluconzole-resistant Candida, methicillin-resistant S. aureus (MRSA), vancomycin-resistant Enterococci (VRE) and now S. aureus with reduced susceptibility to vancomycin. Given the dramatic increase in the incidence of multiple drug-resistant organisms—and now—the mounting evidence of resistance transfer from one organism to another, we will certainly witness a combined growth of nosocomial pathogens, for which there are no antibiotic solutions. Appropriate infection control measures for such resistant strains depend, in part, on the mechanisms of genetic information exchanged among micro-organisms. Clearly we need to strengthen the basic tenets of infection prevention and control; hygiene, engineering and microbial barriers, to prevent transinfection. We need to control horizontal nosocomial transmission of organisms. Contaminated environmental surfaces are a reservoir for resistant organisms such as MRSA (Boyce et al 1997) and VRE (Karanfil et al 1992). Stringent infection control policies need to be developed and implemented. A comprehensively applied infection control programme will reduce the dissemination of resistant strains. Each patient care setting must examine its current practices and review the outcome efficacy. A consensus development conference to develop centres for disease control (CDC) formal guidelines against vancomycin intermediate-level resistant staphylococcus aureus (VISA) and vancomycin-resistant staphylococcus aureus (VRSA) may take a year or more to convene. This paper will

examine the basic considerations currently offered by the CDC which may be valuable starting points for the enhancement of current infection control practices. Perspectives of the Society for Healthcare Epidemiology of America (SHEA) will also be included.

Dominguez M.A. et al. *Antibiotic resistance in respiratory pathogens.* Curr Opin Pulm Med. 1998; 4(3) : 173-9.p Abstract: Antibiotic resistance in respiratory pathogens has dramatically increased during recent years. Resistance to penicillin and multiple antimicrobial agents in pneumococci and resistance to ampicillin in Moraxella catarrhalis and Haemophilus influenzae, as a result of betalactamase production, have become highly prevalent worldwide. The emergence of multiple drug-resistant tuberculosis in different countries is of concern, and has become a therapeutic challenge.

Donskey C.J. et al. *A polyclonal outbreak of predominantly VanB vancomycin-resistant enterococci in northeast Ohio. Northeast Ohio Vancomycin-Resistant Enterococcus Surveillance Program.* Clin Infect Dis. 1999; 29(3) : 573-9.p Abstract: We studied the molecular epidemiology of vancomycin-resistant enterococci (VRE) isolated in northeast Ohio during 1996 and examined the association between isolation of VRE from samples other than stool and antimicrobial purchases for five Cleveland hospitals. Susceptibility testing and pulsed-field gel electrophoresis were used to analyze 363 isolates from individual patients from 13 hospitals. Susceptibility testing indicated that 287 strains (79%) expressed the VanB phenotype and 76 (21%) expressed the VanA phenotype. The outbreak was polyclonal, with 30 total genotypes. Both VanA and VanB VRE demonstrated multiple genotypes. One genotype was present in all hospitals, suggesting spread between hospitals. For five teaching hospitals, rates of isolation from non-stool sources and from blood correlated positively with purchases of ticarcillin/clavulanic acid (P =.005). In summary, this outbreak demonstrates transmission of VRE between several hospitals in a geographic region and suggests that use of certain beta-lactam antibiotics may be associated with an increased prevalence of VRE.

Dore M.P. et al. *Effect of pretreatment antibiotic resistance to metronidazole and clarithromycin on outcome of Helicobacter pylori therapy: a meta-analytical approach.* Dig Dis Sci. 2000; 45(1) : 68-76.p Abstract: Our purpose was to define the effect of pretreatment Helicobacter pylori resistance to metronidazole or to clarithromycin on the success of antimicrobial therapy. We used 75 key words to perform a literature search in MEDLINE as well as manual searches to identify clinical treatment trials that provided results in relation to H. pylori susceptibility to metronidazole and clarithromycin or both during the period 1984-1997 (abstracts were not included). Meta-analysis was done with both fixed- and random-effect models; results were shown using Galbraith's radial plots. We identified 49 papers with 65 arms for metronidazole (3594 patients, 2434 harboring H. pylori strains sensitive to metronidazole and 1160 harboring resistant strains). Metronidazole resistance reduced effectiveness by an average of 37.7% (95% CI = 29.6-45.7%). The variability in the risk difference for metronidazole was 122.0 to -90.6 and the chi-square value for heterogeneity was significant (P<0.001). Susceptibility tests for clarithromycin were performed in 12 studies (501 patients, 468 harboring H. pylori strains sensitive to clarithromycin and 33 harboring resistant strains). Clarithromycin resistance reduced effectiveness by an average of 55% (95% CI = 33-78%). We found no common factors that allowed patients to be divided into subgroups with additional factors significantly associated with resistance. In conclusion, metronidazole or clarithromycin pretreatment resistant H. pylori are the main factors responsible for treatment failure with regimens using these compounds. If H. pylori antibiotic resistance continues to increase, pretherapy antibiotic sensitivity testing might become necessary in many regions.

Dormedy E.S. et al. *Validation of acid washes as critical control points in hazard analysis and critical control point systems.* J Food Prot. 2000; 63(12) : 1676-80.p Abstract: A 2% lactic acid wash used in a large meat-processing facility was validated as an effective critical control point (CCP) in a hazard analysis and critical control point (HACCP) plan. We examined the microbial profiles of beef carcasses before the acid wash, beef carcasses immediately after the acid wash, beef carcasses 24 h after the acid wash, beef subprimal cuts from the acid-washed carcasses, and on ground beef made from acid-washed carcasses. Total mesophilic, psychrotrophic, coliforms, generic Escherichia coli, lactic acid bacteria, pseudomonads, and acid-tolerant microorganisms were enumerated on all samples. The presence of Salmonella spp. was also determined. Acid washing significantly reduced all counts except for pseudomonads that were present at very low numbers before acid washing. All other counts continued to stay significantly lower ($P < 0.05$) than those on pre-acid-washed carcasses throughout all processing steps. Total bacteria, coliforms, and generic E. coli enumerated on ground beef samples were more than 1 log cycle lower than those reported in the U.S. Department of Agriculture Baseline data. This study suggests that acid washes may be effective CCPs in HACCP plans and can significantly reduce the total number of microorganisms present on the carcass and during further processing.

Dos Santos C. et al. *Antimicrobial resistance patterns in respiratory pathogens isolated in an Italian university hospital during a period of eight years: a statistical analysis.* Chemotherapy. 2000; 46(3) : 166-72.p Abstract: The antimicrobial resistance patterns of respiratory pathogens isolated during an 8-year period (1990-1997) in an Italian hospital from patients with bronchopulmonary infections were investigated. A global variation in the resistance of Staphylococcus aureus to all relevant antibiotics was observed during the years 1990-1997. With the exception of penicillin and amoxicillin, to which Staphylococci were always resistant, and vancomycin, to which they were always susceptible, in the first period (1990-1992) the percentage of resistance to beta-lactams, aminoglycosides, macrolides, fluoroquinolones and cotrimoxazole was about 15%, while in the last period (1993-1997) it was about 35%. No global variation in resistance to the antimicrobials examined during the study period was observed for gram-negative bacteria. The percentages of resistance to the more recent beta-lactams, aminoglycosides and fluoroquinolones were generally less than 10% for the KES group, less than 20% for Pseudomonas aeruginosa, and less than 30% for other Pseudomonas species. A high percentage of resistance was observed for the KES group to amoxicillin + clavulanic acid (60%) and to cefoxitin (48%). Copyright 2000 S. Karger AG, Basel.

Dossche K.M. et al. *Allograft aortic root replacement in prosthetic aortic valve endocarditis: a review of 32 patients.* Ann Thorac Surg. 1997; 63(6) : 1644-9.p Abstract: BACKGROUND: This study was conducted to evaluate allograft aortic root replacement in the setting of complicated prosthetic valve endocarditis with extensive annular destruction. METHODS: From January 1990 through March 1996, 32 patients diagnosed with complicated prosthetic valve endocarditis underwent allograft root replacement. Mean age was 58.3 +/- 13.2 years; 23 patients were men. Mean preoperative New York Heart Association functional class was 3.4. Staphylococcus epidermidis (50%) and Enterococcus faecalis (19%) were the predominant causative microorganisms. Annular abscesses were found in 26 patients (81%), aortic-mitral discontinuity in 14 patients (43%), and left ventricular-aortic discontinuity in 11 patients (34%). A cryopreserved allograft was used in 31 patients (97%) and a fresh antibiotic-treated allograft was used in 1 patient (3%). Mean aortic cross-clamp time was 150 +/- 29 minutes. Mean duration of the postoperative antibiotic treatment was 38.5 +/- 11.8 days. RESULTS: There were three operative deaths (9.4%); causes of death were multiorgan failure in 2 patients (6.2%) and low cardiac output in 1 patient (3.2%). Six patients (18%) had complete heart block (4 patients already before the operation), 3 patients (9.4%) had temporary respiratory insufficiency, and 1 patient (3.2%) needed temporary hemodialysis. Mean follow-up was 37.4 +/- 22.4 months. Two late deaths occurred: 1 patient had recurrent endocarditis, leading to a false

aneurysm, and died at reoperation; another patient died of lung cancer. Actuarial 5-year survival was 87.3% (70% confidence interval, 76.8% to 97.8%); actuarial 5-year freedom from recurrent endocarditis was 96.5% (70% confidence interval, 90.0% to 100%). CONCLUSIONS: Allograft aortic root replacement is a valuable technique in the complex setting of prosthetic valve endocarditis with involvement of the periannular region. Mortality and morbidity are low.

Douzinas E.E. et al. *Prevention of infection in multiple trauma patients by high-dose intravenous immunoglobulins.* Crit Care Med. 2000; 28(1) : 8-15.p Abstract: OBJECTIVE: To investigate the activity of intravenous immunoglobulin (IVIG) as a prophylactic agent against infection in trauma victims. DESIGN: Prospective, randomized, double-blind, placebo-controlled study. SETTING: A 20-bed university intensive care unit. PATIENTS: Thirty-nine trauma patients with injury severity scores (ISSs) of 16-50. INTERVENTIONS: Penicillin was given at the time of admission and continued at least until day 4. Twenty-one patients received IVIG and 18 patients received human albumin at 1 g/kg in four divided doses (days 1, 2, 3, and 6). The two groups had similarities in age, gender, Acute Physiology and Chronic Health Evaluation II score, risk of death, and Glasgow Coma Scale score, but differing ISSs (p =.02), at the time of admission. Blood was collected on days 1, 4, and 7. MEASUREMENTS AND MAIN RESULTS: Clinical variables related to infection were recorded. The complement components C3c, C4 and CH50, IgG, and the fractions of IgG were measured. The serum bactericidal activity (SBA) was assessed at 37 degrees C (98.6 degrees F) and 40 degrees C (104.0 degrees F) at the time of admission and during the course of IVIG administration. Controlling for ISS, IVIG-treated patients had fewer pneumonias (p =.003) and total non-catheter-related infections (p =.04). Catheter-related infections (p =.76), length of stay in the intensive care unit, antibiotic days, and infection-related mortality did not differ between the two groups. A significantly increased trend in IgG and its subclasses was shown on days 4 and 7 in the IVIG group but not in the control group (p<.000001). No important differences were noted in complement fractions. The SBA of the groups was similar on day 1, but significantly higher on days 4 and 7 (p<.000001) in the IVIG group, remaining so controlling for complement and ISS. SBA was higher at 40 degrees C (104.0 degrees F) compared with 37 degrees C (98.6 degrees F) (p<.0001) under all three conditions. In both groups, low SBA (on days 1, 4, and 7) was associated with increased risk of pneumonia (p<.01) and non-catheter-related infections (p =.06 for day 1; p<.01 for days 4 and 7). CONCLUSIONS: Trauma patients receiving high doses of IVIG exhibit a reduction of septic complications and an improvement of SBA. Early SBA measurement may represent an index of susceptibility to infection.

Dowell S.F. et al. *Acute otitis media: management and surveillance in an era of pneumococcal resistance. Drug-Resistant Streptococcus Pneumoniae Therapeutic Working Group.* Nurse Pract. 1999; 24(10 Suppl) : 1-9; quiz 15-6.p Abstract: Experts in the management of otitis media and the Drug-resistant Streptococcus pneumoniae Therapeutic Working Group were convened by the Centers for Disease Control and Prevention to respond to changes in antimicrobial susceptibility among pneumococci. The objective was to provide consensus recommendations for the management of acute otitis media (AOM) and for the surveillance of drug-resistant Streptococcus pneumoniae. After summarizing published and unpublished data from the scientific literature and the experience of the panel members, the group concluded that oral amoxicillin should remain the first-line antimicrobial agent for treating AOM. For patients with clinically defined treatment failure after 3 days of therapy, useful alternative agents include amoxicillin-clavulanate, cefuroxime axetil, and intramuscular ceftriaxone. The group also made recommendations to improve surveillance and to obtain antimicrobial susceptibility patterns for local geographic areas.

Dowell S.F. et al. *Acute otitis media: management and surveillance in an era of pneumococcal resistance—a report from the Drug-resistant Streptococcus pneumoniae Therapeutic Working Group.* Pediatr Infect Dis J. 1999; 18(1) : 1-9.p Abstract: OBJECTIVE: To provide recommendations [corrected] for the management of acute otitis media (AOM) and the surveillance of drug-resistant Streptococcus pneumoniae (DRSP). Five questions were addressed: (1) Can amoxicillin remain the best initial antimicrobial agent for treating AOM in the current period of increasing prevalence of DRSP? (2) What are suitable alternative agents for use if amoxicillin fails? (3) Should empiric treatment of AOM vary by geographic region? (4) Where can clinicians learn about resistance patterns in their patient populations? (5) What modifications to laboratory surveillance would improve the utility of the information for clinicians treating AOM? PARTICIPANTS: Experts in the management of otitis media and the DRSP Therapeutic Working Group. This group was convened by the CDC to respond to changes in antimicrobial susceptibility among pneumococci and includes clinicians, academicians and public health practitioners. EVIDENCE: Published and unpublished data summarized from the scientific literature and experience from the experts present. PROCESS: [corrected] After group presentations and review of background materials, subgroup chairs prepared draft responses to the five questions, discussed the responses as a group and edited those responses [corrected]. CONCLUSIONS: Oral amoxicillin should remain the first line antimicrobial agent for treating AOM. In view of the increasing prevalence of DRSP, the safety of amoxicillin at higher than standard dosages and evidence that higher dosages of amoxicillin can achieve effective middle ear fluid concentrations, an increase in the dosage used for empiric treatment from 40 to 45 mg/kg/day to 80 to 90 mg/kg/day is recommended. For patients with clinically defined treatment failure after 3 days of therapy, useful alternative agents include oral amoxicillin-clavulanate, cefuroxime axetil and intramuscular ceftriaxone. Many of the 13 other Food and Drug Administration-approved otitis media drugs lack good evidence for efficacy against DRSP. Currently local surveillance data for pneumococcal resistance that are relevant for the clinical management of AOM are not available from most areas in the United States. Recommendations to improve surveillance include establishing criteria for setting susceptibility breakpoints for clinically appropriate antimicrobials to ensure relevance for treating AOM, testing middle ear fluid or nasal swab isolates in addition to sterile site isolates and testing of drugs that are useful in treating AOM. The management of otitis media has entered a new era with the development of DRSP. These recommendations are intended to provide a framework for appropriate clinical and public health responses to this problem.

Dowell S.F. et al. *Resistant pneumococci: protecting patients through judicious use of antibiotics.* Am Fam Physician. 1997; 55(5) : 1647-54, 1657-8.p Abstract: Increasing resistance to antimicrobial agents has occurred among many pathogens, but the emergence of resistant Streptococcus pneumoniae will have the greatest impact on the practice of outpatient medicine. Consequences of resistance include complicated management of acute otitis media and meningitis treatment failures. Pneumococci have acquired resistance to penicillin, third-generation cephalosporins and other antibiotics at an alarming rate; in some areas, 25 percent of isolates are nonsusceptible to penicillin. In areas with high resistance rates, the addition of vancomycin to cefotaxime or ceftriaxone is warranted for empiric treatment of bacterial meningitis. Changes in empiric therapy for pneumonia, bacteremia and otitis media may eventually be necessary. Previous antibiotic use is a risk factor for invasive disease with resistant pneumococci. Patients may be best protected by avoiding unnecessary use of antibiotics. Patient education materials as well as recommendations for avoiding the use of antibiotics for some upper respiratory tract infections are currently being developed to help physicians achieve this goal.

Dowzicky M. et al. *Evaluation of in vitro activity of quinupristin/dalfopristin and*

comparator antimicrobial agents against worldwide clinical trial and other laboratory isolates. Am J Med. 1998; 104(5A) : 34S-42S.p Abstract: This report summarizes the activities of quinupristin/dalfopristin (Q/D) and appropriate comparator antibiotics, including ciprofloxacin, erythromycin, gentamicin, rifampin, teicoplanin, and vancomycin, against selected gram-positive pathogens, including Enterococcus faecium, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus agalactiae, and Streptococcus pyogenes. The study pathogens were obtained from 2 sources: (1) clinical isolates taken from patients participating in Q/D worldwide Phase III comparative and noncomparative (emergency-use program) clinical trials; and (2) other isolates collected from the laboratories of 45 geographically distinct medical centers around the world. Q/D was highly active, with minimum inhibitory concentrations (MICs) < or = 1.0 microg/mL against most isolates, including those known to be resistant to methicillin, vancomycin, or erythromycin. Q/D was active (MICs < or = 1 microg/mL) against 95% of the vancomycin-resistant E. faecium strains, for example, whereas ciprofloxacin was active against 6%. Q/D was equally active against methicillin-susceptible or -resistant S. aureus strains (MIC90=1 microg/mL), as was vancomycin (MIC90=2 microg/mL), whereas ciprofloxacin was much less active against methicillin-resistant strains than against methicillin-susceptible strains (MIC90=32 vs 1 microg/mL). Given its spectrum of activity, Q/D may provide a viable option for the treatment of severe respiratory and skin and skin-structure infections caused by gram-positive bacteria, especially when strains with known or suspected resistance to other commonly used antibiotics are present.

Drabick J.J. et al. *Microbiological laboratory results from Haiti: June-October 1995.* Bull World Health Organ. 1997; 75(2) : 109-15.p Abstract: From June to October 1995, the U.S. Army's 86th Combat Support Hospital was deployed in Haiti in support of the United Nations peacekeeping mission. The hospital's mission was to provide comprehensive health care to United Nations military and civilian personnel in Haiti. The hospital's laboratory, with microbiological and parasitological capability, was a critical asset in light of the infectious disease threats in Haiti. A total of 356 microbiological (5.4%) and 887 parasitological (13.4%) tests were performed, out of a total of 6628 laboratory tests. One finding was the discovery of antibiotic-resistant urinary isolates of Escherichia coli. These were from community-acquired infections and included strains resistant to ampicillin (6/15), trimethoprim+sulfamethoxazole (6/15), and ciprofloxacin (2/15). Ampicillin (8/15) and trimethoprim+sulfamethoxazole (3/15) resistance was also noted in Shigella spp. However, no chloroquine-resistant strains of malaria were encountered. Dengue virus, also mosquito borne, was a major pathogen. Antimicrobial-resistant nosocomial pathogens were also encountered. Deployed laboratories should be able to determine antimicrobial susceptibility and perform microbial identification to guide clinical management, conduct medical surveillance, and detect emerging resistance.

Drago L. et al. *In vitro antimicrobial activity of propolis dry extract.* J Chemother. 2000; 12(5) : 390-5.p Abstract: In this study the antibacterial and antifungal properties of propolis, a natural product of bees, have been investigated against different pathogens. Minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBCs) were determined according to NCCLS standards on 320 strains including Staphylococcus aureus, Group A beta-hemolytic streptococci, Streptococcus pneumoniae, Moraxella catarrhalis, Haemophilus influenzae, Klebsiella pneumoniae, Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa and Candida albicans. Time-kill curves were assessed for susceptible microorganisms, testing 0, 0.5, 1, 2, 4 x MIC for propolis, by counting viable bacteria after 0, 3, 6, 24 hours and viable yeasts after 0, 3, 6, 24 and 48 hours. Propolis showed good antimicrobial activity against most of the isolates, particularly S. pneumoniae, H. influenzae and M. catarrhalis, but not against Enterobacteriaceae. Time-kill curves demonstrated bacteriostatic rather than bactericidal activity of propolis, the latter being evident only at high concentrations.

Drinkovic D. et al. *Prospective vancomycin audit in Auckland healthcare hospitals.* N Z Med J. 1999; 112(1095) : 336-9.p Abstract: AIM: In response to emerging vancomycin resistance among gram-positive cocci, it is recommended that hospitals develop guidelines for the appropriate use of glycopeptides and identify situations where glycopeptide use should be discouraged. The aim of this study was to audit the use of vancomycin in Auckland Healthcare hospitals. METHOD: Patients prescribed vancomycin were recorded by pharmacy staff at Auckland, Starship, Green Lane and National Women's Hospitals. Clinical and laboratory information was collected for each course of vancomycin treatment. Standard definitions were used to classify prophylactic, empirical or specific directed therapy as appropriate or inappropriate. Continuing vancomycin when cultures were negative for beta-lactam-resistant, gram-positive organisms and/or initial choice of vancomycin when it was not necessary for the presumed source of infection were reasons for inappropriate empirical use. Reasons for inappropriate specific directed therapy included vancomycin prescribed for methicillin susceptible S. aureus and coagulase-negative staphylococci, or penicillin susceptible viridans streptococci when there was no history of beta-lactam allergy. RESULTS: One hundred and sixty-eight courses of vancomycin were prescribed for 146 patients; 42 in children (<16 years) and 126 in adults. Thirty-two per cent of all vancomycin courses were in renal patients, 26% in surgical specialities, 17% in haematology/oncology patients, 14% in medical specialities and 10% in intensive care unit patients. Eighty-six (51%) courses of vancomycin were considered inappropriate. The majority, 54/86 (63%) of inappropriate use, was for empirical therapy. It was an inappropriate initial choice in 25 instances, the duration of treatment was inappropriate, given no beta-lactam-resistant organisms were isolated in nine instances and both its initial choice and duration were inappropriate in 20 instances. Switching to other antimicrobial agents sooner when culture results and susceptibilities became available would have shortened the duration of 58/86 (67%) of the inappropriate courses. Of the inappropriate courses, 44/86 (51%) were prescribed for renal patients, 22 for empirical use, e.g. for peritoneal dialysis-related peritonitis, wound infections and presumed line infections and 22 for specific therapy of beta-lactam susceptible isolates because of dosing convenience in patients with renal failure. CONCLUSION: Half of the vancomycin use in Auckland Healthcare hospitals could potentially be modified. The majority of inappropriate use (63%) was for empirical therapy. The microbiology laboratory's ability to promptly and accurately report culture and susceptibility results and convey these to the prescribing clinician is important in reducing unnecessary doses. This study identified areas where interventions will be focused to reduce vancomycin use.

Droffner M.L. et al. *Survival of E. coli and Salmonella populations in aerobic thermophilic composts as measured with DNA gene probes.* Zentralbl Hyg Umweltmed. 1995; 197(5) : 387-97.p Abstract: Aerobic, thermophilic composting is a widely practiced method for disposal of organic wastes. The wastes which are composted include biosolids from waste water treatment plants (WWTP), and biowastes (food scraps and yardwaste). Important hygiene issues are involved in composting since many potential pathogens may be present in the fresh wastes. In this study, the survival of Salmonella and Escherichia coli is examined during aerobic composting of municipal solid wastes, municipal wastewater sludge and biowastes. A laboratory compost was prepared by inoculating with 10(7) Salmonella typhimurium Q and Escherichia coli B. In both industrial and laboratory trials, gene probes were used to determine at what time during the composting and at what temperature these bacteria became undetectable. It was observed that Salmonella and E. coli survived for 59 days at about 60 degrees C in an industrial compost. The bacteria became undetectable after the temperature decreased from 62 degrees C to about 40 degrees C in the compost curing. The bench scale trials showed that E. coli B survived for at least 9 days at 60-70 degrees C in a

biowaste (food waste) compost or a waste water sludge compost. Salmonella typhimurium Q survived for at least 9 days over 60 degrees C in the food biowaste compost and at least 5 days in the waste water sludge compost. Data collected show that the temperature or the time of high temperature is difficult to correlate to the destruction of the pathogen, Salmonella, or the pathogen indicator, E. coli. These results suggest that the mechanism for removal of these microorganisms during aerobic composting is complex and not simply the result of a thermal physical environment.

Drogari-Apiranthitou M. et al. *The effect of mannan-binding lectin on opsonophagocytosis of Neisseria meningitidis.* Immunopharmacology. 1997; 38(1-2) : 93-9.p Abstract: Mannan-binding lectin (MBL), an acute phase protein with a structure and a function very similar to that of C1q, is known to act as an opsonin binding to a number of microorganisms. In order to investigate the effect of MBL on the phagocytic killing of meningococci, a serogroup B meningococcal strain (H44/76) and its unencapsulated variant v24, as well as a serogroup A meningococcal strain were opsonized with MBL (purified from normal human plasma at the State Serum Institute, Denmark) and used in a phagocytic killing assay at a density of 7 x 10(3) CFU/ml. Polymorphonuclear cells (PMNs) from one healthy donor were isolated by density gradient centrifugation over Percoll and added to the system (7 x 10(6) cells/ml). In a first set of experiments without addition of serum or complement, no influence of MBL was observed on the killing of any of these strains. Addition of MBL to non-opsonized bacteria of the serogroup A strain did not result in enhanced killing either; on the contrary, the growth of this strain increased significantly when a high MBL concentration (40 micrograms/ml) was used in the presence of PMNs. Further investigations were performed using sera of five individuals with late complement component deficiency (LCCD) and a concomitant MBL deficiency, vaccinated with a tetra-valent (ACYW135) meningococcal capsular polysaccharide vaccine. Pre- and post-vaccination sera (50% final concentration) were tested against a group A strain opsonized or not with MBL. In only one patient was there a moderate increase of killing of the opsonized bacteria after vaccination compared to pre-vaccination serum. Our results suggest that MBL may not play a significant role in the opsonophagocytosis of meningococci, irrespective of its binding to unencapsulated and serogroup A strains.

Dubois J. et al. *In vitro study of the post-antibiotic effect and the bactericidal activity of Cefditoren and ten other oral antimicrobial agents against upper and lower respiratory tract pathogens.* Diagn Microbiol Infect Dis. 2000; 37(3) : 187-93.p Abstract: The in vitro post-antibiotic effect (PAE) and batericidal activity of cefditoren was compared to that of cefixime, cefuroxime, loracarbef, cefaclor, amoxicillin, amoxicillin/clavulanate, clarithromycin, azithromycin, erythromycin, and ciprofloxacin against ATCC culture strains and clinical respiratory isolates. A PAE > 1 h was observed for cefditoren and generally for the macrolides against Streptococcus pneumoniae, beta-lactamase-negative Moraxella catarrhalis, and Streptococcus pyogenes, whereas the other beta-lactams showed mixed results. Cefditoren was the only beta-lactam showing significant bactericidal activity (>3 log reduction of viable cells) within 4 h against penicillin-resistant S. pneumoniae. Only cefditoren and ciprofloxacin showed significant bactericidal activity against beta-lactamase-negative (after 24 h) and beta-lactamase-positive strains of H. influenzae (after 12 h). Against beta-lactamase-positive strains of M. catarrhalis, cefditoren was the only agent to show significant bactericidal activity at 6 h (versus cefuroxime and ciprofloxacin at 12 h).

Dubost J.J. et al. *Pyogenic arthritis in adults.* Joint Bone Spine. 2000; 67(1) : 11-21.p Abstract: Septic arthritis has shown no change in incidence, and despite advances in antimicrobial therapy is often responsible for residual functional impairment and for a high mortality rate among debilitated patients. Risk factors include older age, diabetes mellitus, rheumatoid arthritis, immunodeficiency, and a preexisting joint disease (e.g., rheumatoid arthritis) to which the symptoms of septic arthritis are sometimes ascribed. Staphylococcus aureus contributes over two-thirds of identified organisms; a range of streptococci and gram-negative bacilli are next in frequency. The most common site is the knee, followed by the hip and shoulder. Over 10% of patients have polyarticular involvement reflecting bacteremia and diminished resistance to infection; (over 50% of polyarticular forms occur in rheumatoid arthritis patients). Prosthetic joint infection is becoming increasingly common; chronic forms due to intraoperative contamination and resulting in septic loosening should be distinguished from acute hematogenous infection in which emergency treatment can allow to salvage the prosthesis. Demonstration of the organism in the joint is the key to the diagnosis. Joint aspiration should be performed on an emergency basis, if needed after identification of radiographic landmarks or under ultrasonographic guidance. Seeding the fluid on blood culture flasks immediately after aspiration increases the yield. Antibiotics should be started as soon as the microbiological specimens have been collected. When aspiration is difficult (hip) or inadequate, arthroscopic drainage usually makes arthrotomy unnecessary. Early antiinflammatory therapy (nonsteroidal antiinflammatory drugs, systemic or local glucocorticoids, anticytokines, and antiinflammatory cytokines) are being considered as tools for limiting joint damage; their efficacy and safety will first have to be established in animal studies.

Duch-Samper A.M. et al. *Endophthalmitis following open-globe injuries.* Curr Opin Ophthalmol. 1998; 9(3) : 59-65.p Abstract: Endophthalmitis following open-globe injuries is caused by a specific range of microorganisms, of which Bacillus sp. and coagulase-negative Staphylococcus are the most frequent. Risk factors include the presence of an intraocular foreign body, injury inflicted by organic material, delay in surgery, and the type of wound involved. Despite important advances in medical and surgical management, this type of endophthalmitis continues to pose a poor prognosis. In this sense, we consider prevention to be the best approach. We report our protocols for the prevention and treatment of endophthalmitis following open-globe injuries, based on recent experimental studies on the ocular pharmacokinetics of antibiotics and on multicenter studies of the treatment of endophthalmitis.

Ducons J.A. et al. *Impact of clarithromycin resistance on the effectiveness of a regimen for Helicobacter pylori: a prospective study of 1-week lansoprazole, amoxycillin and clarithromycin in active peptic ulcer.* Aliment Pharmacol Ther. 1999; 13(6) : 775-80.p Abstract: BACKGROUND: Clarithromycin is a key antimicrobial in the combinations used to cure Helicobacter pylori infections, so there is a need to define the impact of in vitro resistance on in vivo results. METHODS: A prospective trial was designed to study the effectiveness of the 1-week combination of lansoprazole, clarithromycin and amoxycillin in 102 consecutive patients with active peptic ulcer. The pre-treatment and post-treatment sensitivity to amoxycillin, metronidazole and clarithromycin were studied by E-test, and H. pylori status was defined by histology, culture and urease test at diagnosis and one month after treatment, and by urea-breath test 2 months after treatment. RESULTS: The eradication rate (intention-to-treat analysis) was 77% (95% CI: 69-86). No clinical factor was found to be different between eradicated and non-eradicated patients. Clarithromycin-resistant strains were found in 10 (10%; CI: 5-17) patients. The eradication rate was 20% (CI: 3-56) in these patients vs. 83% (CI: 75-91) in patients harbouring clarithromycin-sensitive strains ($P < 0.001$). A logistic-regression analysis confirmed clarithromycin resistance as the only factor associated with treatment failure. CONCLUSIONS: Clarithromycin resistance significatively impairs the effectiveness of the combination of lansoprazole, amoxycillin, and clarithromycin. The 80% efficacy goal will be difficult to reach in areas with high (>10%) primary clarithromyicin resistance, if currently recommended proton pump inhibitor-triple therapies are used.

Dull J.S. et al. *Non-surgical treatment of biliary liver abscesses: efficacy of endoscopic drainage and local antibiotic lavage with nasobiliary catheter.* Gastrointest Endosc. 2000; 51(1) : 55-9.p Abstract: BACKGROUND: It is universally recognized that the most frequent cause of hepatic abscess is biliary disease. The aim of this study was to determine the efficacy of endoscopic drainage and local antibiotic lavage via nasobiliary catheter in the treatment of liver abscesses of biliary origin. METHOD: From January 1994 to December 1995, twenty-two cases of pyogenic liver abscess were treated. Diagnosis was established with ultrasound, computed tomography, endoscopic retrograde cholangiography, and laboratory tests. All patients were assigned prospectively to endoscopic or other non-surgical forms of therapy, depending on the etiology of the pyogenic process. Patients in whom this treatment failed underwent surgical drainage. Twenty patients had hepatic abscesses of biliary origin. In this subgroup, a nasobiliary catheter was placed into the biliary tree for continuous antibiotic lavage (infusion technique: 1 to 1.5 mL/min for 8 to 10 days) after endoscopic sphincterotomy. Two patients had hepatic abscesses of hematogenous and amebic origin, respectively. They were treated only with the appropriate systemic antibiotics. RESULTS: Nineteen patients of the biliary subgroup (95%) and the two patients with non-biliary disease (100%) had complete resolution of the abscesses. "Salvage" surgical drainage was required in only one patient (4.5%). There was no treatment related mortality. CONCLUSION: Endoscopic sphincterotomy and local antibiotic lavage via an endoscopically placed nasobiliary catheter is a safe and effective treatment for biliary liver abscesses. It should be considered as first-line treatment in this subgroup of patients with liver abscesses. Percutaneous or surgical drainage modalities should be reserved for patients in whom endoscopic treatment fails.

Dung S.Z. *Effects of mutans streptococci, Actinomyces species and Porphyromonas gingivalis on collagen degradation*. Chung Hua I Hsueh Tsa Chih (Taipei). 1999; 62(11) : 764-74.p Abstract: BACKGROUND: While Streptococcus mutans and Actinomyces spp are considered to be major pathogenic microorganisms of root caries, their roles in the degradation of organic matrix components of human root dentin need clarification. METHODS: Ten laboratory strains and 11 clinical isolates of mutans streptococci and Actinomyces species, and positive bacterial or purified enzyme controls (Porphyromonas gingivalis whole cell lysates, trypsin or clostridial collagenase) were used to establish the degradation of azocollagen (AC), insoluble type I collagen (IC) or human dentin collagen (DC) from dentin powder in two types of experiments investigating collagenolytic activity either during or after bacterial growth. Ultraviolet-irradiated dentin powder and gamma-irradiated IC were used to assess the collagenolytic activity of test strains during bacterial growth. AC, IC and acid-treated dentin powder were used to determine the collagenolytic activity of sonicated bacterial whole cells and cell-free culture supernatants recovered from test strains after growth. Hydroxyproline or spectrophotometric assays were used to analyze the level of degraded collagen. RESULTS: Data from this study showed that in contrast to the positive controls, none of the laboratory strains or clinical isolates elicited significant degradation of AC, IC or DC. CONCLUSIONS: Results indicated that mutans streptococci and Actinomyces species had no significant collagenolytic activity, but may be involved in the root caries process through other mechanisms. In addition, proteolytic enzymes from other oral bacteria such as Porphyromonas gingivalis or from host cells such as neutrophils may also participate in the pathogenesis of root caries.

Dunne W.M. Jr. *Comparison of selective broth medium plus neomycin-nalidixic acid agar and selective broth medium plus Columbia colistin-nalidixic acid agar for detection of group B streptococcal colonization in women*. J Clin Microbiol. 1999; 37(11) : 3705-6.p Abstract: The combination of neomycin-nalidixic acid (NNA) agar and a selective broth medium (SBM) has recently been shown to improve the sensitivity of screening cultures for group B streptococcal (GBS) carriage in women. Because of the relatively high cost of NNA agar, a study was initiated to determine whether Columbia colistin-nalidixic acid (CNA) agar would be an equally sensitive, more economical alternative. A total of 580 cervical-vaginal and/or rectal specimens submitted for detection of GBS were included in the study. Each was plated onto NNA and CNA agar and then inoculated into SBM. GBS were recovered from 95 of 580 (16.4%) specimens, including 61 isolates from CNA, 74 from NNA, 73 from the CNA-SMB combination, and 86 from the NNA-SMB tandem. Of those, 22 isolates were recovered on NNA but not CNA, 9 were cultured on CNA but not NNA, 52 were isolated on both media, and 12 were recovered from subcultures of SBM only. The overall sensitivity of CNA alone (64. 2%) was statistically significantly less than that of NNA agar (77. 9%), as was the sensitivity of combination of CNA plus SBM (76.8%) compared to that of NNA plus SBM (90.5%). Based on these findings, CNA should not be considered an acceptable alternative to NNA for the detection of GBS colonization in women despite potential cost savings.

Dunne W.M. Jr et al. *Antimicrobial activity of merocyanine 540: a photosensitizing dye.* Diagn Microbiol Infect Dis. 1998; 32(2) : 101-5.p Abstract: The antimicrobial activity of merocyanine 540 (MC 540), a photosensitizing dye previously used to purge malignant cells from autologous bone marrow grafts, was evaluated against a panel of Gram-positive and Gram-negative bacteria and Candida albicans in the presence and absence of light. In the absence of light, MC 540 demonstrated no antibacterial activity against any of the organisms tested. When combined with increasing intervals of photoillumination, growth inhibition was observed with all Gram-positive organisms tested except Mycobacterium fortuitum. Photosensitizing growth inhibition was also observed with Moraxella catarrhalis but not with any other Gram-negative bacilli including members of the Enterobacteriaceae, Pseudomonas aeruginosa, Acinetobacter baumannii, Stenotrophomonas maltophila, or Burkhoderia cepacia. These results suggested that differences in cell wall structure confer resistance to the photodamaging effects of the dye. MC 540 exhibited no antimicrobial activity against C. albicans in the presence or absence of light.

Durban J.J. et al. *Antimicrobial efficiency of hydrogel contact lens soaking solutions marketed in Spain*. Optom Vis Sci. 1998; 75(2) : 126-31.p Abstract: The antimicrobial efficiency of 20 commercially available solutions for soaking and rinsing soft contact lenses was studied in relation to 5 bacteria (Escherichia coli, Staphylococcus epidermidis, Pseudomonas aeruginosa, Bacillus subtilis, and Serratia marcescens) and 1 fungus (Candida albicans). Each product was separately inoculated with each of six microorganisms, and samples of the inoculated contact lens solutions were taken at predetermined times, placed in a recovery medium, and incubated. Where there was growth, the colonies were counted. There were differences in performance even between solutions labeled as having the same antimicrobial content. One of the solutions marketed in Spain to soak hydrogel contact lenses failed to inactivate all six test strains.

Durmaz B. et al. *Methicillin-resistance among Turkish isolates of Staphylococcus aureus strains from nosocomial and community infections and their resistance patterns using various antimicrobial agents.* J Hosp Infect. 1997; 37(4) : 325-9.p Abstract: The purposes of this study were to determine the prevalence of Turkish isolates of methicillin-resistant Staphylococcus aureus (MRSA) in nosocomial and community infections and their antibiotic resistant patterns. The oxacillin disk diffusion method for the detection of methicillin resistance and the Kirby-Bauer disk diffusion for antibiotic susceptibility tests were used. A total 383 S. aureus strains were identified from different patients. The prevalence of methicillin resistance among S. aureus strains was 31.3% (120/383). The proportions of MRSA isolated from nosocomial and community infections were 26.4% (46/174) and 35.4% (74/209), respectively. The resistance rates of MRSA to other antibiotics were as follows: 71% resistant to erythromycin, 54% to clindamycin, 52% to gentamicin, 44.5% to trimethoprim-sul-

famethoxazole and 36% to ciprofloxacin. No strain resistant to vancomycin was recorded in this study.

Dussurget O. et al. *Interdependence of mycobacterial iron regulation, oxidative-stress response and isoniazid resistance.* Trends Microbiol. 1998; 6(9) : 354-8.p Abstract: Iron is an essential cofactor for vital functions in microorganisms. Bacterial pathogens have developed efficient iron-acquisition systems to counteract the defensive sequestration of iron by their hosts. In mycobacteria, the recently described protein, IdeR, negatively controls iron-uptake systems. This protein also has a role in the oxidative-stress response, as well as in resistance to the front-line antimycobacterial drug isoniazid.

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Eandi M. et al. *Economic impact of resistance in the community.* Int J Clin Pract Suppl. 1998; 95 : 27-38.p Abstract: Antimicrobial resistance is assumed to be an important health problem and an economic burden to society. However, the relationship between the emergence of in vitro microbiological resistance and its clinical and socioeconomic consequences has not yet been satisfactorily determined for either nosocomial or community-acquired infection. In the case of both nosocomial and community-acquired infection, previous exhaustive reviews of published and unpublished reports concluded that mortality, likelihood of hospitalization, and length of hospital stay were usually at least twice as great for patients infected with drug-resistant strains as for those infected with drug-susceptible strains of the same bacteria. However, evaluation of the economic impact of resistance is still problematic and the adverse economic and health effects of drug-resistant bacterial infections can only be roughly quantified. Decision analysis models, such as decision trees, can aid evaluation of the impact of resistance on health and economic outcomes from the perspective of a given decision maker. A model of cost analysis should be based on a knowledge of the incremental consumption of resources specifically dependent on the dynamics of antimicrobial resistance in a given clinical setting (e.g. home care or hospital care). In general, we can assume that the increased rate of isolation of resistant strains from community-acquired infections correlates positively with an increase in morbidity, mortality, risk of hospitalization and the need for additional days in hospital and for more expensive and powerful antibiotics. We implemented and simulated a general decision-tree model to analyse the influence of antibiotic resistance on the economic outcomes of community-acquired lower respiratory tract infections, from the perspective of both society and the health-care local organization (HCLO). This model allows simulation of the impact of different degrees of resistance on the direct costs of an antibiotic therapy as well as on the cost-effectiveness of antibiotics with different degrees of resistance.

Eatock M.M. et al. *A dose-finding study of raltitrexed (tomudex) with cisplatin and epirubicin in advanced gastro-oesophageal adenocarcinoma.* Br J Cancer. 2000; 82(12) : 1925-31.p Abstract: The standard treatment for advanced gastro-oesophageal cancer in the UK is epirubicin, cisplatin and continuous infusion 5-fluoruracil by an indwelling central venous catheter (ECF), which has significant morbidity. Raltitrexed (tomudex), a specific inhibitor of thymidylate synthase with a long plasma terminal half-life (50-100 h) has activity in gastro-intestinal tract malignancy. To reduce the Hickman line-associated morbidity of ECF; we have conducted a dose-finding study of tomudex combined with epirubicin and cisplatin. Twenty-four patients (22 males, two female), median age 63 years (range 21-75), ECOG performance status < or =2 with histologically proven, unresectable or metastatic gastric (14 patients), gastro-oesophageal junction (nine patients) or oesophageal (one patient) adenocarcinoma received treatment with 3-weekly cisplatin 60 mg m(-2), epirubicin 50 mg m(-2) and tomudex at doses of 2 mg m(-2), 2.5 mg m(-2) or 3 mg m(-2) in successive cohorts. Six patients were treated per dose level with no intra-patient dose escalation. Dose escalation occurred after six patients had completed at least one cycle of chemotherapy at the previous dose level. After defining the maximum tolerated dose a further six patients were treated at the preceding dose level to assess toxicity at the proposed phase II dose. A total of 102 cycles (50% completed 6 cycles) were administered. The dose-limiting toxicities are neutropenia and diarrhoea occurring in 2/6 patients at the 3 mg m(-2) dose level. Of those patients evaluable for response, there were eight partial and one complete response (overall response rate 38%). The median survival was 9.9 months. ECT is an active regimen in oesophagogastric adenocarcinoma. The recommended dose of tomudex for further study in combination with epirubicin and cisplatin is 2.5 mg m(-2).

Eaves-Pyles T. et al. *Bacterial invasion is not required for activation of NF-kappaB in enterocytes.* Infect Immun. 1999; 67(2) : 800-4.p Abstract: Pathogenic enteric microorganisms induce the NF-kappaB-dependent expression of proinflammatory genes in intestinal epithelial cells. The purpose of the present study was to clarify the contribution of microbial invasion to the degradation of the regulatory protein Ikappa Balpha and the subsequent activation of NF-kappaB in cultured intestinal epithelial cells. Caco-2BBe cells were incubated with Salmonella dublin, Salmonella typhimurium, or a weakly invasive strain of E. coli. S. dublin and S. typhimurium (10(7) organisms/ml) induced equivalent concentration-dependent gel mobility shifts of an NF-kappaB consensus sequence that was preceded by Ikappa Balpha degradation. E. coli (10(7) organisms/ml) did not induce Ikappa Balpha degradation or NF-kappaB translocation. Pretreatment with cytochalasin D blocked invasion of all three strains but had no effect on Ikappa Balpha degradation or NF-kappaB activation. S. dublin and S. typhimurium adhered to Caco-2BBe cells 3- to 10-fold more than E. coli. NF-kappaB activation was prevented by physical separation of S. dublin from Caco-2BBe cells by a 0. 4-micrometers-pore-size filter. Our results imply that bacterial adhesion, rather than invasion or release of a secreted factor, is sufficient to induce IkappaBalpha degradation and NF-kappaB activation in intestinal epithelial cells. Our data suggest that strategies to reduce enteric inflammation should be directed to the reduction of bacterial enterocyte adhesion.

Echaniz-Aviles G. et al. *Predominance of the multiresistant 23F international clone of Streptococcus pneumoniae among isolates from Mexico.* Microb Drug Resist. 1998; 4(3) : 241-6.p Abstract: During a surveillance study to determine the relative prevalence of capsular types of Streptococcus pneumoniae and antimicrobial susceptibility of invasive isolates in children <5 years old in Mexico City, 220 isolates were collected. The serotype 23F was the most common found, followed by types 6A + B, 14, 19F, and 19A. Diminished susceptibility to penicillin was detected in 106 isolates (48.2%), and high penicillin resistance was found in 49 strains (22.2%), 31 belonging to type 23F. Resistance was also observed to erythromycin (13.1%), to chloramphenicol (43.1%), and to cefotaxime (10.9%). No strains were resistant to ofloxacin or vancomycin. Forty-four of the highly penicillin resistant isolates (penicillin MIC > or =2.0 microg/ml) were examined with molecular fingerprinting techniques; 29 (65.9%) of these isolates (all except two strains) were serotype 23F and shared subtype variants of PFGE type A characteristic of the internationally spread Spanish/USA clone of S. pneumoniae. These strains were also resistant to trimethoprim/sulfametoxasole (TMP/SMX), chloramphenicol, and tetracycline, and most of them were susceptible to erythromycin. Another 6 of the highly penicillin-resistant strains (serogroups 9 and 14) showed PFGE fingerprints and antimicrobial susceptibility pattern characteristic of a second internationally spread clone (French/Spanish clone) and carried resistance to penicillin and TMP/SMX. The rest of the 9 penicillin-resistant isolates were represented by 7 distinct additional PFGE types. The findings suggest that almost 80% of all highly penicillin resistant strains may have been "imported" into Mexico.

Echaniz-Aviles G. et al. *Antimicrobial susceptibilities and capsular types of invasive Streptococcus pneumoniae isolated in children in Mexico City.* Microb Drug Resist. 1997; 3(2) : 153-7.p Abstract: As part of the Sistema Regional de Vacunas (SIREVA) initiative, we conducted a surveillance study to determine the relative prevalence of capsular types of Streptococcus pneumoniae and antimicrobial susceptibility of invasive isolates in children less than 5 years old. We collected 220 isolates and found 33 of the 90 known types, with type 23F as the most common followed by types 6A+B, 14, 19F, and 19A. High penicillin resistance was found in 49 strains (22.2%), 31 belonging to type 23F. Twenty-nine (13.1%) were resistant to erythromycin, 95 (43.1%) were resistant to chloramphenicol, and 24 (10.9%) were resistant to cefotaxime. No strains were resistant to vancomycin.

Echeverria M.J. et al. *[In vitro activity of 9 antibiotics and 3 beta-lactamase inhibitors against 107 clinical isolates of Acinetobacter baumanii].* Enferm Infecc Microbiol Clin. 1997; 15(6) : 319-22.p Abstract: BACKGROUND: Acinetobacter sp. is an important cause of nosocomial infections and it is often resistant to many antibiotics. In our hospital it often causes infections in patients on the intensive care unit. The aim of this study was to know the susceptibility of Acinetobacter sp. strains isolated in our hospital. METHODS: The in vitro activities of nine antimicrobial agents (ticarcillin, piperacillin, ceftazidime, imipenem, meropenem, gentamicin, tobramycin, amikacin and colistin) and three beta-lactamase inhibitors (sulbactam, clavulanate and tazobactam) against 107 clinical isolates of Acinetobacter baumannii were studied. MICs were determined by a dilution agar method, except for colistin, which we used the disk-diffusion agar method. RESULTS: Of the antimicrobial agents tested imipenem and colistin were highly active against all isolates (100% susceptibility), meropenem presented good activity (96.3% susceptibility), ticarcillin presented moderated activity (84.1% susceptibility). Most of the strains were resistant to ceftazidime (4.7% susceptibility), piperacillin (3.7% susceptibility) and the aminoglycosides (amikacin 21.5% susceptibility, gentamicin 2.8% susceptibility and tobramycin 4.7% susceptibility). Sulbactam was the most active agent among the beta-lactamase inhibitors studied (CMI90 = 4 micrograms/ml). CONCLUSIONS: Recent trends indicate increasing antimicrobial resistance of Acinetobacter baumannii, posing a serious threat to hospitalized patients. An strict attention to maintain a good housekeeping and control of the environment and of the antimicrobial usage, appears the measures most likely to control the spread of Acinetobacter baumannii in hospitals.

Edenharder R. et al. *Soil mutagens are airborne mutagens: variation of mutagenic activities induced in Salmonella typhimurium TA 98 and TA 100 by organic extracts of agricultural and forest soils in dependence on location and season.* Mutat Res. 2000; 472(1-2) : 23-36.p Abstract: As our hypothesis was that soil mutagens are airborne mutagens, possibly modified by soil microorganisms, we checked solvent extracts from agricultural and forest soils collected during late summer in the environment of Mainz, a region highly charged by anthropogenic air pollution, or near Bayreuth, a rural low charged region of Germany, or in a remote region of western Corsica without anthropogenic air pollution for the presence of mutagenicity in Salmonella typhimurium. Levels of mutagenic activities were quantified by calculation of revertants/g from the initial slope of dose-response curves applying tester strains S. typhimurium TA 98 and TA 100 in the absence and presence of an activation system from rat liver (S9). Three soils from Corsica did not induce mutagenicity under any test condition. However, most soils from Germany exhibited mutagenic activities, though preferentially in strain TA 98, but no statistically significant differences could be detected between 27 soils from the Mainz and nine soils from the Bayreuth regions. On the other hand, no correlation could be detected between the levels of mutagenic activities at any test condition and agricultural practice - rye growing, viniculture, fruit growing, meadow, and fallow - texture of soils - % composition of clay, slit, and sand - or the contents of organic matter. The only significant difference of mutagenicity was, however, found with S. typhimurium TA 98-S9 between forest soils of pH approximately 4.0 as compared with agricultural soils of pH approximately 7.0. The presence of antimutagens in soil as demonstrated by the course of dose-response curves of the three soils from Corsica may be another possible confounder. Calculation of mean values of mutagenic activities for all soils from Germany gave the following results: S. typhimurium TA 98: 69.7+/-153.2 (-S9); 63.0+/-176.3 (+S9); S. typhimurium TA 100:-144.7+/-399.4 (-S9); 43.3+/-172.0 (+S9) revertants/g of dry soil. In another series of experiments, soil mutagenicity in 10 rye fields near Mainz was monitored for 1 year. It became evident that low levels of mutagenic activities in late summer increased during autumn, reached a peak in late winter, and subsequently, decreased during spring and summer. These results agree with the hypothesis of an airborne origin of soil mutagens, deposition, and an adjacent transformation to non-mutagenic compounds by soil microorganisms.

Edlund C. et al. *Effect of vancomycin on intestinal flora of patients who previously received antimicrobial therapy.* Clin Infect Dis. 1997; 25(3) : 729-32.p Abstract: To evaluate the ecological disturbances of peroral vancomycin administration following cephalosporin administration, 20 healthy volunteers received cefuroxime axetil tablets (250 mg) perorally twice a day for 1 week, and 10 of these volunteers subsequently received vancomycin capsules (125 mg) perorally four times daily for 7 days. The concentration of vancomycin in feces after 1 week of vancomycin administration was high (mean +/- SD, 520 +/- 197 mg/kg), which correlated with the ecological disturbances noted in the vancomycin recipients. Vancomycin administration resulted in a rapid decrease in the numbers of intestinal Enterococcus faecium, Enterococcus faecalis, and Enterococcus durans ($P < or = .05$), while there was a significant emergence of motile enterococci with decreased susceptibility to vancomycin (Enterococcus gallinarum and Enterococcus casseliflavus; minimum inhibitory concentration, 4-16 mg/L) ($P < or = .01$). Because of vancomycin administration, there was also a significant overgrowth of vancomycin-resistant Pediococcus species and lactobacilli as well as of Klebsiella species, Citrobacter species, and Enterobacter species ($P < or = .01$). The numbers of bifidobacteria and Bacteroides species were significantly reduced during vancomycin administration. None of the enterococcal strains carried vanA or vanB. Twenty-two of the 27 motile enterococci carried the vanC-1 gene specific for E. gallinarum, whereas five strains carried the vanC-2(C-3) gene, thus implicating that they were E. casseliflavus or Enterococcus flavescens.

Edlund C. et al. *Resistance of the normal human microflora to mercury and antimicrobials after exposure to mercury from dental amalgam fillings.* Clin Infect Dis. 1996; 22(6) : 944-50.p Abstract: The concentrations of mercury in saliva and feces and the resistance pattern of the gastrointestinal microflora were investigated for 20 subjects. Ten patients, with a mean number of 19 amalgam surfaces, had all amalgam fillings removed during one dental session. Ten subjects without amalgam fillings served as a control group. Saliva and fecal samples were collected before amalgam removal and 2, 7, 14, and 60 days afterward. Mercury levels in saliva and feces correlated significantly with the number of amalgam surfaces. No differences in the resistance pattern of the oral microflora were detected between the two groups. In the amalgam group there was an increase in the relative number of intestinal microorganisms resistant to mercury, ampicillin, cefoxitin, erythromycin, and clindamycin on days 7-14. This was not statistically significant in light of the normal variations of the control group. A significant correlation between the prevalence of mercury resistance and multiple antimicrobial resistance in intestinal bacterial strains was observed.

Edmiston C.E. Jr et al. *Airborne particulates in the OR environment.* AORN J. 1999; 69(6) : 1169-72, 1175-7, 1179 passim.p Abstract: Intraoperative sampling of airborne particulates is rarely performed in the OR environment because of technical difficulties associated with sampling methodologies and because of the common belief

that airborne contamination is infrequently associated with surgical site infections (SSIs). In this study, investigators recovered non-viable (i.e., lint) and viable (i.e., microorganisms) particulates during vascular surgery using a personal cascade impactor sampling device. The predominant nonviable particulates recovered during intraoperative sampling were wood pulp fibers from disposable gowns and drapes. Several potential nosocomial pathogens (e.g., Staphylococcus aureus, Staphylococcus epidermidis) and other drug-resistant isolates frequently were recovered from an area adjacent to the surgical field. The widespread presence of airborne particulates during surgery suggests that further studies are warranted to assess the role these particles may play in the development of SSIs or in dissemination of nosocomial pathogens within the OR and hospital environment.

Edmond M.B. et al. *Vancomycin-resistant Enterococcus faecium bacteremia: risk factors for infection*. Clin Infect Dis. 1995; 20(5) : 1126-33.p Abstract: We describe an outbreak of vancomycin-resistant Enterococcus faecium (vanA phenotype) bacteremia on the oncology ward of a tertiary care community hospital. In 10 of the 11 cases the patients had leukemia and were neutropenic (median duration of neutropenia, 21 days) at the time of bacteremia. On average, patients received six antibiotic agents for a total of 61 agent-days prior to development of vancomycin-resistant E. faecium bacteremia. The mortality rate was 73%. Molecular typing of 22 isolates revealed that the majority (83%) represented a common strain, indicating nosocomial spread. When the 11 cases were compared to 22 matched control patients, gastrointestinal colonization with vancomycin-resistant E. faecium (odds ratio [denominator, 0] infinity, P =.005) and the use of antimicrobial agents with significant activity against anaerobes (metronidazole, clindamycin, and imipenem; odds ratio infinity, P =.02) were found to be risk factors for the development of vancomycin-resistant E. faecium bacteremia. Since no proven therapy for such infection exists, there is an urgent need to identify effective measures to prevent and control the development of vancomycin-resistant E. faecium bacteremia.

Edmond M.B. et al. *Nosocomial bloodstream infections in United States hospitals: a three-year analysis.* Clin Infect Dis. 1999; 29(2) : 239-44.p Abstract: Nosocomial bloodstream infections are important causes of morbidity and mortality. In this study, concurrent surveillance for nosocomial bloodstream infections at 49 hospitals over a 3-year period detected >10,000 infections. Gram-positive organisms accounted for 64% of cases, gram-negative organisms accounted for 27%, and 8% were caused by fungi. The most common organisms were coagulase-negative staphylococci (32%), Staphylococcus aureus (16%), and enterococci (11%). Enterobacter, Serratia, coagulase-negative staphylococci, and Candida were more likely to cause infections in patients in critical care units. In patients with neutropenia, viridans streptococci were significantly more common. Coagulase-negative staphylococci were the most common pathogens on all clinical services except obstetrics, where Escherichia coli was most common. Methicillin resistance was detected in 29% of S. aureus isolates and 80% of coagulase-negative staphylococci. Vancomycin resistance in enterococci was species-dependent—3% of Enterococcus faecalis strains and 50% of Enterococcus faecium isolates displayed resistance. These data may allow clinicians to better target empirical therapy for hospital-acquired cases of bacteremia.

Edmond M.B. et al. *Vancomycin-resistant Staphylococcus aureus: perspectives on measures needed for control*. Ann Intern Med. 1996; 124(3) : 329-34.p Abstract: Given the dramatic increase in the incidence of vancomycin resistance among the enterococci and experimental evidence for the transfer of vancomycin resistance from enterococci to Staphylococcus aureus, there is concern that strains of S. aureus will emerge that are resistant to vancomycin. The result would be a highly virulent pathogen for which effective antimicrobial therapy would not be available. To prevent the nosocomial transmission of such an organism, stringent infection control policies need to be developed and implemented. We offer proposals that are based on the limited data available on the transmission and control of S. aureus and that may be used as starting points for the development of formal guidelines for the isolation of colonized and infected patients and for microbiology laboratory precautions.

Edson R.S. et al. *The aminoglycosides.* Mayo Clin Proc. 1999; 74(5) : 519-28.p Abstract: Despite the introduction of newer, less toxic antimicrobial agents, the aminoglycosides continue to serve a useful role in the treatment of serious enterococcal, mycobacterial, and gram-negative bacillary infections. Gentamicin, because of its low cost, remains the aminoglycoside of choice in hospitals with low levels of resistance among Enterobacteriaceae and Pseudomonas aeruginosa. Typically, it is administered in combination with beta-lactam antibiotics, but it may also be used as monotherapy for urinary tract infections or tularemia. Amikacin is useful against gentamicin-resistant gram-negative bacilli and also in the treatment of infections caused by susceptible Nocardia and nontuberculous mycobacteria. Streptomycin serves an important role in the treatment of multidrug-resistant tuberculosis and may be useful in the treatment of some gentamicin-resistant enterococcal infections. Despite an alarming increase in aminoglycoside-resistant enterococci, most institutions have noted little change in patterns of resistance among gram-negative bacilli. Although the development of newer, less toxic aminoglycosides is unlikely in the near future, single daily dosing regimens have been proposed as a convenient, cost-effective strategy. In selected patients, this novel approach seems to be as safe and effective as traditional, multidose regimens.

Edwards R.K. et al. *Expanded-spectrum antibiotics with preterm premature rupture of membranes.* Obstet Gynecol. 2000; 96(1) : 60-4.p Abstract: OBJECTIVE: To compare maternal infection rates, neonatal sepsis rates, and bacterial resistance patterns in cases of neonatal sepsis for three antibiotic protocols for women with preterm premature rupture of membranes (PROM). METHODS: From January 1, 1988 to February 28, 1998, women with preterm PROM not requiring immediate delivery were treated according to one of three antibiotic protocols. During three distinct periods, patients received no antibiotics, intravenous ampicillin for 48 hours followed by oral amoxicillin, or intravenous ticarcillin-clavulanic acid for 48 hours followed by oral amoxicillin-clavulanic acid. Rates of chorioamnionitis, endometritis, and neonatal sepsis were compared, as were antimicrobial resistance patterns. Statistical analysis was done using chi(2) analysis, Fisher exact test, and the log-likelihood ratio test. The Bonferroni correction was used for multiple comparisons. RESULTS: During the three periods, preterm PROM was diagnosed in 1695 women. The incidence of endometritis was lower during the third (5.3%) compared with the first (15.1%, P <.001) and second (11.6%, P <.001) protocols. Chorioamnionitis rates were 13.6%, 12.7%, and 15.6% (P =.34) for the first, second, and third periods, respectively, and neonatal sepsis rates were 2.2%, 0.6%, and 1.1% (P =.08), respectively. Neonatal sepsis with gram-negative (P =.02) and ampicillin-resistant (P =.04) organisms was more likely when mothers received antepartum ampicillin or ticarcillin-clavulanic acid. CONCLUSION: Antibiotic therapy for patients with preterm PROM was associated with a decrease in the rate of endometritis and a trend toward less neonatal sepsis but an increase in the proportion of gram-negative and ampicillin-resistant organisms causing neonatal sepsis.

Egerer G. et al. *Efficacy of continuous infusion of ceftazidime for patients with neutropenic fever after high-dose chemotherapy and peripheral blood stem cell transplantation*. Int J Antimicrob Agents. 2000; 15(2) : 119-23.p Abstract: Neutropenia is an important complication of high-dose chemotherapy (HDCT). Neutropenic patients presenting with fever are routinely hospitalized for treatment with broad-spectrum antibiotics. Neutropenia up to 10 days is associated with a low-risk profile, and antimicrobial therapy administered on an outpatient basis might be an alternative to admission to hospital. This prospective study evaluates the safety of a continuous infusion of ceftazidime in

neutropenic patients after HDCT and peripheral blood stem cell transplantation (PBSCT). From September 1995 to October 1999, 81 patients received a 2 g intravenous bolus of ceftazidime, followed by a 4 g continuous infusion per 24 h of ceftazidime using a portable infusion pump. If the fever persisted for 72 h, a glycopeptide antibiotic was added. The median patients' age was 44 years. Fifty-two of 81 patients (64%) responded to the monotherapy with ceftazidime. After addition of a glycopeptide antibiotic, a further 17 patients (21%) became afebrile. The causes of fever were septicaemia in 11 patients, pneumonia in two and fever of unknown origin in 68 patients. Fifty-eight episodes (72%) were successfully managed by outpatient treatment alone. The reason for admission to hospital was the change to imipenem/cilastin, which had to be administered three times per day (12 patients), severe mucositis with parenteral nutrition (eight patients), or a Karnovsky index </=60 (three patients). In six of these cases, outpatient treatment was resumed after a brief period of in-patient care. In no case was the treatment terminated because of failure of the pump. With daily follow-up and close monitoring for development of complications, it is possible to discharge patients earlier after HDCT and PBSCT, thereby decreasing costs.

Egger S.F. et al. *[Contamination of intraocular fluid in pars plana vitrectomy].* Ophthalmologe. 1996; 93(2) : 126-9.p Abstract: Endophthalmitis after pars plana vitrectomy is rare, with an incidence of 0.05-0.14%. The aim of this study was to evaluate the microbiological situation during pars plana vitrectomy and to ascertain what organisms and how many enter the eye during the operation. PATIENTS AND METHODS: Twenty-five consecutive subjects undergoing primary pars plana vitrectomy were included in the study. Patients were excluded if they had evidence of local or systemic infections or had undergone antibiotic therapy within 3 weeks before surgery. A standard three-port pars plana vitrectomy was performed on each patient. Preoperative smears of the conjunctiva and intraoperative aspirates of the vitreous were taken immediately after sclerotomy, and aspirates of the intraocular fluid at the conclusion of operation. RESULTS: We obtained preoperative smears from the conjunctival sac of all patients, and found that 19 patients (76%) had positive cultures, with coagulase-negative staphylococci as the most commonly isolated organisms, (n = 14; 56%). Vitreous—aspirated immediately after sclerotomy—was sterile in 68% (n = 17). In 32% (n = 8) contamination occurred, the microorganisms isolated being coagulase-negative staphylococci (20%) and Staphylococcus aureus (12%). Five of the samples (20%) of intraocular fluid from the vitreous cavity—aspirated before wound closure—were contaminated, coagulase-negative staphylococci (8%) and Staphylococcus aureus (12%) again being found in culture. In no case did postoperative endophthalmitis develop. CONCLUSIONS: This study demonstrates that bacteria enter the eye during pars plana vitrectomy and that there is a change in the contaminating bacterial species during operation. Even if bacteria remain in the eye after pars plana vitrectomy, postoperative endopthalamitis does not necessarily develop.

Eggers C. et al. *Rapid clearance of human immunodeficiency virus type 1 from ventricular cerebrospinal fluid during antiretroviral treatment.* Ann Neurol. 2000; 47(6) : 816-9.p Abstract: To understand the pathogenesis of human immunodeficiency virus-induced neuropathology, it is critical to know the dynamics of viral replication in the central nervous system. Viral decay kinetics were mathematically analyzed from multiple serial specimens of ventricular cerebrospinal fluid and plasma during antiretroviral therapy in a patient with asymptomatic human immunodeficiency virus infection and an external ventricular catheter for hydrocephalus. A rapid exponential decay of virus with an elimination half-life of 4.2 days in ventricular cerebrospinal fluid and 2.3 days in plasma was found. Sequencing the V3 loop-encoding envelope gene of virus in both compartments revealed high sequence homology. The combined data suggest that virus in ventricular cerebrospinal fluid is at least partly contributed by rapidly replicating virus-producing cells recruited from the circulation.

Eggimann P. et al. *Impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care.* Lancet. 2000; 355(9218) : 1864-8.p Abstract: BACKGROUND: Intravascular devices are a leading cause of nosocomial infection. Specific prevention strategies and improved guidelines for the use of intravascular devices can decrease the rate of infection; however, the impact of a combination of these strategies on rates of vascular-access infection in intensive-care units (ICUs) is not known. We implemented a multiple-approach prevention programme to decrease the occurrence of vascular-access infection in an 18-bed medical ICU at a tertiary centre. METHODS: 3154 critically ill patients, admitted between October, 1995, and November, 1997, were included in a cohort study with longitudinal assessment of an overall catheter-care policy targeted at the reduction of vascular-access infections and based on an educational campaign for vascular-access insertion and on device use and care. Incidence of ICU-acquired infections was measured by means of on-site surveillance. FINDINGS: 613 infections occurred in 353 patients (19.4 infections per 100 admissions). The incidence density of exit-site catheter infection was 9.2 episodes per 1000 patient-days before the intervention, and 3.3 episodes per 1000 patient-days afterwards (relative risk 0.36 [95% CI 0.20-0.63]). Corresponding rates for bloodstream infection were 11.3 and 3.8 episodes per 1000 patient-days, respectively (0.33 [0.20-0.56]) due to decreased rates of both microbiologically documented infections and clinical sepsis. Rates of respiratory and urinary-tract infections remained unchanged, whereas those of skin or mucous-membrane infections decreased from 11.4 to 7.0 episodes per 1000 patient-days (0.62 [0.41-0.93]). Overall, the incidence of nosocomial infections decreased from 52.4 to 34.0 episodes per 1000 patient-days (0.65 [0.54-0.78]). INTERPRETATION: A multiple-approach prevention strategy, targeted at the insertion and maintenance of vascular access, can decrease rates of vascular-access infections and can have a substantial impact on the overall incidence of ICU-acquired infections.

Eginton P.J. et al. *Quantification of the ease of removal of bacteria from surfaces.* J Ind Microbiol. 1995; 15(4) : 305-10.p Abstract: This paper describes a technique which reproducibly quantifies the ease of removal of microorganisms from surfaces. Tiles (22 mm x 22 mm) of various materials were colonised with Staphylococcus epidermidis NCTC 11047, Escherichia coli K12 HB101 or Pseudomonas aeruginosa PaWH, by submersion, for various times (2 min-48 h), in inoculated Tryptone Soya broth (37 degrees C). Colonised tiles were blotted onto a Tryptone Soya agar plate for 1 min and the process was repeated through a succession of agar plates. The final plate contained tetrazolium salts (0.05% w/v) and was incubated in situ with the tile. Tetrazolium plates indicated that very few organisms remained on the tiles after 15 successive blots. In all instances, the number of recovered colonies per plate decreased exponentially with plate succession number, according to the relationship, CFU = A.10-kN, where CFU is the number of colonies transferred, k is the removal exponent, A is the intercept and N is the plate succession number. Removal exponents differed significantly between organisms ($P > 0.95$), depended on the nature of the test surface, and decreased as the inital attachment and colonisation time was increased from 2 min-48 h. Intercept values (A) but not the gradients were dependent upon the initial numbers of bacteria in suspension. These data indicate that the gradients derived from counting recoverable viable cells from successive blots of test tiles onto agar is a measure of the strength of attachment of the organisms to the surface.

Ehret J.M. et al. *A clinical isolate of Neisseria gonorrhoeae with in vitro resistance to erythromycin and decreased susceptibility to azithromycin.* Sex Transm Dis. 1996; 23(4) : 270-2.p Abstract: BACKGROUND AND OBJECTIVES: Erythromycin is a recommended treatment for penicillin-allergic pregnant women with gonorrhea, and azithromycin has been suggested as therapy for coexisting gonococcal and chlamydial infections. Although gonococcal resistance to

erythromycin is not uncommon, decreased resistance to azithromycin is rare. A clinical isolate of Neisseria gonorrhoeae with in vitro resistance to erythromycin and decreased susceptibility to azithromycin is reported. STUDY DESIGN: This is a case report. RESULTS: Antimicrobial susceptibility testing of a clinical isolate of N. gonorrhoeae revealed a minimal inhibitory concentration (MIC) of 2 micrograms/ml to azithromycin and 32 micrograms/ml to erythromycin. Five hundred other urethral isolates were tested, resulting in an MIC for erythromycin ranging from 0.015 to 2 micrograms/ml. The range for azithromycin was 0.015 to 0.5 micrograms/ml. There was a strong correlation between erythromycin and azithromycin MICs ($r = 0.73$; $P < 0.0001$). CONCLUSIONS: Continued national monitoring is needed to detect the appearance and early dissemination of new types of gonococcal resistance.

Eick S. et al. *Antimicrobial susceptibility of anaerobic and capnophilic bacteria isolated from odontogenic abscesses and rapidly progressive periodontitis.* Int J Antimicrob Agents. 1999; 12(1) : 41-6.p Abstract: In dentistry antimicrobials are used in the treatment of progressive periodontitis and odontogenic abscesses, therefore the susceptibility to commonly used antibiotics of capnophilic and anaerobic species causing these diseases should be investigated. The activity of penicillin, amoxycillin, cefoxitin, clindamycin, doxycycline, metronidazole and ciprofloxacin was investigated. One hundred and sixty four isolates from subgingival plaque samples of 66 patients with progressive periodontitis and 192 bacterial strains from pus of 74 patients with odontogenic abscesses were included in this study. The majority of species tested were gram-negative anaerobes (Prevotella spp., Porphyromonas spp., Fusobacterium spp.), and were highly susceptible to clindamycin and metronidazole. Nearly 6% of the periodontal isolates and 22% of the bacteria obtained from pus samples produced beta-lactamases. With the exception of the periodontopathogenic species Actinobacillus actinomycetemcomitans and Eikenella corrodens, clindamycin seemed to be a useful antibiotic and could be recommended for empirical antimicrobial treatment.

Eisen D.P. et al. *Candida tropicalis vertebral osteomyelitis complicating epidural catheterisation with disease paralleled by elevated D-arabinitol/L-arabinitol ratios.* Eur J Clin Microbiol Infect Dis. 2000; 19(1) : 61-3.p Abstract: Deep-seated Candida infections are challenging to diagnose by noninvasive means, and new modalities are needed to improve the yield of such investigations. Reported here is a case of Candida tropicalis vertebral osteomyelitis complicating epidural catheterisation in a diabetic patient with complicated abdominal sepsis. The diagnosis was supported by detection of increased D-arabinitol/L-arabinitol ratios in urine samples, and failure of medical management was indicated by elevated D-arabinitol/L-arabinitol ratios, which later decreased to baseline with successful surgical debridement and prolonged antifungal therapy.

Eisenburger P. et al. *Acute renal failure and rhabdomyolysis after inadvertent intra-arterial infusion of excessive doses of epinephrine during cardiopulmonary resuscitation.* Wien Klin Wochenschr. 2000; 112(4) : 174-6.p Abstract: Severe renal dysfunction or even acute renal failure necessitating renal replacement therapy are rather infrequent observations in patients following cardiopulmonary resuscitation. A low flow situation alone does not seem to be sufficient for renal breakdown and in addition other factors, such as preexisting renal disease, severe infections or congestive heart failure must be present. We report a patient, in whom during cardiopulmonary resuscitation a central venous catheter was placed which inadvertently was located in the aortic arch. Through this malpositioned line increasing and finally excessive amounts of epinephrine (in total 150 mg) were injected because of inadequate therapeutic response. After finally successful resuscitation the patient developed rhabdomyolysis and acute renal failure, which required hemodialyis therapy. Intraarterial infusion of the vasoconstrictor catecholamine obviously caused a critical reduction in renal and skeletal muscle perfusion. Nevertheless, the patient was discharged from hospital in good neurologic condition and with normal renal function.

El-Karsh T. et al. *Antimicrobial resistance and prevalence of extended spectrum beta-lactamase among clinical isolates of gram-negative bacteria in Riyadh.* J Chemother. 1995; 7(6) : 509-14.p Abstract: The activity of ciprofloxacin, imipenem and 12 other commonly used antibiotics was evaluated against 106 documented clinical isolates from a medical Intensive Care Unit (ICU). The resistance rates to ceftriaxone, cefotaxime, aztreonam and ceftazidime were 42, 25, 24 and 21%, respectively. Apart from Pseudomonas aeruginosa, all isolates were sensitive to ciprofloxacin and imipenem. Complete cross resistance among tested beta-lactam groups was uniformly evident in Enterobacter cloacae, Citrobacter freundii and P. aeruginosa. On the other hand, penicillins and second generation cephalosporins showed cross resistance among Escherichia coli and Klebseilla pneumoniae isolates. Induction experiments indicate that 70 and 62% of P. aeruginosa and E. cloacae or C. freundii produce class I cephalosporinase, respectively. Among all tested isolates, plasmid mediated extended spectrum beta-lactamase (ESBL) was detected in one isolate of K. pneumoniae. The plasmid mediated beta-lactamase is transferable and inhibited by beta-lactamase inhibitors. The transconjugates not only expressed resistance to extended spectrum beta-lactams and aztreonam but also toward tested aminoglycoside antibiotics, with the exception of gentamicin. The obtained transconjugates conferred high level resistance to ceftazidime and aztreonam but considerably low resistance to ceftriaxone and cefotaxime. The isoelectric point for the extended-spectrum beta-lactamase is 8.2.

el-Shaaer H.M. et al. *Synthesis, antimicrobial activity and bleaching effect of some reaction products of 4-oxo-4H-benzopyran-3-carboxaldehydes with aminobenzothiazoles and hydrazides.* Farmaco. 1998; 53(3) : 224-32.p Abstract: The synthesis of the biologically active novel systems derived from reaction of 3-formylchromones with three types of amino derivatives, 6-R2-2-aminobenzothiazoles, 6-amino-2-R3-thiobenzothiazoles and hydrazide derivatives (derived from cyanoacetic, isonicotine, salicylic and gallic acids) was carried out. The structures of the prepared compounds have been proved by elemental analysis, 1H NMR and IR spectra. Antimicrobial activity was studied against the following microorganisms—bacteria G+ (Staphylococcus aureus 29/58, Bacillus subtilis 18/66), G- (Escherichia coli 326/71, Pseudomonas aeruginosa); yeasts: Candida albicans, Saccharomyces cerevisiae; moulds: Microsporum gypseum, Aspergillus niger, Scopulariopsis brevicaulis; and against typical and atypical mycobacteria: Mycobacterium tuberculosis (H37Rv), Mycobacterium kansasii (PFG 8), Mycobacterium avium (My 80/72), Mycobacterium fortuitum (1021). The hereditary bleaching effect on the plastid system of Euglena gracilis, a unique phenomenon of the biological activity of chromone derivatives, is reported. The bleaching test on E. gracilis is used for detecting extranuclear mutations.

Elbim C. et al. *Defective priming of the phagocyte oxidative burst in a child with recurrent intracellular infections.* Microbes Infect. 1999; 1(8) : 581-7.p Abstract : Human phagocytes (polymorphonuclear neutrophils and monocytes) play a critical role in host defense against invading microorganisms. Recent studies reported that circulating phagocytes undergo a final maturation process, in particular in terms of oxidative burst, during extravasation and migration to local sites of inflammation. This process is known as priming. We report here on a nine-year-old boy with successive disseminated infections due to intracellular microorganisms (Mycobacterium bovis, BCG, and Salmonella typhimurium). No T- or B-cell quantitative or qualitative defects were found. Polymorphonuclear neutrophil (PMN) migration and NADPH oxidase in PMNs and monocytes stimulated with various agents at optimal concentrations were normal, ruling out a leukocyte adhesion deficiency syndrome, a Chediak Higashi syndrome, and a chronic granulomatous disease. Nevertheless, the patient's PMNs and monocytes showed defective priming capacity, as measured by H(2)O(2) production after pretreatment with LPS (5

microg/mL for 30 min), TNFalpha (100 units/mL for 30 min), or IL-8 (50 ng/mL for 30 min) in response to bacterial N-formyl peptides (fMLP 10(-6) M for 5 min). In these conditions, H(2)O(2) production of PMNs and monocytes from the patient did not exceed that of the samples treated with fMLP or LPS alone, while the controls strongly produced H(2)O(2). Moreover, monocytes from the patient showed an impaired capacity to kill S. typhimurium in vitro. Such an impairment could be related at least in part to the priming deficiency of phagocyte oxidative burst. This case suggests, for the first time, that in vivo priming processes are critical in host defence against intracellular pathogens.

Elduayen B. et al. *Central venous catheter placement in the inferior vena cava via the direct translumbar approach*. Eur Radiol. 2000; 10(3) : 450-4.p Abstract: The aim of this study was to evaluate the technical aspects and efficacy of placing tunneled central venous access catheters (CVA) in the inferior vena cava (IVC) via a direct translumbar approach. Between August 1994 and July 1998, 50 CVA (Hickman 13.5 F) were placed in the IVC via a direct translumbar approach in 46 patients (10 males, 36 females) with a mean age of 39.9 years (age range 10-87 years). The indications were chemotherapy administration plus leukoaphoresis (n = 39), bone marrow transplantation (n = 2) and hemodialysis (n = 5). The reasons for placing the CVA in the IVC were cosmetic (n = 34), supradiaphragmatic venous thrombosis (n = 8), previous catheter infection (n = 2), and non-functioning arteriovenous fistula (n = 2). There were no immediate complications. The mean period of time the CVA was in place was 3 months (15 days to 15 months), during which the function was excellent. The commonest late complication was infection (4 local, 6 bacteremia). Others included: pain (n = 2), ureteric fistula (n = 1), pericatheter fibrin sheath formation (n = 6) and catheter-tip impaction (n = 2). Two catheters were damaged due to postprocedural inappropriate manipulations and two others fell off due to incorrect fixation. Due to these complications, it was necessary to remove ten catheters, replace an additional four and reposition two. Direct translumbar catheterization of the IVC is a safe and effective way of placing a long-term CVA with a moderate complication rate.

Eliopoulos G.M. *In vitro activity of fluoroquinolones against gram-positive bacteria*. Drugs. 1995; 49 Suppl 2 : 48-57.p Abstract: This paper reviews the in vitro activities of several newer fluoroquinolone antimicrobials that exhibit enhanced potency against Gram-positive bacteria. Several of these agents demonstrate 10-fold greater activity than older members of this class against Staphylococcus aureus and inhibit [minimum inhibitory concentration (MIC90) values < or = 2 mg/L] many isolates resistant to ciprofloxacin or ofloxacin. Markedly enhanced activity is also noted against Streptococcus pneumoniae, 90% of isolates being inhibited at concentrations 10- to 100-fold lower than those of the older agents. Enterococci also exhibit greater susceptibility to several of the newer fluoroquinolones, although relative cross-resistance with the earlier drugs is noted. As determined by dilution techniques, the new fluoroquinolones generally demonstrate bactericidal activity at concentrations at or near their MIC values. The activities of the new compounds described here are decreased at low pH, but are not affected by the addition of up to 50% human serum to the test medium. Resistance is rarely detected (frequency < 10(-9)) when high density bacterial suspensions are plated in the presence of 4 times the MIC of these compounds. However, colonies displaying relative resistance to the new agents can be selected by serial passage in incremental antimicrobial concentrations.

Eliopoulos G.M. et al. *Characterization of vancomycin-resistant Enterococcus faecium isolates from the United States and their susceptibility in vitro to dalfopristin-quinupristin*. Antimicrob Agents Chemother. 1998; 42(5) : 1088-92.p Abstract: In the course of clinical studies with the investigational streptogramin antimicrobial dalfopristin-quinupristin, isolates of vancomycin-resistant Enterococcus faecium were referred to our laboratory from across the United States. Seventy-two percent of the strains were of the VanA type, phenotypically and genotypically, while 28% were of the VanB type. High-level resistance to streptomycin or gentamicin was observed in 86 and 81%, respectively, of the VanA strains but in only 69 and 66%, respectively, of the VanB strains. These enterococci were resistant to ampicillin (MIC for 50% of the isolates tested [MIC50] and MIC90, 128 and 256 microg/ml, respectively) and to the other approved agents tested, with the exception of chloramphenicol (MIC90, 8 microg/ml) and novobiocin (MIC90, 1 microg/ml). Considering all of the isolates submitted, dalfopristin-quinupristin inhibited 86.4% of them at concentrations of < or = 1 microg/ml and 95.1% of them at < or = 2 microg/ml. However, for the data set comprised of only the first isolate submitted for each patient, 94.3% of the strains were inhibited at concentrations of < or = 1 microg/ml and 98.9% were inhibited at concentrations of < or = 2 microg/ml. Multiple drug resistance was very common among these isolates of vancomycin-resistant E. faecium, while dalfopristin-quinupristin inhibited the majority at concentrations that are likely to be clinically relevant.

Elliott J.A. et al. *Antimicrobial susceptibilities of Lactococcus lactis and Lactococcus garvieae and a proposed method to discriminate between them*. J Clin Microbiol. 1996; 34(5) : 1296-8.p Abstract: The MICs of antimicrobial agents contained in the SCEPTOR Streptococcus MIC panels (Becton Dickinson Microbiology Systems) were determined for Lactococcus lactis, L. garvieae, and unknown Lactococcus species. Several isolates had reduced susceptibilities to many of the antimicrobial agents contained in the panel. For L. garvieae, the MICs of penicillin and, possibly, cephalothin were higher than for L. lactis, and unlike L. lactis, L. garvieae was resistant to clindamycin, indicating that knowledge of the Lactococcus species causing an infection might influence the choice of antimicrobial therapy. Susceptibility to clindamycin can also be used to differentiate between L. lactis and L. garvieae.

Elliott T. *Intravascular catheter-related sepsis—novel methods of prevention*. Intensive Care Med. 2000; 26 Suppl 1 : S45-50.p Abstract: Intravascular catheter-related sepsis continues to cause a significant degree of morbidity and mortality, and accounts for the majority of staphylococcal bacteraemias and septicaemias in hospitalised patients. Methods designed to prevent these infections include those directed at aseptic techniques involving the patient and improvements in catheter design. More recently catheters which are either coated or have incorporated into their polymers antimicrobial agents have been developed. The antimicrobial agents have included both antimicrobials which are used to treat infections as well as antiseptics. The antimicrobial catheters currently available appear to only give protection for relatively short periods of time (approximately 14 days). The use of these antimicrobial catheters needs to be restricted to the situation where infection rates and the risk to the patient of sepsis are relatively high. Further novel approaches for the prevention of these infections include the combination of low voltage electric current together with antimicrobials; these await clinical evaluation.

Elliott T.S. et al. *Antibacterial resistance in the intensive care unit: mechanisms and management*. Br Med Bull. 1999; 55(1) : 259-76.p Abstract: The incidence of multiple antimicrobial resistance of bacteria which cause infections in the intensive care unit is increasing. These include methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci, penicillin-resistant Streptococcus pneumoniae and cephalosporin and quinolone resistant coliforms. More recently, pan antibiotic resistant coliforms, including carbapenems, have emerged. The rapidity of emergence of these multiple antibiotic-resistant organisms is not being reflected by the same rate of development of new antimicrobial agents. It is, therefore, conceivable that patients with serious infections will soon no longer be treatable with currently available antimicrobials. Strict management of antibiotic policies and surveillance programmes for multiple resistant organisms, together with infection control procedures, need to be implement-

ed and continuously audited. As intensive care units provide a nidus of infection for other areas within hospitals, this is critically important for prevention of further spread and selection of these resistant bacteria.

Elliott T.S. et al. *Novel approach to investigate a source of microbial contamination of central venous catheters.* Eur J Clin Microbiol Infect Dis. 1997; 16(3) : 210-3.p Abstract: The potential route of contamination by skin microorganisms onto the distal tip of central venous catheters during insertion was investigated. Thirty patients undergoing cardiac surgery who required a central venous catheter (CVC) as part of their clinical management were studied. Following catheter placement, the device insertion equipment and the skin at the insertion site were sampled for microorganisms. The distal tips of the CVCs were also sampled in situ within 90 min post insertion. Bacteria were isolated from 20 of 30 (66%) CVC skin insertion sites, from 15 of 30 (50%) guidewires, and from five of 30 (16%) catheter distal tips in situ. These findings suggest that despite rigorous skin disinfection and strict aseptic technique, viable microorganisms are impacted during insertion onto the distal tip of the CVC, which may act as a subsequent nidus of infection.

Elliott T.S. et al. *Improved recovery of antibiotic-stressed microorganisms on inclusion of saponin in aerobic blood culture media.* Eur J Clin Microbiol Infect Dis. 1998; 17(8) : 566-9.p Abstract: The recovery rates and times to detection of microorganisms isolated from two similar blood culture media, one containing saponin, were compared. A total of 2117 blood cultures were analysed in a prototype automated blood culture system. Significantly more gram-positive organisms ($P<0.05$) and gram-negative organisms ($P<0.05$), including Enterobacteriaceae ($P<0.05$) were recovered from the lytic medium. Average time to detection in the lytic medium was 15.8 h, compared to 22.7 h in the other medium ($P<0.001$). The improved recovery of microorganisms was most pronounced in blood samples obtained from patients being treated with antibiotics at the time of venesection. In vitro experiments on antibiotic affected bacteria confirmed the protective effect of saponin.

Ellstrom K.E. *Breathing easier in the intensive care unit. Pneumonia.* Crit Care Nurs Clin North Am. 1999; 11(4) : 409-22.p Abstract: Pneumonia, whether it is community-acquired, hospital-acquired, or ventilator-acquired, has a high incidence with associated high morbidity and mortality. The continuing emergence of resistant organisms is an indication that appropriate measures are still not effective or are not being used effectively to control the incidence of HAP and VAP as well as evidence of the overuse of antibiotics. Nurses are key in identifying patients at risk and instituting preventive measures. Continuing issues are the use of an adequate handwashing technique and elevation of the head of the bed for prevention of HAP and VAP and immunization of all patients at risk for CAP. Effective interventions can be evaluated by following best practices, using quality and process improvement methodology, and measuring appropriate outcomes.

Elmer G.W. et al. *Biotherapeutic agents. A neglected modality for the treatment and prevention of selected intestinal and vaginal infections.* JAMA. 1996; 275(11) : 870-6.p Abstract: OBJECTIVE: To evaluate the potential of biotherapeutic agents (microorganisms with therapeutic properties) for the prevention and/or treatment of selected intestinal and vaginal infections. DATA SOURCES: The MEDLINE database was searched for all relevant articles published between 1966 and September 1995. Search terms used were biotherapeutic agent, probiotic, Lactobacillus, Saccharomyces, Bifidobacterium, Candida, gastrointestinal- system, vaginitis, vaginosis-bacterial, and related terms. The bibliographies of obtained articles were also reviewed. STUDY SELECTION AND DATA EXTRACTION: All placebo-controlled human studies on biotherapeutic agents were reviewed. English-language open trials, case series and reports, and animal studies were reviewed only if they were especially relevant to providing information on the potential efficacy, adverse effects, or mechanisms of action of these agents. DATA SYNTHESIS: Placebo-controlled studies have shown that biotherapeutic agents have been used successfully to prevent antibiotic-associated diarrhea (Lactobacillus caseiGG, bifidobacterium longum, B longum with L acidophilus, and Saccharomyces boulardii), to prevent acute infantile diarrhea (Bifidobacterium bifidum with Streptococcus thermophilus), to treat recurrent Clostridium difficile disease (S boulardii), and to treat various other diarrheal illnesses (Enterococcus faecium SF68, L caseiGG, and S boulardii). There is also evidence for Lactobacillus acidophilus in the prevention of candidal vaginitis. Few adverse effects have been reported. However, many of the studies tested only small numbers of patients or volunteers. CONCLUSIONS: There is now evidence that administration of selected microorganisms is beneficial in the prevention and treatment of certain intestinal and, possibly, treatment of vaginal infections. In an effort to decrease the reliance on antimicrobials, the time has come to carefully explore the therapeutic applications of biotherapeutic agents.

Eloubeidi M.A. et al. *The great imitator: Rocky Mountain spotted fever occurring after hospitalization for unrelated illnesses.* South Med J. 1997; 90(9) : 943-5.p Abstract: We describe two patients who had Rocky Mountain spotted fever after they were admitted to the hospital for emergency and elective surgical procedures. We initially thought one patient had a hospital-acquired infection; the correct diagnosis was deduced from epidemiologic clues elicited by consultants. These two cases were also unusual in that one patient had a recurrent rash after an abbreviated course of low-dose doxycycline therapy and the other patient had transient and self-limiting postinfectious polyneuropathy. These cases illustrate that community-acquired infection with Rickettsia rickettsii can occur simultaneously with other disease processes and sometimes mimic a nosocomial infection.

Elsakr R. et al. *Antimicrobial treatment of intra-abdominal infections.* Dig Dis. 1998; 16(1) : 47-60.p Abstract: There have been several recent changes that influence the management of intra-abdominal infections. These changes include important developments in antibiotic resistance such as increases in pneumococcal resistance, emergence of multi-drug-resistant enterococcal isolates, and decreasing sensitivity of anaerobes and gram-negative rods. In addition there are new antibiotics such as piperacillin/tazobactam, and new antibiotic dosing regimens such as single daily dosing of aminoglycosides. In this article, we will review the therapeutic approach to intra-abdominal infections with special emphasis on the various forms of peritonitis, cholecystitis, cholangitis, and diverticulitis. Several new concepts about the treatment of enterococcus, the management of bacterial and fungal peritonitis, and the prevention of spontaneous bacterial peritonitis will also be reviewed. Specific recommendations for the management of the different infections including antibiotic doses and costs will be provided. Finally the role of invasive procedures in the management of some of the infections will be explored.

Elsner H.A. et al. *In vitro susceptibilities of enterococcal blood culture isolates from the Hamburg area to ten antibiotics.* Chemotherapy. 2000; 46(2) : 104-10.p Abstract: Treatment of enterococcal infections is often difficult because of intrinsic and acquired resistance to a variety of antimicrobial agents. Between January 1993 and May 1997, enterococci were isolated from blood cultures of 117 patients at the Institute of Medical Microbiology and Immunology, University Hospital Eppendorf, Hamburg, Germany. Eightynine (76%) isolates were phenotypically identified as Enterococcus faecalis, and 24 (21%) as Enterococcus faecium. All E. faecalis isolates, but only 17% of the E. faecium isolates were susceptible to ampicillin. Two E. faecium isolates (8%) but no E. faecalis were vancomycin resistant (vanA genotype). Quinupristin/dalfopristin shows a high degree of susceptiblity of E. faecium (79%) and may be suitable for the therapy of infections caused by glycopeptide-resistant E. faecium strains.

Eltahawy A.T. *Gram-negative bacilli isolated from patients in intensive care unit: prevalence and antibiotic susceptibility.* J Chemother. 1997; 9(6) : 403-10.p Abstract: The surveillance of 100 gram-negative bacilli that were recovered from patients in the intensive care unit (ICU) at King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia showed that Pseudomonas aeruginosa, Klebsiella pneumoniae, Escherichia coli, and Enterobacter species, in this order, were the most frequently isolated organisms. The most common sites were respiratory tract (34%), wounds (24%), urinary tract (18%), and blood (11%). The resistance patterns towards different antimicrobial agents were determined by the minimal inhibitory concentration (MIC) using the E test. Imipenem, ciprofloxacin and amikacin were the most active agents against the isolates. Of the gram-negative isolates, 31% were resistant to at least two of the four major antibiotic groups (e.g. aminoglycosides, fluoroquinolones, third generation cephalosporins, and carbapenems), and 6% to three of the groups. Twenty-nine percent of the gram-negative bacilli were resistant to ceftazidime. Ceftazidime-resistant bacteria were frequently resistant to monobactams, piperacillin/tazobactam and gentamicin.

Eltringham I.J. et al. *Multiple drug resistant tuberculosis: aetiology, diagnosis and outcome.* Br Med Bull. 1998; 54(3) : 569-78.p Abstract: Tuberculosis is an increasing problem worldwide both in terms of disease burden and resistance to conventional antibiotic therapy. Studies of outbreaks involving resistant strains have highlighted the need for both improved infection control and the rapid provision of accurate susceptibility data. Each patient should undergo a risk assessment for possible resistance and those in whom risk factors exist should be investigated by means of rapid molecular techniques or other phenotypic methods, so that appropriate management can be instituted with minimal delay. The ultimate outcome will vary according to whether the patient is immunosuppressed, the time taken to make a diagnosis, the severity of disease as well as the degree of resistance. The prognosis can be improved when adequate antibiotic therapy is started as soon as resistance is suspected. Adjuncts to conventional treatment, such as surgery and perhaps immunotherapy may be considered when response to antimicrobial chemotherapy has been suboptimal.

Elving G.J. et al. *Antimicrobial activity of synthetic salivary peptides against voice prosthetic microorganisms.* Laryngoscope. 2000; 110(2 Pt 1) : 321-4.p Abstract: OBJECTIVES: To investigate whether synthetic salivary antimicrobial peptides have an inhibitory effect on the growth of bacteria and yeasts isolated from used silicone rubber voice prostheses. METHODS: The antimicrobial activities of six synthetic salivary peptides (histatin 5, dhvarl, dhvar4, dhvar5, lactoferrin b 1730 [LFb 17-30], and cystatin S1-15) at concentrations of 2 and 4 mg/mL were determined against different oropharyngeal yeast (four) and bacterial (eight) strains and against a "total microflora" isolated from explanted voice prostheses using agar diffusion tests. The spectrum of susceptible microorganisms was determined qualitatively. RESULTS: Histatin 5 and cystatin S1-15 did not show any antimicrobial activity against the microorganisms involved in this study. Dhvar1 was active against some of the oropharyngeal microorganisms tested, including the yeast strains, but not against Rothia dentocariosa, Staphylococcus aureus, Escherichia coli, and the total microflora Dhvar4 was active against all microorganisms tested, including the total microflora. Dhvar5 lacked activity against E coli and the total microflora LFb 1730 did not inhibit the growth of any of the yeast strains involved and showed only minor activity against some of the bacterial strains. LFb 1730 slightly inhibited the growth of the total microflora from an explanted prosthesis. CONCLUSIONS: The synthetic salivary peptide dhvar4 has a broad antimicrobial activity against all microorganisms that are commonly isolated from explanted voice prostheses, including yeasts. Therewith, it may represent a useful drug, as an alternative for antibiotics and antimycotics employed in various ways to prolong the lifetime of voice prostheses in laryngectomees.

Elvira J. et al. *[A prospective study of meningitis diagnosed in a 3rd-level hospital during a 1-year period].* Rev Clin Esp. 1999; 199(9) : 576-82.p Abstract: OBJECTIVE: One-year prospective observational study of meningitis diagnosed at a third level hospital. PATIENTS AND METHODS: All patients with a cerebrospinal fluid (CSF) specimen with cyto-biochemical characteristics and clinical picture consistent with meningitis were included in the study. They were followed from admission to hospital up to discharge or exitus. The epidemiologic characteristics of patients, etiology, related risk factors and predisposing situations, CSF characteristics, clinical manifestations, clinical course, and antibiotic susceptibility of the causative agents were analyzed. RESULTS: Ninety-five cases were included. Seventy-six (69.4%) were community acquired and 29 (30.5%) nosocomially acquired meningitis. Among community acquired meningitis, 31 (46.9%) were of bacterial origin (8 N. meningitidis, 3 H. influenzae, 2 S. pneumoniae, 1 Streptococcus group B, 1 Listeria monocytogenes, 1 Staphylococcus aureus, and 1 Brucella spp.); CSF culture was negative in 14 cases (41.2%). In most cases neither risk factor nor predisposing situations were detected. Patients with purulent meningitis and negative CSF culture had a significantly lower number of complications than patients with positive CSF culture. Among patients previously treated with beta-lactam antibiotics (8 cases) the probability of a negative CSF culture was greater than among not treated patients (OR 16.00, 95% CI 1.45-764.68; p = 0.011). The remaining cyto-biochemical characteristics were similar in both groups. Thirty-five cases (53.03%) of community acquisition were lymphocytic meningitis (31 viral, 3 tuberculous, and 1 luetic meningitis). Among nosocomial cases (29 cases, 30.5%), most were caused by gram-negative bacilli and microorganisms of the Staphylococcus genus. Fourteen cases (48.2%) were related to some type of neurosurgical procedure. Overall, only two exitus cases were recorded. CONCLUSIONS: The etiologic agents of community acquired meningitis are mainly N. meningitidis, S. pneumoniae and Haemophilus influenzae. The previous antibiotic therapy did not influence thy cyto-biochemical characteristics of CSF but it did influence the yielding of culture. Meningitis with negative CSF culture has a significantly lower number of complications. The availability of a Neurosurgery Department at a hospital confers a change in the epidemiologic spectrum of diagnosed meningitis, with a higher incidence of nosocomial meningitis. In our environment, a substantial proportion of cases due to Staphylococcus microorganisms was observed.

Emele F.E. *Etiologic spectrum and pattern of antimicrobial drug susceptibility in bacterial meningitis in Sokoto, Nigeria.* Acta Paediatr. 2000; 89(8) : 942-6.p Abstract: Etiologic agents of meningitis were prospectively investigated among patients admitted to Usman Danfodio University Teaching Hospital, Sokoto. Of 1097 cerebrospinal fluid (CSF) samples submitted to the microbiology laboratory from various wards of the hospital, 289 (26%) were microscopically, culturally and/or serologically proven to be bacterial meningitis. The etiologic spectrum was as follows: Neisseria meningitidis (61%), Streptococcus pneumoniae (18%), Haemophilus influenzae (10%), Staphylococcus aureus (6%), Coliform bacilli (3%), Escherichia coli (0.7%), Mycobacterium tuberculosis (0.7%), Listeria monocytogenes (0.4%), Flavobacterium meningosepticum (0.4%) and Pseudomonas putrifasciens (0.4%). Bacterial meningitis was most prevalent (195 or 68%) among children aged 1-9 y, while adults and neonates were least affected. Coliform bacilli caused five of eight neonatal cases. Males were more frequently affected than females (chi2 = 12.50; p < 0.05). Culture and microscopy were comparatively less efficient than the search for bacterial antigens, especially in the diagnosis of Haemophilus meningitis. Antimicrobial susceptibility of N. meningitidis to ampicillin and benzyl penicillin reduced progressively over the years (F = 406.98; p < 0.001). Nineteen (11%) of the isolates (5 Meningococci, 7 Staph. aureus, 1 Haem. influenza and 6 others) showed simultaneous resistance to chloramphenicol, ampicillin and benzyl penicillin.

Emele F.E. et al. *Microorganisms associated with wound infection in Ekpoma, Nigeria.* West Afr J Med. 1999; 18(2) : 97-100.p Abstract: Bacteria associated with wound infection in Ekpoma, Nigeria, and their antimicrobial susceptibility profile was investigated by standard microbiological methods, using hospital as well as non-hospital patients. Of 40 patients seen, 25 (62.5%) were males, while the rest were females. Those aged 30 years and above accounted for 63% of the patients, and post-operative sepsis was the most frequently encountered wound infection. Of the organisms encountered, Staphylococcus aureus was the most frequently occurring organism (39%), followed by coliform bacilli (24%), which was the most prevalent organism (44%) in post-operative sepsis. Twenty-one percent of the isolates were Pseudomonas aeruginosa. The majority of the bacterial isolates from the infected wounds were susceptible to Gentamicin, as follows: 92% of the Staph. aureus, 100% of Streptococcus faecalis, Escherichia coli and Pseud. aeruginosa, and 75% of the coliform bacilli. It is suggested that gentamicin, in combination with metronidazole, be used not only for empirical treatment of wound infections in Ekpoma locality but also for prophylactic coverage of surgical operations.

Endtz H.P. et al. *Comparative in vitro activities of trovafloxacin (CP-99,219) against 445 gram-positive isolates from patients with endocarditis and those with other bloodstream infections.* Antimicrob Agents Chemother. 1997; 41(5) : 1146-9.p Abstract: The in vitro activity of trovafloxacin (CP-99,219), a new fluoroquinolone, was compared with the in vitro activities of other commonly used quinolones and other antimicrobial agents against 445 gram-positive microorganisms isolated between 1986 and 1995 from patients with endocarditis and those with other bloodstream infections. The MICs at which 90% of the isolates are inhibited (MIC90) of trovafloxacin for methicillin-susceptible staphylococci, viridans group streptococci, and enterococci were 0.06, 0.25, and 0.5 mg/liter, respectively. The MIC90 of trovafloxacin for vancomycin-resistant enterococci as well as for methicillin-resistant Staphylococcus aureus and methicillin-susceptible and ciprofloxacin-resistant S. aureus, isolated from sources other than blood, was 1 mg/liter. For the quinolones the rank order of activity was trovafloxacin > sparfloxacin > ciprofloxacin = ofloxacin > pefloxacin. Depending on the species tested, trovafloxacin was 4- to 64-fold more active than ciprofloxacin. Further experimental and in vivo studies are warranted to evaluate the efficacy of trovafloxacin in the treatment of bacterial endocarditis and other infections caused by gram-positive organisms.

Endtz H.P. et al. *Vancomycin resistance: status quo and quo vadis.* Eur J Clin Microbiol Infect Dis. 1999; 18(10) : 683-90.p Abstract: The prevalence of vancomycin resistance is steadily rising among clinical isolates of Enterococcus spp., thereby limiting the treatment options for infections caused by vancomycin-resistant enterococci. The precise nature of the glycopeptide resistance genes has been elucidated, and many studies on gene reservoirs and strain-versus-resistance-gene epidemiology have been performed. The prevalence of vancomycin-resistant enterococci in various clinical and environmental settings in relation to nosocomial and veterinary applications of antimicrobial glycopeptides is discussed in detail in this review. Novel molecular tools for the identification of vancomycin-resistant enterococci genomes or the various resistance genes have been applied in order to expand current insight into the overall epidemiology of the resistance trait itself. The risk of the spread of vancomycin resistance to other bacterial species was recently underscored by the emergence of staphylococci showing clinical resistance to vancomycin. The topics mentioned above are elaborated on and discussed in light of the increasing medical concern on the future detection of microbial infections beyond chemotherapeutic cure.

Endtz H.P. et al. *Comparative in-vitro activity of meropenem against selected pathogens from hospitalized patients in The Netherlands. MASTIN Study Group.* J Antimicrob Chemother. 1997; 39(2) : 149-56.p Abstract: Thirty laboratories evaluated the in-vitro activity of meropenem and 15 commonly used antibiotics against selected microorganisms isolated in 1994-95 from hospitalized patients with serious infections requiring antibacterial treatment. Isolates (2169) from blood, sputum, pus or CSF were included. MICs were determined with Etest and NCCLS breakpoints were used. In general, the MICs of meropenem for Gram-positive isolates were found to be one- to six-fold higher than those of imipenem, except for Enterococcus faecalis. The MIC90 of meropenem for E. faecalis was high (32 mg/L) and distinctly higher than the MIC90 of imipenem (2 mg/L). The MICs of meropenem for Gram-negative isolates were two- to 24-fold lower, with the exception of Acinetobacter spp. Gram-negative fermentative strains, Enterobacter spp. in particular, isolated from patients in intensive care units (ICU) were more resistant to the -lactam antibiotics than those isolated from patients in non-intensive care wards. However, all Enterobacteriaceae, with and without inducible -lactamases, isolated from ICU patients were susceptible to meropenem.

Engelhard D. et al. *Nosocomial coagulase-negative staphylococcal infections in bone marrow transplantation recipients with central vein catheter. A 5-year prospective study.* Transplantation. 1996; 61(3) : 430-4.p Abstract: The purpose of this study was to examine coagulase-negative staphylococcal infections in bone marrow transplantation (BMT) patients with central vein catheters by investigating incidence, clinical relevance, risk factors, methicillin resistance, clinical impact of initial empiric antimicrobial therapy without vancomycin, and management of documented catheter-related infections. A 5-year prospective study was conducted with daily evaluation of 242 BMT patients during hospitalization, including clinical assessment and blood culture via the Hickman/Broviac catheter. If fever or infected appearance occurred, peripheral blood cultures or exit site cultures, respectively, were done. Results showed a septicemia incidence of 7.0%, including in 6 patients following colonization, in 1 patient with tunnel infection, in 1 patient with thrombophlebitis, in 1 patient with exit site infection, and in 8 patients with septicemia of unknown origin. Total colonization incidence was 7%, with colonization only in 11 patients who had 16 episodes; incidence of exit site infection was 3.7%. Age > or = 18 years was the only identified risk factor for developing staphylococcal infection (P = 0.03). Despite a methicillin resistance rate of 45% and omission of vancomycin from the routine initial empiric antimicrobial regimen, the clinical course of coagulase-negative staphylococcal infections was relatively benign. A single patient, who experienced marrow rejection, died on day +31 with septicemia and only one patient experienced microbiological failure with recurrent colonization. Bacteria grown in both aerobic and anaerobic bottles were more likely true bacteremia than contaminant (P = 0.03). We conclude that the hazard of coagulase-negative staphylococcal infection does not mandate inclusion of a glycopeptide in the initial empiric antimicrobial regimen in BMT patients, even during febrile neutropenia. Hickman/Broviac-related staphylococcal infections, except for tunnel infection or thrombophlebitis, can usually be treated successfully without removing the catheter.

Engels D. et al. *Epidemic dysentery caused by Shigella dysenteriae type 1: a sentinel site surveillance of antimicrobial resistance patterns in Burundi.* Bull World Health Organ. 1995; 73(6) : 787-91.p Abstract: Annual epidemics of bacillary dysentery have been a public health problem in Burundi for the last 14 years. Recent civil unrest, resulting in the displacement of large numbers of people into refugee settlements, has aggravated the situation. We report the results of a nationwide, health-centre based, sentinel site survey to check the drug resistance of Shigella dysenteriae type 1 (Sd1), the causal organism of such epidemics. Shigella spp. (of which 97% were Sd1) were isolated from 73% of the 126 specimens collected from six main sites around the country. There was no difference in culture results from fresh and frozen stool specimens. Overall Sd1 resistance to commonly available antibiotics (sulfamethoxazole + trimethoprim, ampicillin, tetracycline, and chloramphenicol) varied from 77% to 99% and was fairly

uniformly distributed over the country. All Sd1 isolates were susceptible to newer drugs, such as ciprofloxacin and ceftriaxone. Resistance to nalidixic acid, the current first line of treatment for bacillary dysentery in Burundi, varied from 8% to 83% in the different sentinel sites; global resistance was 57%.

Engler H.D. et al. *Clinical evaluation of the BacT/Alert and isolator aerobic blood culture systems.* Am J Clin Pathol. 1996; 105(6) : 774-81.p Abstract: The BacT/Alert (BTA) (Organon Teknika, Durham, NC) and Isolator 10 (ISO) (Wampole Laboratories, Cranbury, NJ) blood culture systems were evaluated for their ability to detect aerobic and facultatively anaerobic microorganisms in blood of adult patients. For each culture 8 mL of blood was inoculated into both the aerobic standard BTA bottle and the ISO tube. Of 7,259 paired culture sets, 1,168 organisms were recovered, and 667 (57.1%) of these were considered clinically significant. This represented 540 clinically significant positive cultures from 266 patients. Of the significant isolates, 410 were recovered by both systems, 108 by BTA only and 149 by ISO only (P <.025). Overall, the BTA detected 77.7% of the significant isolates, whereas ISO detected 83.8%. The ISO recovered significantly more isolates of Staphylococcus aureus (P =.0001), coagulase-negative Staphylococcus spp (P <.01), and non-Enterobacteriaceae gram-negative rod species (P <.0025), whereas the BTA detected significantly more isolates of Streptococcus spp (P <.0025). Growth of S aureus (P <.0025), Enterococcus spp (P <.0025), and Streptococcus spp (P <.0075) was detected earlier by the BTA when laboratory coverage was available during the first shift only (7:30 AM to 4:00 PM), and additionally of Enterobacteriaceae (P <.0005) and other gram-negative rod species (P <.0001) if coverage was extended to 12:00 AM. Yeasts were detected more rapidly by the ISO (P <.0025). The ISO contamination rate (5.9%) was six times that of the BTA. Taking into account its ability to rapidly detect most organisms, its automated and thus labor-saving features, and the minimal contamination rate associated with its use, the BTA appears to be a reliable alternative to the ISO as a blood culturing system, although improvement in detection of staphylococci and non-Enterobacteriaceae gram-negative rods would be desirable.

Enjuanes L. et al. *Interference with virus and bacteria replication by the tissue specific expression of antibodies and interfering molecules.* Adv Exp Med Biol. 1999; 473 : 31-45.p Abstract: Historically, protection against virus infections has relied on the use of vaccines, but the induction of an immune response requires several days and in certain situations, like in newborn animals that may be infected at birth and die in a few days, there is not sufficient time to elicit a protective immune response. Immediate protection in new born could be provided either by vectors that express virus-interfering molecules in a tissue specific form, or by the production of animals expressing resistance to virus replication. The mucosal surface is the largest body surface susceptible to virus infection that can serve for virus entry. Then, it is of high interest to develop strategies to prevent infections of these areas. Virus growth can be interfered intracellularly, extracellularly or both. The antibodies neutralize virus intra- and extracellularly and their molecular biology is well known. In addition, antibodies efficiently neutralize viruses in the mucosal areas. The autonomy of antibody molecules in virus neutralization makes them functional in cells different from those that produce the antibodies and in the extracellular medium. These properties have identified antibodies as very useful molecules to be expressed by vectors or in transgenic animals to provide resistance to virus infection. A similar role could be played by antimicrobial peptides in the case of bacteria. Intracellular interference with virus growth (intracellular immunity) can be mediated by molecules of very different nature: (i) full length or single chain antibodies; (ii) mutant viral proteins that strongly interfere with the replication of the wild type virus (dominant-negative mutants); (iii) antisense RNA and ribozyme sequences; and (iv) the product of antiviral genes such as the Mx proteins. All these molecules inhibiting virus replication may be used to obtain transgenic animals with resistance to viral infection built in their genomes. We have developed two strategies to target into mucosal areas either antibodies to provide immediate protection, or antigens to elicit immune responses in the enteric or respiratory surfaces in order to prevent virus infection. One strategy is based on the development of expression vectors using coronavirus derived defective RNA minigenomes, and the other relies on the development of transgenic animals providing virus neutralizing antibodies in the milk during lactation. Two types of expression vectors are being engineered based on transmissible gastroenteritis coronavirus (TGEV) defective minigenomes. The first one is a helper virus dependent expression system and the second is based on self-replicating RNAs including the information required to encode the TGEV replicase. The minigenomes expressing the heterologous gene have been improved by using a two-step amplification system based on cytomegalovirus (CMV) and viral promoters. Expression levels around 5 micrograms per 10(6) cells were obtained. The engineered minigenomes will be useful to understand the mechanism of coronavirus replication and for the tissue specific expression of antigen, antibody or virus interfering molecules. To protect from viral infections of the enteric tract, transgenic animals secreting virus neutralizing recombinant antibodies in the milk during lactation have been developed. Neutralizing antibodies with isotypes IgG1 or IgA were produced in the milk with titers of 10(6) in RIA that reduced virus infectivity by one million-fold. The recombinant antibodies recognized a conserved epitope apparently essential for virus replication. Antibody expression levels were transgene transgene copy number independent and were related to the transgene integration site. This strategy may be of general use since it could be applied to protect newborn animals against infections of the enteric tract by viruses or bacteria for which a protective MAb has been identified. Alternatively, the same strategy could be used to target the expression of antibio.

Ennis D.M. et al. *The newer cephalosporins. Aztreonam and imipenem.* Infect Dis Clin North Am. 1995; 9(3) : 687-713.p Abstract: Many of the antimicrobial agents described here exhibit great advances over older drugs in terms of antimicrobial spectrum, clinical utility, and, sometimes, safety. The newer cephalosporins are useful for treatment of many common outpatient and inpatient infections. Aztreonam provides excellent coverage against a broad range of aerobic gram-negative bacteria, without the toxicity associated with aminoglycosides. Imipenem exhibits activity against an impressive array of pathogens. These antimicrobials are expensive, however, and some offer no advantages over older agents. Finally, all—including imipenem—are faced with increasing resistance of bacteria.

Enright M.C. et al. *Multilocus sequence typing for characterization of methicillin-resistant and methicillin-susceptible clones of Staphylococcus aureus.* J Clin Microbiol. 2000; 38(3) : 1008-15.p Abstract: A multilocus sequence typing (MLST) scheme has been developed for Staphylococcus aureus. The sequences of internal fragments of seven housekeeping genes were obtained for 155 S. aureus isolates from patients with community-acquired and hospital-acquired invasive disease in the Oxford, United Kingdom, area. Fifty-three different allelic profiles were identified, and 17 of these were represented by at least two isolates. The MLST scheme was highly discriminatory and was validated by showing that pairs of isolates with the same allelic profile produced very similar SmaI restriction fragment patterns by pulsed-field gel electrophoresis. All 22 isolates with the most prevalent allelic profile were methicillin-resistant S. aureus (MRSA) isolates and had allelic profiles identical to that of a reference strain of the epidemic MRSA clone 16 (EMRSA-16). Four MRSA isolates that were identical in allelic profile to the other major epidemic MRSA clone prevalent in British hospitals (clone EMRSA-15) were also identified. The majority of isolates (81%) were methicillin-susceptible S. aureus (MSSA) isolates, and seven MSSA clones included five or more isolates. Three of the MSSA clones included at least five isolates from patients with community-acquired invasive disease and may represent virulent clones with an increased ability to

cause disease in otherwise healthy individuals. The most prevalent MSSA clone (17 isolates) was very closely related to EMRSA-16, and the success of the latter clone at causing disease in hospitals may be due to its emergence from a virulent MSSA clone that was already a major cause of invasive disease in both the community and hospital settings. MLST provides an unambiguous method for assigning MRSA and MSSA isolates to known clones or assigning them as novel clones via the Internet.

Entenza J.M. et al. *Levofloxacin versus ciprofloxacin, flucloxacillin, or vancomycin for treatment of experimental endocarditis due to methicillin-susceptible or -resistant Staphylococcus aureus.* Antimicrob Agents Chemother. 1997; 41(8) : 1662-7.p Abstract: Levofloxacin is the L isomer of ofloxacin, a racemic mixture in which the L stereochemical form carries the antimicrobial activity. Levofloxacin is more active than former quinolones against gram-positive bacteria, making it potentially useful against such pathogens. In this study, levofloxacin was compared to ciprofloxacin, flucloxacillin, and vancomycin for the treatment of experimental endocarditis due to two methicillin-susceptible Staphylococcus aureus (MSSA) and two methicillin-resistant S. aureus (MRSA) isolates. The four test organisms were susceptible to ciprofloxacin, the levofloxacin MICs for the organisms were low (0.12 to 0.25 mg/liter), and the organisms were killed in vitro by drug concentrations simulating both the peak and trough levels achieved in human serum (5 and 0.5 mg/liter, respectively) during levofloxacin therapy. Rats with aortic endocarditis were treated for 3 days. Antibiotics were injected with a programmable pump to simulate the kinetics of either levofloxacin (350 mg orally once a day), ciprofloxacin (750 mg orally twice a day), flucloxacillin (2 g intravenously four times a day), or vancomycin (1 g intravenously twice a day). Levofloxacin tended to be superior to ciprofloxacin in therapeutic experiments (P = 0.08). More importantly, levofloxacin did not select for resistance in the animals, in contrast to ciprofloxacin. The lower propensity of levofloxacin than ciprofloxacin to select for quinolone resistance was also clearly demonstrated in vitro. Finally, the effectiveness of this simulation of oral levofloxacin therapy was at least equivalent to that of standard treatment for MSSA or MRSA endocarditis with either flucloxacillin or vancomycin. This is noteworthy, because oral antibiotics are not expected to succeed in the treatment of severe staphylococcal infections. These good results obtained with animals suggest that levofloxacin might deserve consideration for further study in the treatment of infections due to ciprofloxacin-susceptible staphylococci in humans.

Enting R.H. et al. *Antimicrobial susceptibility of Haemophilus influenzae, Neisseria meningitidis and Streptococcus pneumoniae isolates causing meningitis in The Netherlands, 1993-1994.* J Antimicrob Chemother. 1996; 38(5) : 777-86.p Abstract: The increasing antimicrobial resistance among pathogens frequently isolated from patients with bacterial meningitis formed the rationale to perform a surveillance study to determine the prevalence of resistance in The Netherlands. Haemophilus influenzae strains (n = 316) isolated from cerebrospinal fluid (CSF), 1125 meningococcal strains isolated from blood or CSF and 398 pneumococcal strains isolated from CSF in 1993 and 1994 were tested by the Etest for susceptibility to commonly prescribed antibiotics for the treatment of community-acquired meningitis. In H. influenzae strains ampicillin-resistance occurred in 7.0%, resistance to chloramphenicol in 2.2%, and resistance to both antibiotics in 0.9%. The prevalence of intermediate penicillin-resistance in meningococci was 3.3%. Resistance to rifampicin was rarely found (0.1%). Intermediate penicillin-resistance in pneumococci was found in only 0.5% of isolates. All 1839 isolates were susceptible to ceftriaxone. Based on these results, we conclude that empirical therapy of childhood community-acquired bacterial meningitis with amoxycillin and chloramphenicol is no longer justified in children who have not been vaccinated against H. influenzae type b. In vaccinated or older children and adults, amoxycillin is a rational choice for empirical treatment of meningitis. The prophylactic use of rifampicin in contacts of patients with meningococcal disease is still applicable.

Enwere G.C. et al. *The host response in malaria and depression of defence against tuberculosis.* Ann Trop Med Parasitol. 1999; 93(7) : 669-78.p Abstract: Malaria causes significant morbidity and mortality worldwide. Both asymptomatic and symptomatic malarial infections cause immune depression, which predisposes the host to infection with other microorganisms. Specific clinical investigations have shown, for example, that those with malaria-attributable anaemia are particularly likely to have Salmonella septicaemia, and that asymptomatic malarial infection causes diminished response to polysaccharide vaccine. The results of clinical studies and experiments with animal models have revealed that malarial parasites can decrease their vertebrate host's effective humoral and cellular immune responses. In this review, the possible ways in which this malaria-induced immune impairment could affect the host's response to Mycobacterium tuberculosis infection are considered. Could malarial infection be one of the reasons for the persistence of tuberculosis in malaria-endemic regions?

Erard P. *[Is there a role for infectious disease specialists in private practice?].* Rev Med Suisse Romande. 2000; 120(1) : 59-64.p Abstract: For the last 20 years infectious diseases have gained increasing importance for hospital medicine. As a specialty, infectious diseases have been recognized only recently by the Swiss medical association. However, the precise role of infectious disease specialist operating in private practice remain to be defined. The medical community faces many challenges for which infectious disease specialist must provide answers. Knowledge in microbiology has progressed enormously and many very sophisticated and, partly, expensive diagnostic techniques are widely available. New treatment options are introduced while numerous microbial species demonstrate increasing resistance to antimicrobial agents. The intervention of infectious disease specialist could thus contribute to optimize treatment and limit the use of economic resources. Infectious disease specialist in private practice are also facing new activities such as parenteral outpatient treatment for severe infections and HIV infection, which clearly require a specialized professional approach. Infectious disease specialist in private practice will need great care to find a responsible equilibrium between clinical consultation and telephone consultation.

Erasmus J.J. et al. *Percutaneous management of intrapulmonary air and fluid collections.* Radiol Clin North Am. 2000; 38(2) : 385-93.p Abstract: The radiologist's role in the management of intrapulmonary air and fluid collections is becoming more important. Improvements in percutaneous interventional techniques now allow the radiologist to offer patients an alternative treatment option with less morbidity and mortality than surgical resection. The use of CT allows optimal catheter placement and enables safe and effective percutaneous evacuation of intrapulmonary collections. In summary, image-guided percutaneous catheter drainage should (1) be the initial procedure performed to diagnose and treat lung abscesses not responding to conservative therapy; and (2) because of its effectiveness and safety, be considered as a treatment option in the management of symptomatic patients with intrapulmonary mycetomas.

Erez E. et al. *Septic emboli caused by vascular catheters after surgery for congenital heart disease.* Crit Care Med. 2000; 28(3) : 845-7.p Abstract: OBJECTIVE: To review the incidence, diagnosis, and management of septic emboli caused by vascular catheters after surgery for congenital heart disease. DESIGN: Retrospective clinical review. All patients were computer registered. Our database includes daily follow-up and every sign of infection registered. SETTING: Pediatric cardiac surgery intensive care unit in a university hospital. PATIENTS: A total of 720 consecutive pediatric cardiac operations performed in 108 neonates and 612 older children from 1995 to 1997 are reviewed. MEASUREMENTS AND MAIN RESULTS: Septic emboli were defined as erythematous non-tender papulonodular hemorrhagic lesions restricted to the limb and distal to the monitoring catheter. Four patients (0.55%) with catheter-related septic emboli after congenital heart surgery were identified, three

neonates (0.41%) and one older infant (0.14%). The incidence of catheter-related septic emboli in our patients was significantly higher in the neonatal group compared with older infants (p =.0076; odds ratio=17.45). All infants with catheter-associated septic emboli were severely ill and required prolonged intensive care management postoperatively for periods ranging from 27 to 90 days (mean, 50 days). The catheters involved were in place for periods ranging from 5 to 7 days. All patients were treated by catheter removal and intravenous antibiotics without surgical intervention in the vascular access area. The affected limbs healed well without residual damage. CONCLUSIONS: Septic emboli are a rare complication of infected vascular catheters in neonates and small infants undergoing prolonged postoperative intensive care management (0.55%). They may indicate the source of unexplained sepsis involving mainly Gram-negative bacilli. Generally, treatment consists of removal of the offending catheter and antibiotic administration with no need for surgical intervention.

Ernst R.K. et al. *Specific lipopolysaccharide found in cystic fibrosis airway Pseudomonas aeruginosa*. Science. 1999; 286(5444) : 1561-5.p Abstract: Cystic fibrosis (CF) patients develop chronic airway infections with Pseudomonas aeruginosa (PA). Pseudomonas aeruginosa synthesized lipopolysaccharide (LPS) with a variety of penta- and hexa-acylated lipid A structures under different environmental conditions. CF patient PA synthesized LPS with specific lipid A structures indicating unique recognition of the CF airway environment. CF-specific lipid A forms containing palmitate and aminoarabinose were associated with resistance to cationic antimicrobial peptides and increased inflammatory responses, indicating that they are likely to be involved in airway disease.

Ersan S. et al. *Synthesis and antimicrobial activity of 1-dialkylaminomethyl- 2-(p-substituted phenyl)-5-substituted benzimidazole derivatives.* Arzneimittelforschung. 1997; 47(4) : 410-2.p Abstract: 1-(Dialkylaminomethyl)-2-(p-substituted phenyl)-5-substituted benzimidazole derivatives 1 have been synthesized by reacting 2-phenylbenzimidazole derivatives with formaldehyde and a secondary amine. The derivatives of 2-phenylbenzimidazole were obtained by reacting the bisulfide addition product of substituted benzaldehydes with 4-substituted-o-phenylenediamines. Their structures were confirmed by microanalysis, IR and NMR spectral analysis. Antimicrobial activity of the compounds was investigated by the microdilution susceptibility test in Mueller-Hinton Broth and Sabouraud Dextrose Broth was used for the determination of antibacterial and antifungal activities. Test organisms: Staphylococcus aureus ATCC 29213 and Enterococcus faecalis ATCC 29212 as Gram-positive bacteria, Escherichia coli ATCC 25922 and Pseudomonas aeruginosa ATCC 27853 as Gram-negative bacteria, and Candida albicans, C. parapsilosis, C. stellatoidea as yeast-like fungi. Compounds 1a, 1b, 1c, 1e and 1i showed slight to moderate activity against all microorganisms. Compound 1g showed the highest activity. It was found more potent than streptomycin against Enterococcus faecalis and Pseudomonas aeruginosa.

Escalante P. et al. *Genotypic characterization of drug-resistant Mycobacterium tuberculosis isolates from Peru*. Tuber Lung Dis. 1998; 79(2) : 111-8.p Abstract: SETTING: Twenty-nine epidemiological unrelated and mostly multidrug-resistant Mycobacterium tuberculosis (MDR-TB) strains from Peruvian patients. OBJECTIVE: To investigate the molecular genetics of MDR-TB strains recovered in a Latin American country. DESIGN: Antimicrobial agent susceptibility testing, major genetic group designation, IS6110 fingerprinting, spoligotyping, and automated deoxyribonucleic acid sequencing of regions of the katG, rpoB, embB, gyrA, and pncA genes with mutations commonly associated with drug resistance. RESULTS: Nineteen isolates were found to be multidrug-resistant by susceptibility testing. IS6110 typing showed that virtually all isolates were unique and therefore had independently acquired drug resistance. Seventy-nine percent of isoniazid-resistant strains had a Ser315Thr amino acid change in KatG. Ninety-five percent of rifampin-resistant isolates had amino acid replacements in the rifampin-resistance determining region of RpoB. Six of 11 ethambutol-resistant strains had EmbB alterations. Eleven pyrazinamide-resistant strains had distinct mutations in pncA. CONCLUSION: Virtually all organisms evolved drug resistance independently. The types of drug resistance-associated mutations identified were very similar to changes occurring in isolates from other areas of the world. Nucleotide sequence-based strategies for rapid detection of drug resistance-conferring mutants will be applicable to organisms recovered in Peru, and potentially other areas of Latin America.

Esclarin De Ruz A. et al. *Epidemiology and risk factors for urinary tract infection in patients with spinal cord injury.* J Urol. 2000; 164(4) : 1285-9.p Abstract: PURPOSE: To our knowledge risk factors for urinary tract infection associated with various drainage methods in patients with spinal cord injury have never been evaluated overall in the acute period. We identified the incidence and risk factors associated with urinary tract infection in spinal cord injured patients. MATERIALS AND METHODS: We prospectively followed 128 patients at our spinal cord injury reference hospital for 38 months and obtained certain data, including demographic characteristics, associated factors, methods of urinary drainage, bladder type, urological complications and predisposing factors of each infection episode. Logistic regression modeling was done to analyze variables and identify risk factors that predicted urinary tract infection. RESULTS: Of 128 patients 100 (78%) were male with a mean age plus or minus standard deviation of 32 +/- 14.52 years. All patients had a nonfatal condition by McCabe and Jackson guidelines, and 47% presented with associated factors. The incidence of urinary tract infection was expressed as number episodes per 100 patients daily or person-days. The overall incidence of urinary tract infection was 0.68, while for male indwelling, clean intermittent, condom and female suprapubic catheterization, and normal voiding the rate was 2.72, 0.41, 0.36, 0.34 and 0.06, respectively. The risk factors associated with urinary tract infection were invasive procedures without antibiotic prophylaxis, cervical injury and chronic catheterization (odds ratio 2.62, 3 and 4, respectively). Risk factors associated with repeat infection were a functional independence measure score of less than 74 and vesicoureteral reflux (odds ratio 10 and 23, respectively). CONCLUSIONS: Spinal cord injured patients with complete dependence and vesicoureteral reflux are at highest risk for urinary tract infection.

Eskola J. *Immunogenicity of pneumococcal conjugate vaccines.* Pediatr Infect Dis J. 2000; 19(4) : 388-93.p Abstract: BACKGROUND: Prevention of pneumococcal infections is a public health priority because of the high impact of the disease and because of the increasing problems due to antimicrobial resistance. Traditional vaccines, consisting of purified capsular polysaccharides (PSs) of Streptococcus pneumoniae, are not immunogenic in young children. In addition they confer only limited protection in patients with immunodeficiencies and hematologic malignancies. IMMUNOGENICITY OF PNEUMOCOCCAL CONJUGATE VACCINES: Immunogenicity of the PS vaccine has been enhanced by coupling pneumococcal PSs to proteins to produce a conjugate vaccine. Conjugate molecules are designed to possess T cell dependent properties, such as immunogenicity in early infancy, stimulation of high levels of IgG isotype antibodies and enhanced immunologic memory responses. In the clinical studies multivalent pneumococcal conjugate vaccines have been shown to induce an IgG-dominating serum antibody response against common pneumococcal serotypes causing infections in children. A booster dose later in life creates a robust and rapid antibody response, indicating the existence of immunologic memory in primed children. Antibodies induced by conjugate vaccines are functionally active, as demonstrated by their high avidity and opsonophagocytic activity.

Esper M.R.N.R. et al. *Salmonella: sorotipos identificados das cepas isoladas de pacientes hospitalizados e não hospitalizados, na Região de Presidente*

Prudente, SP, no período de 1978-1997. Rev. Inst. Adolfo Lutz. 1998; 57(2) : 45-50.p Abstract: No período de 1978-1997, foram identificadas 413 cepas de Salmonella, isoladas de coproculturas de origem ambulatorial e hospitalar, no Setor de Microbiologia do Laboratório I Regional de Presidente Prudente. Determinou-se a sensibilidade aos agentes antimicrobianos de 394 cepas de Samonella. Entre as cepas isoladas de coproculturas de origem ambulatorial observou-se grande diversidade de sorotipos (27 sorotipos) com predomin∫ncia de S. Enteritidis 24,4(por cento), S. Infantis 19,3 (por cento) e S. Agona 10,1(por cento). Em relação …s cepas isoladas de pacientes hospitalizados, foram identificados 8 diferentes sorotipos, sendo que a S. Typhimurium representou o sorotipo prevalente 95,6(por cento), seguido de S. Typhi 1(por cento) e S. I4,12:i:-1(por cento). Com relação … sensibilidade aos agentes antimicrobianos, as cepas de origem hospitalar apresentam multirresistência, enquanto que aquelas de origem ambulatorial foram sensíveis … maioria dos antimicrobianos utilizados.

Esteban J. et al. *Microbiological characterization and clinical significance of Corynebacterium amycolatum strains.* Eur J Clin Microbiol Infect Dis. 1999; 18(7) : 518-21.p Abstract: The laboratory records of patients with bacillus isolates identified as Corynebacterium xerosis were reviewed in an attempt to establish the clinical significance of the isolates, and the isolated strains were reidentified. Of the 22 strains available for reidentification, four were identified as Corynebacterium striatum and 18 as Corynebacterium amycolatum. Forty-one patients were considered to have Corynebacterium amycolatum isolates, and in 13 (31.7%) of these patients a genuine clinical infection occurred, comprising catheter-related infection in seven cases, surgical wound infection in five cases, and pilonidal cyst infection in one case. Most patients were treated with antimicrobial agents (vancomycin in seven cases and amoxicillin/clavulanic acid in four cases). All patients were cured. Corynebacterium amycolatum can cause genuine infection, usually hospital-acquired, and the clinical significance of isolates must be determined to ensure proper management of patients.

Estevao Belchior S. et al. *[Microbiological controls and control points in a hake fillets manufacturing process for exportation].* Arch Latinoam Nutr. 2000; 50(2) : 171-6.p Abstract: Indicator and foodborne pathogens microorganisms in the "for export" hake fillets manufacturing were investigated in this study. Critical control points were identified and prevention activities and control were proposed during seafood elaboration process. 45 samples of hake from sequential processing operation stages, 15 ice samples and 12 water samples from utensil washing, were collected. The samples were analyzed for their content of aerobic mesophilic bacteria, psychrotrophic bacteria, enterobacteria, total and fecal coliform bacteria, Staphylococcus aureus and the presence of Escherichia coli, Salmonella and Shigella. The analysis of the samples collected from the factory revealed that the amounts of aerobic mesophiles bacteria increased during manual filleting and packaging, in comparison with raw material. Psychrotrophic bacteria were the predominant microorganisms, specially in hake samples. In addition, high levels of enterobacteria, which do not occur normally in fish, were detected in raw hake samples. Staphylococcus aureus, Escherichia coli, Salmonella and Shigella, were not isolated from any samples in this study. The goal of this work is to establish microbiological risks in the hake fillets manufacturing process and, therefore to make possible corrective and control actions to assure the quality and safety of seafood.

Esteves Echanique M. et al. *Logros de la inmunofarmacoterapia.* Educ. med. contin. 1996; (51) : 11-9.p Abstract: Se trata sobre los procedimientos e inmunofarmacos (inmunoestimulantes e inmunosupresores) aplicados en un vasto campo clínico y experimental que abarca enfermedades infecciosas, inmunodeficiencias (primarias y secundarias), enfermedades autoinmunes, cáncer y enfermedades alérgicas. A lo largo del texto se habla sobre el transplante de médula ósea (TMO), timoestimulina (TP-1) y hormonas tímicas, interferones (IFNs), anticuerpos monoclonales e inmunoglobulinas (Igs), factor de transferencia (extracto leucocitario dializado), methisoprinol (Inosine pranobex), glicofos fopeptical (AM3) y levamisol. Se enumera a los antivirales inhibidores de la transcriptasa reversa. Asimismo, se hace referencia a los glucocorticosteroides (CSS), azatioprina (Aza) y ciclosporina A (C y A). Se menciona algunos tipos de ensayos inmunoterapéuticos antineoplasicos. Finalmente, se describe el tratamiento inmunitario de las enfermedades alérgicas en base a la desensibilización usando antígenos (alergenos) y al bloqueo terapéutico del enlace de IgE por medio de inmunoglobulinas (alergoglobulina). (AU).

Estrela C. et al. *Antimicrobial evaluation of calcium hydroxide in infected dentinal tubules.* J Endod. 1999; 25(6) : 416-8.p Abstract: The objective of this study was to evaluate the antimicrobial activity of calcium hydroxide in infected dentinal tubules. Four microorganisms, strains of ATCC (Streptococcus faecalis (ATCC-29212), Staphylococcus aureus (ATCC-6538), Bacillus subtilis (ATCC-6633), and Pseudomonas aeruginosa (ATCC-27853)) and one mixture of these were used. These strains were inoculated in brain heart infusion (BHI) and incubated at 37 degrees C for 24 h. Sixty-three human maxillary central incisors were prepared and sterilized by autoclaving. Five groups of 12 teeth each were contaminated for 28 days using new 24-h cultures every 72 h, prepared and adjusted to tube 2 of the MacFarland scale (6 x 10(8) cells/ml). Root canals were then irrigated with 5 ml of saline, dried, and completely filled with calcium hydroxide paste. At intervals of 0, 48, and 72 h, and 7 days, dressings were removed and teeth were immersed in 5 ml of BHI and incubated at 37 degrees C for 48 h to observe the growth and multiplication of the microorganisms. Three uninoculated teeth were maintained in a humid environment as an aseptic control. These teeth were immersed in BHI and maintained at 37 degrees C for 7 days to determine microbial growth. Bacterial growth was shown by turbidity of the culture medium and confirmed by seeding these broths on BHI agar at 37 degrees C for 24 h. The positive BHI tubes were selected, and inoculum was spread on the surface of BHI agar, followed by the same incubation conditions. Gram stain was conducted from BHI growth and from colonies growing on solid medium. Calcium hydroxide in infected dentinal tubules showed no antimicrobial effect on S. faecalis, S. aureus, B. subtilis, P. aeruginosa, or on the bacterial mixture used throughout the experiment.

Estrela C. et al. *In vitro determination of direct antimicrobial effect of calcium hydroxide.* J Endod. 1998; 24(1) : 15-7.p Abstract: The objective of this study was to determine in vitro the time required for calcium hydroxide in direct contact with microorganisms to express its antimicrobial effect. The microorganisms used were: Micrococcus luteus (ATCC-9341), Staphylococcus aureus (ATCC-6538), Fusobacterium nucleatum (ATCC-25586), Pseudomonas aeruginosa (ATCC-27853), Escherichia coli, and Streptococcus sp. The strains were cultivated in Brain Heart Infusion (BHI), with the exception of F. nucleatum (BHI-PRAS). Pure and mixed suspensions of the microorganisms were prepared. Paper cones immersed in these substances were covered with calcium hydroxide paste, and after 0, 1, 2, 6, 12, 24, 48, and 72 h and 7 days they were transferred to an appropriate medium to observe the growth and multiplication of the microorganisms. Incubation was conducted at 37 degrees C for 48 h, according to the requirements of oxygen of each microorganism. The antimicrobial effect of calcium hydroxide was shown to occur after 12 h on M. luteus and F. nucleatum, 24 h on Streptococcus sp, 48 h on E. coli, and 72 h on S. aureus and P. aeruginosa. Mixture II (M. luteus + Streptococcus sp + S. aureus) was sensitive to calcium hydroxide antimicrobial potential after 48 h, whereas mixture I (M. luteus + E. coli + P. aeruginosa), mixture III (E. coli + P. aeruginosa), and mixture IV (S. aureus + P. aeruginosa) were inactivated after 72 h of exposure.

Evans J. et al. *Aortic laceration secondary to palmaz stent placement for treatment of superior vena cava syndrome.* Catheter Cardiovasc Interv. 2000;

49(2) : 160-2.p Abstract: Aortic laceration secondary to Palmaz Stent placement for treatment of superior vena cava syndrome is reported. This potentially life-threatening complication should be considered when rigid balloon expandable stents are used to treat superior vena cava syndrome of benign origin. Cathet. Cardiovasc. Intervent. 49:160-162, 2000. Copyright 2000 Wiley-Liss, Inc.

Evans M.E. et al. *Polymyxin B sulfate and colistin: old antibiotics for emerging multiresistant gram-negative bacteria.* Ann Pharmacother. 1999; 33(9) : 960-7.p Abstract: BACKGROUND: Polymyxin B sulfate and colistin, also known as colistimethate, have not been used for many years because less toxic antimicrobials are available. Gram-negative bacteria that are resistant to the aminoglycosides, beta-lactams, and fluoroquinolones are becoming more common. These bacteria are often susceptible to the polymyxins. OBJECTIVE: To present a review of the chemistry, antibacterial spectrum, dosing, pharmacokinetics, toxicity, and indications for polymyxin B sulfate and colistin. DATA SOURCE: A MEDLINE search (1966-1998) of the English-language literature was performed to identify primary literature on the polymyxins. Older citations (1949-1965) were identified through the bibliographies of these articles. STUDY SELECTION: All available reports of in vitro antibacterial activity, animal and clinical trials, and case reports were reviewed. DATA SYNTHESIS: The polymyxins are amphipathic molecules that interact with lipopolysaccharide in the bacterial outer membrane. They have potent antiendotoxic properties and antibacterial activity against Pseudomonas aeruginosa and many of the Enterobacteriaceae. Polymyxin B and colistin are usually given at a dose of 1.5-2.5 and 5 mg/kg/d, respectively, in two divided doses. Dosing must be altered in renal failure since the kidney is the primary route of elimination. Distribution into pleural fluid, joints, and cerebrospinal fluid is poor. Toxic effects involve the kidney and central nervous system. The polymyxins are recommended for serious systemic infections caused by gram-negative bacteria that are resistant to other agents. CONCLUSIONS: Polymyxin B sulfate and colistin have a role in the therapy of multidrug-resistant gram-negative bacterial infections.

Evins G.M. et al. *The emerging diversity of the electrophoretic types of Vibrio cholerae in the Western Hemisphere.* J Infect Dis. 1995; 172(1) : 173-9.p Abstract: Since the Latin American cholera epidemic began in 1991, 447 isolates of Vibrio cholerae O1 from the Western Hemisphere have been assayed by multilocus enzyme electrophoresis (MEE) to determine allelic variation among 16 enzyme-encoding genes. Two electrophoretic types (ETs) were identified among toxigenic isolates from Latin America: 323 were ET 4, the ET associated with the Latin American epidemic, and 29 were ET 3. Twenty-three of these ET 3 isolates had a distinctive antimicrobial resistance pattern also seen in isolates imported into the United States from Latin America and Southeast Asia. These resistant isolates had an identical ribotype and nearly identical pulsed-field gel electrophoresis (PFGE) patterns. Most nontoxigenic isolates analyzed were not precursors or descendants of toxigenic epidemic strains. MEE provided a population genetic frame-work for the interpretation of PFGE and ribotype data from the isolates in this study. All three methods identified 2 distinct strains of toxigenic V. cholerae O1 currently epidemic in Latin America.

Ewig S. et al. *Pneumonia acquired in the community through drug-resistant Streptococcus pneumoniae.* Am J Respir Crit Care Med. 1999; 159(6) : 1835-42.p Abstract: The aim of the study was to determine the incidence of and risk factors for drug resistance of Streptococcus pneumoniae, and its impact on the outcome among hospitalized patients of pneumococcal pneumonia acquired in the community. Consecutive patients with culture-proven pneumococcal pneumonia were prospectively studied with regard to the incidence of pneumococcal drug resistance, potential risk factors, and in-hospital outcome variables. A total of 101 patients were studied. Drug resistance to penicillin, cephalosporin, or a macrolide drug was found in pneumococci from 52 of the 101 (52%) patients; 49% of these isolates were resistant to penicillin (16% intermediate resistance, 33% high resistance), 31% to cephalosporin (22% intermediate and 9% high resistance), and 27% to a macrolide drug. In immunocompetent patients, age > 65 yr was significantly associated with resistance to cephalosporin (odds ratio [OR]: 5.0; 95% confidence interval [CI]: 1.3 to 18.8, p = 0. 01), and with the presence of > 2 comorbidities with resistance to penicillin (OR: 4.7; 95% CI: 1.2 to 19.1; p < 0.05). In immunosuppressed patients, bacteremia was inversely associated with resistance to penicillin and cephalosporin (OR: 0.04; 95% CI: 0.003 to 0.45; p < 0.005; and OR: 0.46; 95% CI: 0.23 to 0.93; p < 0.05, respectively). Length of hospital stay, severity of pneumonia, and complications were not significantly affected by drug resistance. Mortality was 15% in patients with any drug resistance, as compared with 6% in those without resistance. However, any drug resistance was not significantly associated with death (relative risk [RR]: 2. 5; 95% CI: 0.7 to 8.9; p = 0.14). Moreover, attributable mortality in the presence of discordant antimicrobial treatment was 12%, as compared with 10% (RR: 1.2; 95% CI: 0.3 to 5.3; p = 0.67) in the absence of such treatment. We conclude that the incidence of drug-resistant pneumococci was high. Risk factors for drug resistance included advanced age, comorbidity, and (inversely) bacteremia. Outcome was not significantly affected by drug resistance.

Ewig S. et al. *Evaluation of antimicrobial treatment in mechanically ventilated patients with severe chronic obstructive pulmonary disease exacerbations.* Crit Care Med. 2000; 28(3) : 692-7.p Abstract: OBJECTIVE: To study microbial and susceptibility patterns and antimicrobial treatment responses in patients with severe, acute exacerbations of chronic obstructive pulmonary disease requiring mechanical ventilation. DESIGN: Microbial investigation using tracheobronchial aspirates, bronchoscopy with a protected specimen brush, and bronchoalveolar lavage, as well as paired serologies. Evaluation of antimicrobial treatment by results of the initial investigation, susceptibility testing, and a repeated microbial investigation (tracheobronchial aspirates, bronchoscopy with a protected specimen brush, and bronchoalveolar lavage) after 72 hrs. SETTING: A respiratory intensive care unit of a 1,000-bed teaching hospital. PATIENTS: Fifty severely exacerbated and mechanically ventilated patients with chronic obstructive pulmonary disease. INTERVENTIONS: Initial empirical antimicrobial treatment according to clinical judgment. MEASUREMENTS AND MAIN RESULTS: Overall, 36 of 50 patients (72%) had evidence of a microbial origin. Community-acquired endogenous pathogens were present in 70% of patients, and Gram-negative enteric bacilli and Pseudomonas/Stenotrophomonas species were present in 30%. All five isolates of Streptococcus pneumoniae were resistant to penicillin (three intermediately and two highly), and three were resistant to multiple antibiotics. Pseudomonas species revealed multiresistance in four of nine isolates (44%), and Stenotrophomonas maltophilia revealed multiresistance in one of two isolates. Antimicrobial treatment was modified according to diagnostic results in 11 of 31 patients (36%) with potentially pathogenic microorganisms. In patients who underwent a repeat investigation after 72 hrs, 24% of the initially present and potentially pathogenic microorganisms persisted. Inappropriate initial antimicrobial therapy was associated significantly with bacterial persistence (p <.002). CONCLUSIONS: Considering the diversity of microbial pathogens and the resistance rates especially to S. pneumoniae in this patient population, antimicrobial treatment should be based on the constant study of local microbial and susceptibility patterns along with routine microbial investigation of the individual patient.

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Fabre-Teste B. et al. *[Calmette Hospital, Phnom Penh, Cambodia. Assessment of the implementation of the Medical Information System (SIM). Global analysis of the 1998 results].* Sante. 1999; 9(6) : 367-

75.p Abstract: Calmette is a national university hospital with 220 adult beds. It has emergency, surgical, medical and gynecology and obstetrics departments, along with a radiology unit, a laboratory for medical analyses, a central pharmacy and an outpatient clinic. This hospital has an unusual statute, with managerial autonomy and a system of cost recovery that currently provides 64% of the hospital's income. Since 1994, it has benefited from a French cooperation program. The French NGO, Medecins du Monde, has been present at Calmette since 1990, providing support for <<Medicine B>>, the indigent sector of the medical department. The aim of the Medical Information System (SIM) is to develop a simple, reliable and reproducible system so that, for every action undertaken at the hospital (hospitalization, day hospital and outpatient clinic) the following pieces of information are recorded: 1) the disease; 2) the type of patient; 3) the type of management; 4) the means used to treat the patient; 5) the cost. Data are collected and analyzed using programs created with EPIINFO software (CDC, WHO), using the EPIGLUE module. In 1998, 10,814 admissions were recorded at Calmette Hospital, 7,811 (72.2%) of which were to the Emergency Department and 3,003 (27.2%) of which were direct admissions to other wards. We analyzed 10,603 (95%) computerized medical summaries (RMI). About 50% of beds were occupied in the maternity and gynecology ward whereas almost 90% of beds were occupied in the surgical and emergency wards. AIDS and tuberculosis were the conditions most frequently treated by the medical department, despite a marked increase in more specialized areas of medicine such as cardiology and diabetology. The surgical department reflected the concentration on emergency services of the hospital, with cranial traumatism the primary reason for admission for the hospital as a whole. The mean age of patients was 27 years for the maternity ward and 49 years for the medicine A ward. The mortality rate was about 5% for the medical wards (mainly due to AIDS) and almost 50% in the emergency department (cerebrovascular neurologic disease, cranial traumatism). The proportion of nonpaying patients was high (about 40% in terms of stays in hospital and about 50% of all days spent in hospital). The training of a Cambodian manager for the SIM is a key priority. The point of the SIM is to use the treated data it produces to improve management and decision-making. The data it produces should be used to define the profile of the patients treated, both from a medical point of view and in terms of their ability to pay. This is a fundamental step towards identifying activities that should receive priority as part of a development strategy for a structure evolving in a highly competitive environment. The SIM data are also invaluable for the short-term management of the hospital through the contribution they make to the development of effective analytical accounting, making it possible to evaluate costs and to adjust charges appropriately. Finally, the involvement of the SIM in the setting up and functioning of the Comite de Lutte Contre les Infections Nosocomiales (CLIN; the Hospital-Acquired Infections Committee) in 1999 to 2000 is not utopia, it is the logical continuation of improvements in the overall quality of care It involves, in particular, the training of nurses and head nurses, initiated by nurses acting as technical assistants in the French cooperation program. The definition of the role of the hygiene nurse and the selection of such a nurse from the trained head nurses are also part of this process.

Facklam R. et al. *Identification of Streptococcus porcinus from human sources.* J Clin Microbiol. 1995; 33(2) : 385-8.p Abstract: Streptococcus porcinus is normally associated with infections in swine. Cultures of this streptococcal species are rarely reported from human infections. In the past 10 years, we have identified 13 cultures of S. porcinus from human sources from persons living in the United States and Canada. Seven of the strains were identified in the past 15 months. Nine of the strains were of a single serogroup, provisionally called C1. In addition, nine of the strains were isolated from the genitourinary tract of reproductive-age female patients, some with delivery problems. S. porcinus strains could be identified by hemolytic, serologic, and physiologic characteristics. All strains were susceptible to penicillin, erythromycin, and other antimicrobial agents. Fifty-four percent of the strains were resistant to tetracycline. These findings suggest that we may be seeing a change in the flora of the genitourinary tract of humans. Whether these isolates are significant pathogens is unknown at this time.

Fagon J.Y. et al. *Hospital-acquired pneumonia: methicillin resistance and intensive care unit admission.* Am J Med. 1998; 104(5A) : 17S-23S.p Abstract: Although epidemiologic investigations of hospital-acquired pneumonia have certain intrinsic limitations because of the heterogeneity of the study populations, the difficulties in making a clinical diagnosis of nosocomial pneumonia, and the need for better microbiologic assays, recent studies have provided new and important data concerning the role of Staphylococcus aureus in this disease. This pathogen has now been identified as the most frequent cause of nosocomial pneumonia in hospitals in both Europe and the United States among patients in general hospital units as well as in the intensive care unit (ICU). Patients who have been treated with mechanical ventilation are at especially high risk for S. aureus pneumonia. The incidence of nosocomial pneumonia related to methicillin-resistant S. aureus (MRSA) has increased in recent years in many countries, especially among patients in the ICU. Because hospitalized patients with suspected nosocomial pneumonia often have many risk factors for MRSA infection, it seems advisable to include coverage of MRSA in the initial therapeutic regimen for these patients until MRSA infection is excluded.

Fairchok M.P. et al. *Carriage of penicillin-resistant pneumococci in a military population in Washington, DC: risk factors and correlation with clinical isolates.* Clin Infect Dis. 1996; 22(6) : 966-72.p Abstract: To assess the carriage of penicillin-resistant pneumococci (PRP) in our local (military) population, we retrospectively reviewed our laboratory isolates from the period of January 1990 through May 1994 and prospectively obtained nasopharyngeal culture specimens from 179 children during January through May 1994. The incidence of PRP increased from 0% of pneumococcal isolates in 1990 to 36.2% by 1994. Fifty-two of 179 subjects (29%) were carriers of S. pneumonia, and 25 (48%) of them carried PRP; 11 (21.7%) of these isolated were highly resistant to penicillin (MIC, > 1.0 microgram/mL), and 14 (26.9%) were intermediately resistant (MIC, 0.1-1.0 micrograms/mL). Exposure to a health care worker was correlated with pneumococcal carriage (P <.007). Frequent courses of antimicrobial treatment correlated both with carriage of pneumococci (P <.009) and with carriage of PRP (P <.0001). In contrast, antimicrobial prophylaxis was protective against carriage of pneumococci (P <.002). We conclude that there is a high proportion of PRP among carriers of pneumococci in our community, as corroborated by the risk in laboratory isolation of PRP. Children who have had frequent antimicrobial courses are at particular risk.

Falagas M.E. et al. *Bacteroides, Prevotella, and Porphyromonas species: a review of antibiotic resistance and therapeutic options.* Int J Antimicrob Agents. 2000; 15(1) : 1-9.p Abstract: Recent basic and clinical research efforts have shed more light on the taxonomy, microbiology, epidemiology, antimicrobial susceptibility and treatment of Bacteroides, Prevotella, and Porphyromonas species. Of all anaerobic bacteria, Bacteroides is the most frequently isolated pathogen from clinical specimens, including blood. Bacteroides, Prevotella and/or Porphyromonas species have been isolated from clinical specimens in cases of infection from almost all anatomic sites. Several multicentre surveys have documented an alarming gradual increase of resistance rates of Bacteroides, Prevotella and Porphyromonas species worldwide. Antimicrobial agents active against >99% of clinical isolates of Bacteroides are metronidazole, chloramphenicol and carbapenems. Agents active against 95-99% of Bacteroides fragilis isolates are the beta-lactam/beta-lactamase inhibitor combinations. B. fragilis group species other than B. fragilis are more likely to be resistant to beta-lactam/beta-lactamase inhibitor combinations than B. fragilis.

Falcao M.C. et al. *Urinary tract infection in full-term newborn infants: risk factor analysis.* Rev Hosp Clin Fac Med Sao Paulo. 2000; 55(1) : 9-16.p

Abstract: OBJECTIVE: To analyze the correlation of risk factors to the occurrence of urinary tract infection in full-term newborn infants. PATIENTS AND METHODS: Retrospective study (1997) including full-term infants having a positive urine culture by bag specimen. Urine collection was based on: fever, weight loss > 10% of birth weight, nonspecific symptoms (feeding intolerance, failure to thrive, hypoactivity, debilitate suction, irritability), or renal and urinary tract malformations. In these cases, another urine culture by suprapubic bladder aspiration was collected to confirm the diagnosis. To compare and validate the risk factors in each group, the selected cases were divided into two groups: Group I - positive urine culture by bag specimen collection and negative urine culture by suprapubic aspiration, and Group II - positive urine culture by bag specimen collection and positive urine culture by suprapubic aspiration. RESULTS: Sixty one infants were studied, Group I, n = 42 (68.9%) and Group II, n = 19 (31.1%). The selected risk factors (associated infectious diseases, use of broad-spectrum antibiotics, renal and urinary tract malformations, mechanical ventilation, parenteral nutrition and intravascular catheter) were more frequent in Group II ($p<0.05$). Through relative risk analysis, risk factors were, in decreasing importance: parenteral nutrition, intravascular catheter, associated infectious diseases, use of broad-spectrum antibiotics, mechanical ventilation, and renal and urinary tract malformations. CONCLUSION: The results showed that parenteral nutrition, intravascular catheter, and associated infectious diseases contributed to increase the frequency of neonatal urinary tract infection, and in the presence of more than one risk factor, the occurrence of urinary tract infection rose up to 11 times.

Falkler W.A. Jr et al. *Isolation of Fusobacterium necrophorum from cancrum oris (noma).* Am J Trop Med Hyg. 1999; 60(1) : 150-6.p Abstract: A study of the predominant microflora in active sites of noma (cancrum oris) lesions was carried out in eight noma patients 3-15 years of age in Sokoto State in northwestern Nigeria. Paper point sampling and conventional anaerobic microbiologic techniques were used. Fusobacterium necrophorum was recovered from 87.5% of the noma lesions. Oral microorganisms included Prevotella intermedia, alpha-hemolytic streptococci, and Actinomyces spp. which were isolated from 75.0%, 50.0%, and 37.5% of the patients, respectively. Peptostreptococcus micros, Veillonella parvula, Staphylococcus aureus, and Pseudomonas spp. were each recovered from one lesion. The F. necrophorum and P. intermedia isolates were tested for antibiotic sensitivity to clindamycin, tetracycline, metronidazole, and penicillin using the E-test, and all strains were observed to be sensitive to all of the antibiotics tested with the exception of one strain of P. intermedia, which showed resistance to penicillin. The first reported isolation from human noma lesions of F. necrophorum, a pathogen primarily associated with animal diseases, may have important etiologic and animal transmission implications.

Falkler W.A. Jr et al. *Microbiological understandings and mysteries of noma (cancrum oris).* Oral Dis. 1999; 5(2) : 150-5.p Abstract: The microbiologic history of noma was reviewed. Studies have associated the disease process with large numbers of fusiform bacilli and spirochetal organisms. In order to study the microbiology of the staging and infection periods of noma 62 Nigerian children, aged 3-14 years, 22 children had acute necrotizing ulcerative gingivitis (ANUG) and were also malnourished, 20 exhibited no acute necrotizing ulcerative gingivitis but were malnourished and 20 were free of acute necrotizing ulcerative gingivitis and in good nutritional state) were evaluated for the presence of viruses and oral microorganisms. The ANUG cases in the malnourished children had a higher incidence of Herpesviridae, the main virus being detected was cytomegalovirus. There were more anaerobic microorganisms recovered, with Prevotella intermedia as the predominant isolate, in the malnourished children as compared to the healthy children. A study of the predominant microflora in active sites of noma lesions was carried out in eight noma patients, 3-15 years of age, in Sokoto State, northwestern Nigeria. Fusobacterium necrophorum was recovered from 87.5% of the noma lesions. Oral microorganisms isolated included Prevotella intermedia, alpha-hemolytic streptococci and Actinomyces spp. which were isolated from 75.0, 50.0 and 37.5% of the patients, respectively. Peptostreptococcus micros, Veillonella parvula, Staphylococcus aureus and Pseudomonas spp. were each recovered from one lesion. All strains were observed to be sensitive to all of the antibiotics tested with the exception of one strain of P. intermedia which showed resistance to penicillin. The pathogenic mechanisms of F. necrophorum as a trigger organism were discussed. The isolation from human noma lesions of F. necrophorum, a pathogen primarily associated with animal diseases, may have important etiologic and animal transmission implications.

Fanchin R. et al. *Microbial flora of the cervix assessed at the time of embryo transfer adversely affects in vitro fertilization outcome.* Fertil Steril. 1998; 70(5) : 866-70.p Abstract: OBJECTIVE: To investigate whether the presence of cervical microorganisms, as detected on catheters used for ET, alters the outcome of IVF-ET. DESIGN: Prospective analysis. SETTING: The assisted reproduction unit of a hospital in Clamart, France. PATIENT(S): Two hundred seventy-nine controlled ovarian hyperstimulation (COH) cycles performed for IVF-ET. Inclusion criteria were a patient age of < or =38 years, a morphologically normal uterus, and > or =2 good-quality embryos transferred. INTERVENTION(S): The tips of catheters used for ruling out possible cervical obstruction before ET were subjected to quantitative (> or =10 colonies = positive culture group; <10 colonies = negative culture group) and qualitative microbial assessment. MAIN OUTCOME MEASURE(S): Pregnancy and implantation rates. RESULT(S): In 143 (51%) of 279 ETs, cultures were positive, predominantly for Escherichia coli (64%) and Streptococcus species (8%). Although data on patients, COH, and embryology were similar in both culture groups, clinical and ongoing pregnancy rates as well as implantation rates were significantly lower in the positive culture group than in the negative culture group (24% versus 37%; 17% versus 28%; and 9% versus 16%, respectively). CONCLUSION(S): The presence of microbial flora of the cervix on ET catheters is associated with poor IVF-ET outcome.

Fang C.T. et al. *Microbiologic features of adult community-acquired bacterial meningitis in Taiwan.* J Formos Med Assoc. 2000; 99(4) : 300-4.p Abstract: BACKGROUND AND PURPOSE: Community-acquired bacterial meningitis (CABM) is a life-threatening disease that requires prompt initiation of appropriate antibiotic therapy. The purpose of this study was to determine the causative microorganisms of CABM and their antimicrobial susceptibility patterns at a major teaching hospital in Taipei from 1993 to 1998. METHODS: A review of medical records and microbiologic data was used to identify cases of CABM and causative pathogens. Antimicrobial susceptibility testing for bacterial isolates was performed by the disk diffusion method. RESULTS: Among the 48 adult patients with a diagnosis of CABM during the study period, the causative pathogens were identified in 36 cases. Unlike reports from other countries, Klebsiella pneumoniae was the leading causative pathogen (33%), followed by Streptococcus pneumoniae (28%), Listeria monocytogenes (11%), Neisseria meningitidis (6%), Staphylococcus aureus (6%), streptococci (6%), and Pseudomonas aeruginosa (6%). The incidence of CABM due to K. pneumoniae increased during the study period ($p = 0.012$, Poisson regression), while the incidence of CABM due to other pathogens remained stable. All of the CABM-associated K. pneumoniae isolates were susceptible to cefotaxime but 25% of the CABM-associated S. pneumoniae strains were not susceptible to penicillin G. CONCLUSIONS: Penicillin G alone was not an appropriate empiric therapy for adult CABM because a high percentage of cases were due to K. pneumoniae or penicillin nonsusceptible S. pneumoniae. While the recommendations for the initial empiric regimen for CABM due to S. pneumoniae in Taiwan remain to be developed, third-generation cephalosporins appear to be an appropriate initial empiric regimen for the treatment of CABM due to K. pneumoniae.

Fang C.T. et al. *Klebsiella pneumoniae meningitis: timing of antimicrobial therapy and prognosis.* QJM. 2000; 93(1) : 45-53.p Abstract: We analysed the clinical course of 30 adult patients with Klebsiella pneumoniae meningitis, 18 community-acquired and 12 hospital-acquired, to assess whether the timing of appropriate antimicrobial therapy had a major effect on prognosis. Of the 30 patients, 29 received appropriate antibiotics. The time from initial symptoms to the start of appropriate therapy, antibiotic resistance of K. pneumoniae isolates, underlying disease severity, diabetes mellitus, age, gender, and acquisition settings were all not significantly correlated with outcome. However, a Glasgow coma scale (GCS) score of 7 points or less at the start of appropriate antimicrobial therapy was a valid predictor of death or a permanent vegetative state (sensitivity 82%, specificity 93%, p=0.005), even after adjusting for the effect of confounding variables by logistic regression. Timing of appropriate antimicrobial therapy, as defined by consciousness level but not by symptom duration, is a major determinant of survival and neurological outcome for patients with K. pneumoniae meningitis, and the first dose of an appropriate antibiotic should be administrated before their consciousness deteriorates to a GCS score of 7 points or less.

Fanos V. et al. *Antimicrobial survey of urinary tract isolates from a pediatric department*. J Chemother. 1999; 11(4) : 255-9.p Abstract: The epidemiology of urinary tract colonization/infection in children admitted during 1996 to the Pediatric Department of the University of Verona has been studied; 501/1959 urine cultures were positive (25.57%). 584 microorganisms (64.89% Gram-negative, 24.82% Gram-positive, 10.27% fungi) were isolated. The highest rate of Gram-negative isolation (80.0%) was observed in infants, while the highest rate of Gram-positive isolation (29.6%) was found in newborns admitted to the neonatal intensive care unit. Escherichia coli was the most frequently isolated microorganism in infants and children, but not in newborns. A 3-fold increase in resistant E. coli strains to cotrimoxazole/sulfamethoxazole and amoxicillin/clavulanic acid was documented during the last 3 years in this pediatric population. Our observations underline the importance of the survey of microbial maps in pediatric departments in order to optimize therapeutic and preventive choices.

Fanos V. et al. *Staphylococcus epidermidis isolation and antibiotic resistance in a neonatal intensive care unit*. J Chemother. 1995; 7(1) : 26-9.p Abstract: Bacterial ecology was studied in 1114 newborns (355 at term, 759 preterm) admitted to a neonatal intensive care unit (NICU) during a three year period. Bacterial samples were taken in each newborn from external ear canal, pharynx and eyes in all patients, and from endotracheal tube, umbilical catheter and blood in selected patients. The predominant flora was characterized by gram-positive microorganisms (63.53%), Staphylococcus epidermidis representing 34.68% of all isolated strains. S. epidermidis isolation increased significantly with time ($p < 0.002$) and was highest in summer. The percentage of S. epidermidis resistant strains to oxacillin (63.8%) and to amikacin (17.8%) was high. This is the antimicrobial combination we commonly employ as empirical treatment of suspected bacterial infection in our NICU. Knowledge of characteristics of local microbial flora seems important in order to optimize preventive and therapeutic policies for neonatal infections.

Farina C. et al. *Human nocardiosis in northern Italy from 1982 to 1992. Northern Italy Collaborative Group on Nocardiosis.* Scand J Infect Dis. 1995; 27(1) : 23-7.p Abstract: We conducted a retrospective survey of nocardiosis in 9 city hospitals in northern Italy from 1982 to 1992. The medical records of 30 patients with documented nocardiosis were reviewed. Microbiological data included morphology, biochemical characteristics, serology and in vitro susceptibility testing. The 29 isolates (1 case was diagnosed on the basis of serological results) were Nocardia asteroides (n = 25) and Nocardia farcinica (n = 4). Predisposing factors including immunosuppression for organ transplant rejection prophylaxis, lung disease (silicotuberculosis and pulmonary fibrosis), solid tumours and hematological malignancies, and AIDS. Three patients had no identified risk factors. 20 cases of pulmonary nocardiosis were observed. Sites of infection in patients without previous pulmonary involvement were: brain abscesses, soft tissues, pericardium, blood, and cerebrospinal fluid. Most strains tested were susceptible to amikacin and imipenem. Resistance to several antimicrobial agents was found, particularly erythromycin, fosfomycin, pefloxacin, sulphonamides and trimethoprim. Antimicrobial chemotherapy included sulphonamides, amikacin, ceftriaxone, imipenem and minocycline. 21 patients survived, although 2 relapsed transiently. Nocardiosis appears to be more common than generally realised by physicians in northern Italy. The local species distribution and disease spectrum are similar to those described elsewhere. Nocardiosis should be part of the differential diagnosis in patients with pulmonary infiltrates or brain abscess, particularly those with predisposing factors.

Farina R. et al. *Vesico-ureteral reflux: diagnosis and staging with voiding color Doppler US: preliminary experience.* Eur J Radiol. 2000; 35(1) : 49-53.p Abstract: INTRODUCTION: The aim of this study is to assess the accuracy of a new US examination: 'voiding color Doppler US ' in the early diagnosis and staging of vesico-ureteral reflux (VUR). The contrast agent US was SH U 508A (Levovist, Schering, Berlin), which produces a chromatic accentuation of the signals picked up by the color Doppler US. Eighteen patients (10 females, eight males) were recruited for the study. In two patients a second examination was performed for follow-up after a VUR conservative therapy. All patients were taken under examination for the evaluation of possible VUR. In all patients the voiding color Doppler US was followed by voiding cystourethrography (VCUG) and the data obtained were compared. MATERIALS AND METHODS: A total of 18 patients aged between 3 months and 10 years, were recruited for the study. The results of the examination were the following: urinary tract infections, follow-up of VUR after conservative or surgical therapy, miscellaneous indications. Voiding color Doppler US was performed, followed by a VCUG. The voiding color Doppler US consists in the trans-catheter introduction of a contrast agent SHU 508 A (Levovist, Schering, Ag. Berlin) into the bladder and a subsequent test with the color Doppler US to show or exclude the presence of reflux into the ureters and/or into the pyelo-caliceal cavity of the kidneys. After the introduction of the contrast agent US the ultrasound scanning of the bladder, the ureters and the pyelo-caliceal cavity was performed to examine the reflux degree. The ultrasonographic investigations were perfomed with AU 590 asyncronus US (Esaote Biomedica, Genova) with a 3.5 MHz convex probe. RESULTS: After the trans-catheter introduction of the contrast agent US, vesico-ureteral reflux occured in 13 patients (77.2%). The reflux degree was also measured by means of ultrasound and was later confirmed by VCUG. The mean times of each examination were as follows: initial US, 10 min; catheterization, 8 min; voiding color Doppler US, 15 min; overall VCURG examination 10 min. The overall mean duration of the voiding color Doppler US examination was 33 min. The comparable mean time for VCUG, including the catheterization time, was 20 min. No reactions of intolerance to the ultrasound contrast agent occurred. DISCUSSION AND CONCLUSIONS: The voiding color Doppler US test has evidenced in all patients the presence of the contrast agent US in the bladder after the introduction. In 13 patients (77.2%) with presence of VUR, the voiding color Doppler US test has established the reflux degree confirmed by cystourethrography. The superimposability of the data obtained with voiding color Doppler US and VCUG would seem to confirm the importance of this new ultrasonographic technique in the diagnosis and staging of VUR.

Farr B.M. et al. *Diagnostic tests: distinguishing good tests from bad and even ugly ones.* Infect Control Hosp Epidemiol. 2000; 21(4) : 278-84.p Abstract: This article focuses on the selection and interpretation of diagnostic tests, emphasizing the importance of understanding how their mathematical parameters affect the information they provide in various settings. The utility and limitations of sensitivity, specificity,

predictive value, and receiver operating characteristic (ROC) curves are discussed using catheter-related bloodstream infections as an example. ROC curves have been used for selecting optimal cutoff values for a positive result and for selecting among several alternative diagnostic tests. For example, 16 different tests have been proposed for diagnosis of catheter-related bloodstream infection; ROC analysis provides an effective way to determine which test offers the best overall performance.

Faruque S.M. et al. *Genomic diversity among Vibrio cholerae O139 strains isolated in Bangladesh and India between 1992 and 1998.* FEMS Microbiol Lett. 2000; 184(2) : 279-84.p Abstract: In order to assess the extent of genomic diversity among Vibrio cholerae O139 strains, restriction fragment length polymorphisms in two genetic loci, rrn and ctx, were studied. Analysis of 144 strains isolated from different regions of Bangladesh and India between 1992 and 1998 revealed the presence of at least six distinct ribotypes (B-I through B-VI) of which three were new ribotypes, and one of these was represented by a nontoxigenic O139 strain. Strains of ribotypes B-I through B-V shared 11 different CTX genotypes (A through K). Antimicrobial resistance patterns of the strains varied independently of their ribotypes and CTX genotypes. Results of this study suggest that V. cholerae O139 is undergoing rapid genetic changes leading to the origination of new variants, and temporal changes in antimicrobial resistance patterns may be contributing to the selection of different variants.

Fattorini L. et al. *Activity of 16 antimicrobial agents against drug-resistant strains of Mycobacterium tuberculosis.* Microb Drug Resist. 1999; 5(4) : 265-70.p Abstract: The in vitro activity of 16 antimicrobial agents against 46 drug-resistant strains of Mycobacterium tuberculosis recently isolated from Italian patients was determined. As for first-line antituberculosis drugs, while isoniazid was ineffective against all the strains tested, resistance to streptomycin, rifampicin, pyrazinamide, and ethambutol was 80.4%, 71.7%, 39.1%, and 8.7%, respectively. Among second-line antituberculous drugs, resistance to ciprofloxacin, ofloxacin, and sparfloxacin and to amikacin and kanamycin was around 20%. About 10% of the strains were resistant to capreomycin and cycloserine and 4.3% were resistant to ethionamide; no strain was found to be resistant to thiacetazone, para-aminosalicylic acid, and viomycin. Although all strains displayed a rather continuous distribution of minimal inhibitory concentrations (MICs), a bimodal distribution was observed for rifampicin, amikacin, and kanamicin, with very high MIC values for resistant strains; relatively low MICs were found for fluoroquinolone-resistant strains. Among the small number of strains resistant to second-line agents, low resistant levels were observed. Restriction fragment length polymorphism analysis showed few strain clusters with resistance to first-line antituberculous drugs and aminoglycosides, fluoroquinolones, or both. Altogether, these results showed that second-line agents were still active against the isoniazid-resistant and multiply first-line resistant strains tested, with none or low resistance levels; these observations can be of importance for the treatment of multidrug-resistant tuberculosis in Italy.

Fayon M.J. et al. *Nosocomial pneumonia and tracheitis in a pediatric intensive care unit: a prospective study.* Am J Respir Crit Care Med. 1997; 155(1) : 162-9.p Abstract: We conducted a prospective study in the multidisciplinary pediatric intensive care unit (pediatric ICU) of a tertiary-care university hospital in order to determine the incidence, risk markers, risk factors, and complications related to bacterial nosocomial pneumonia (BNP) and tracheitis (BNT) in children. A cohort of 1,114 consecutive admissions to the pediatric ICU was enrolled over a 56-wk period; 154 cases were excluded mostly (75%) because they already had a respiratory infection at entry. The final sample included 960 admissions (831 patients). Diagnosis of BNP or BNT was based on Centers for Disease Control of Atlanta criteria using a consensus method involving three experts, who also attributed complications to BNP and BNT. A total of 29 BNP and BNT (3.0%; 95% CI: 1.1 to 4.1%) were diagnosed (BNP: 1.2%, 95% CI: 0.7 to 1.9%; BNT: 1.8%, 95% CI: 0.8 to 2.6%). Three factors were retained by multivariate analysis as independent risk factors or markers for BNP (immunodeficiency, immunosuppression, and neuromuscular blockade), and two for BNT (head trauma and respiratory failure). Gram-negative bacteria and Staphylococcus aureus were the microorganisms most frequently found in the tracheal aspirates. Prescription of antibiotics was commonly attributable to BNP (75%) and BNT (59%). Death, as well as multiple organ system failure, resulted from BNP in 8% of cases, but never from BNT. In BNT, the reintubation rate was 24%. Nosocomial bacterial respiratory infections are rare in critically ill children. However, BNP causes significant complications, and more attention should be focused on BNT in the critically ill child.

Fedorovskaia E.A. et al. *[The characteristics of the causative agents of suppurative-inflammatory complications in hemophiliacs].* Mikrobiol Z. 1998; 60(4) : 88-92.p Abstract: Morphological-cultural and physiological-biochemical properties of 24 strains of microorganisms agents of pyo-inflammatory complications of different localization in patients with hemophilia have been studied. Microorganisms strains presented by the following species: Staphylococcus aureus, S. epidermidis, S. saprophyticus, Proteus vulgaris, P. morganii, Hafnia alvei, Serratia marcescens, have been identified. It was found out that in monoculture staphylococci prove to be the leading etiological agent (60.9%), gram-negative enterobacteria (52.2%) and bacterial associations (8.7%) occur more rarely. Special attention was paid to the study of resistance of antibiotics, circulation and pathogenicity factors that had a direct effect on the main disease severity. It was ascertained that high activity of enzymes and presence of pathogenicity factors were the peculiarities of microorganisms isolated from pyo-septic sites in patients with hemophilia. All the strains possessed multiple resistance to antibiotics.

Fedson D.S. *Pneumococcal vaccination for older adults: the first 20 years.* Drugs Aging. 1999; 15 Suppl 1 : 21-30.p Abstract: During the 20 years following its licensure, pneumococcal vaccine has not been widely used. Although the vaccine was shown to be efficacious in South African gold miners, clinical trials of 'pneumonia vaccine' in older adults that have attempted to demonstrate vaccine efficacy in preventing pneumonia have been inconclusive. Retrospective studies have convincingly demonstrated the effectiveness of vaccination in preventing invasive pneumococcal disease, but these findings have only gradually gained acceptance, largely because some observers reject the findings of observational studies or fail to appreciate the importance of invasive disease. In the 1980s, pneumococcal vaccine was used only in the US, but other countries began vaccination in the mid-1990s, in part due to a better understanding of the disease and the vaccine, but also because of concern about antimicrobial resistance. With greater understanding of the global importance of pneumococcal disease and the promise of conjugate and protein vaccines, during the next 20 years pneumococcal vaccines will become the most important vaccines for adults and children worldwide.

Feikin D.R. et al. *Increased carriage of trimethoprim/sulfamethoxazole-resistant Streptococcus pneumoniae in Malawian children after treatment for malaria with sulfadoxine/pyrimethamine.* J Infect Dis. 2000; 181(4) : 1501-5.p Abstract: Treatment of malaria with sulfadoxine/pyrimethamine and of presumed bacterial infections with trimethoprim/sulfamethoxazole (cotrimoxazole) was assessed to see if either increases the carriage of cotrimoxazole-resistant Streptococcus pneumoniae in Malawian children. Children <5 years old treated with sulfadoxine/pyrimethamine, cotrimoxazole, or no antimicrobial agent were enrolled in a prospective observational study. Nasopharyngeal swabs were taken before treatment and 1 and 4 weeks later. Pneumococci were tested for antibiotic susceptibility by broth microdilution. In sulfadoxine/pyrimethamine-treated children, the proportion colonized with cotrimoxazole-nonsusceptible

pneumococci increased from 38.1% at the initial visit to 44.1% at the 4-week follow-up visit (P=.048). For cotrimoxazole-treated children, the proportion colonized with cotrimoxazole-nonsusceptible pneumococci increased from 41.5% at the initial visit to 52% at the 1-week follow-up visit (P=.0017) and returned to 41.7% at the 4-week follow-up. Expanding use of sulfadoxine/pyrimethamine to treat chloroquine-resistant malaria may have implications for national pneumonia programs in developing countries where cotrimoxazole is widely used.

Fekete T. et al. *Comparative susceptibilities of Klebsiella species, Enterobacter species, and Pseudomonas aeruginosa to 11 antimicrobial agents in a tertiary-care university hospital*. Am J Med. 1996; 100(6A) : 20S-25S.p Abstract: The in vitro activity of cefepime was compared versus that of 10 antimicrobial agents commonly used in the treatment of serious infections caused by common aerobic gram-negative bacteria: aztreonam, cefoperazone, ceftazidime, ceftriaxone, ciprofloxacin, gentamicin, imipenem, piperacillin, ticarcillin-clavulanic acid, and tobramycin. We tested 30 clinical isolates representing a cross section of Klebsiella and Enterobacter species and Pseudomonas aeruginosa collected at our tertiary-care university hospital. The most potent beta-lactams were imipenem and cefepime, which demonstrated significant activity against the majority of strains in all 3 genera of bacteria tested, as did ciprofloxacin and tobramycin. Ceftazidime was active against Pseudomonas aeruginosa but was less potent against Klebsiella and Enterobacter spp. Cefoperazone and ceftriaxone were less active than ceftazidime against Pseudomonas aeruginosa. Cefepime was found to be highly active against many resistant organisms that traditionally have been difficult to treat.

Felmingham D. et al. *The Alexander Project 1996-1997: latest susceptibility data from this international study of bacterial pathogens from community-acquired lower respiratory tract infections.* J Antimicrob Chemother. 2000; 45(2) : 191-203.p Abstract: The Alexander Project was established in 1992 to examine antimicrobial susceptibilities of bacterial isolates from community-acquired infections of the lower respiratory tract. Testing of a range of compounds was undertaken in a central laboratory. From 1992 to 1995, isolates were collected from geographically separated areas in countries in the European Union and various states in the USA. In 1996, the study was extended to include centres in Mexico, Brazil, Saudi Arabia, South Africa, Hong Kong and other European countries not included previously. Data generated by the project during 1996-1997 confirm France and Spain as European centres with high rates of resistance to penicillin among isolates of Streptococcus pneumoniae. Both intermediate (MIC 0. 12-1 mg/L) and resistant (MIC 2 mg/L) phenotypes are present. Combined resistance rates (intermediate and resistant) were >/=50% in 1997. Combined resistance rates in excess of 20% were found in the Republic of Ireland, Portugal, the Slovak Republic and Hungary. Penicillin resistance continues to evolve in the USA, with combined resistance rates of 16.4% (1996) and 18.6% (1997). In the new, non-European centres, e.g. Mexico and, in particular, Hong Kong (where resistant strains accounted for 50% of all isolates of S. pneumoniae in 1996 and 55.5% in 1997), there are centres where rates of resistance are high. Macrolide resistance is increasing generally among both penicillin-resistant and penicillin-susceptible isolates of S. pneumoniae. There is variation between countries, and in four out of the 16 centres for which both 1996 and 1997 data are available, rates of macrolide resistance have fallen. Overall, the percentage of S. pneumoniae strains that is resistant to macrolides exceeds the percentage that is resistant to penicillin. In 1996, 16. 5% of all S. pneumoniae isolates were resistant to macrolides compared with 10.4% resistant to penicillin, and in 1997 respective rates were 21.9% and 14.1%. beta-Lactamase production was the principal mechanism of resistance observed among isolates of Haemophilus influenzae. However, considerable variation in the percentage of isolates producing beta-lactamase (0-37.1%) was observed within this species. Within Europe, in the Republic of Ireland, France and Belgium, more than 15% of isolates were beta-lactamase producers. In Spain rates were as high as 31.7%. Outside Europe and the USA high rates were described in Mexico (25%), Saudi Arabia (27.9%, 16.7%) and Hong Kong (37.1%, 28.9%). Of H. influenzae from the USA, 30.4% were beta-lactamase producers in 1996 and 23.3% in 1997. beta-Lactamase production among isolates of Moraxella catarrhalis was observed in >90% of the isolates tested in 1996 and 1997.

Felmingham D. et al. *A multicentre collaborative study of the antimicrobial susceptibility of community-acquired, lower respiratory tract pathogens 1992-1993: the Alexander Project*. J Antimicrob Chemother. 1996; 38 Suppl A : 1-57.p Abstract: The Alexander Project is a unique, international, collaborative antimicrobial susceptibility surveillance study of bacterial pathogens causing community-acquired lower respiratory tract infection. Fifteen centres, ten in the European Union (EU) and five in the USA, each submitted up to 400 isolated per year for 2 years (1992 and 1993) to a central laboratory for re-identification and determination of MICs of 15 antimicrobials using the Sensititre microbroth incorporation technique. Of the total of 6385 isolates collected, Haemophilus influenzae (2718), Streptococcus pneumoniae (1856) and Moraxella catarrhalis (818) were the most frequently identified pathogens. Staphylococcus aureus (690). Haemophilus parainfluenzae (183) and Klebsiella pneumoniae (120) were identified less commonly. High-level penicillin resistance in S. pneumoniae (MIC > or = 2 mg/L) was found in 222 isolates, an overall prevalence of 12% which varied from < 1% in Germany, Italy, UK and two of the five USA centres, to 3.8-40.4% in the remainder, with the highest prevalence found in France and Spain. Intermediate penicillin resistance (MIC 0.12-1 mg/L) was identified in 228 isolates of S. pneumoniae, an overall prevalence of 12.3%, with individual centre prevalence varying widely (EU, 0-52.3%; USA, 0-20.9%) and not always following that of high-level resistance. Resistance to other, unrelated, antimicrobials, except notably the fluoroquinolones, was strongly associated with beta-lactam resistance. beta-lactamase production was detected in 492 isolates of H. influenzae, an overall prevalence of 18.1%. Rates of detection varied widely between centres from 1.4% in Weingarten, Germany in 1993 to 38.5% in Barcelona, Spain in 1992. In general, the prevalence of beta-lactamase production was higher and less variable in USA centres than in those of the EU. beta-Lactamase was detected consistently in the majority of isolates of M. catarrhalis with an overall prevalence of 81.7%. Virtually no other resistance phenotype was recognised in this species. Of the 690 collected, most isolates of S. aureus produced beta-lactamase with rates of detection varying from 52.2%-89.1%. Isolates from two centres, Genoa, Italy in 1992 and Paris, France in 1993, were associated with a high prevalence of methicillin-resistance (34.8% and 43.8%, respectively). Combined isolates of H. parainfluenzae and K. pneumoniae accounted for only 4.7% of the total collection. Although the current data are insufficient to allow analysis of trends in resistance, the study participants have continued to collect further isolates in 1994 and 1995 which will be reported in the future.

Felmingham D. et al. *Antimicrobial susceptibility of community-acquired lower respiratory tract bacterial pathogens isolated in the UK during the 1995-1996 cold season*. J Antimicrob Chemother. 1998; 41(3) : 411-5.p Abstract: The antimicrobial susceptibility of 1078 isolates of Haemophilus influenzae, 348 Streptococcus pneumoniae and 258 Moraxella catarrhalis was determined. Overall 15.1% of H. influenzae produced beta-lactamase; 98.8% were susceptible to co-amoxiclav, 85.8% to cefaclor, 96% to clarithromycin and 100% to ciprofloxacin. The majority (94.2%) of M. catarrhalis produced beta-lactamase. The overall prevalence of low-level penicillin resistance (MIC = 0.12-1 mg/L) amongst isolates of S. pneumoniae was 3.4% and that of high-level resistance (MIC > or = 2 mg/L) was 3.7%. Most (96.3%) of the isolates of S. pneumoniae were susceptible to amoxycillin (MIC < or = 0.5 mg/L), 96% to cefaclor (MIC < or = 8 mg/L), 90.7% to clarithromycin (MIC < or = 0.25 mg/L) and 89% to ciprofloxacin (MIC < or = 1 mg/L).

Felmingham D. et al. *Trends in the antimicrobial susceptibility of bacterial respiratory tract pathogens—findings of the Alexander Project 1992-1996.* J Chemother. 1999; 11 Suppl 1 : 5-21.p Abstract: The Alexander Project is an ongoing, multicenter surveillance study of the antimicrobial susceptibility of community-acquired lower respiratory tract bacterial pathogens with testing undertaken in a central laboratory. During the period 1992-1995, isolates were collected from geographically separate centers in countries of the EU and various states in the USA. In 1996, the project was extended to centers in Mexico, Brazil, Saudi Arabia, South Africa, Hong Kong and other European countries not previously included. Within Europe, France and Spain are established as centers with a high prevalence of both penicillin-intermediate (MIC 0.12-1 mg/l) and resistant (MIC > or = 2 mg/l) strains of Streptococcus pneumoniae, with combined resistance rates in excess of 40% in Toulouse and Barcelona in 1996. Combined rates of intermediate and resistant strains in excess of 10% were found in 1996, the first year of sampling, in Belgium, Switzerland, the Slovak Republic and Hungary. Penicillin resistance has evolved in the USA during the period of study, with rates for combined pneumococcal isolates increasing from 5.6% in 1992 to 16.4% in 1996. Of the new, non-European centers joining the project in 1996, Mexico (intermediate 31.4%, resistant 15.7%) and, in particular, Hong Kong (intermediate 9.1%, resistant 50%) are centers with a high prevalence of penicillin resistance. Macrolide resistance has increased generally among pneumococcal isolates examined during the study period, both in penicillin-susceptible and resistant isolates, and was evident in 16.5% of the 2160 isolates collected during 1996. In four centers (London, UK; Genoa, Italy; Pokfulum, Hong Kong; Leuven, Belgium), macrolide resistance rates exceeded those of combined penicillin-intermediate and resistant strains; in 12/19 centers (63.2%) macrolide resistance was more prevalent than penicillin resistance. In 1996, macrolide resistance was found in excess of 10% of isolates in Poland, Hungary, London, UK, combined USA isolates, the Slovak Republic, Barcelona, Spain, Genoa, Italy, Mexico, Toulouse, France and Pokfulum, Hong Kong. beta-lactamase production was the principal mechanism of resistance found among isolates of Haemophilus influenzae, with rates in 1996 of around 20% or more in France, Belgium and Spain, and in excess of 10% in the UK and the Czech Republic. In the same year in non-European centers, Mexico (25%), Saudi Arabia (27.9%), Hong Kong (37.1%) and the USA (30.4% of combined isolates) had a high prevalence of beta-lactamase production. Isolates of beta-lactamase-negative, ampicillin-resistant H. influenzae were generally very uncommon, with only Barcelona, Spain consistently associated with rates in excess of 1%. beta-lactamase production in Moraxella catarrhalis was observed in over 90% of isolates tested in 1996.

Feng Q.L. et al. *A mechanistic study of the antibacterial effect of silver ions on escherichia coli and staphylococcus aureus.* J Biomed Mater Res. 2000; 52(4) : 662-8.p Abstract: To investigate the mechanism of inhibition of silver ions on microorganisms, two strains of bacteria, namely Gram-negative Escherichia coli (E. coli) and Gram-positive Staphylococcus aureus (S. aureus), were treated with AgNO(3) and studied using combined electron microscopy and X-ray microanalysis. Similar morphological changes occurred in both E. coli and S. aureus cells after Ag(+) treatment. The cytoplasm membrane detached from the cell wall. A remarkable electron-light region appeared in the center of the cells, which contained condensed deoxyribonucleic acid (DNA) molecules. There are many small electron-dense granules either surrounding the cell wall or depositing inside the cells. The existence of elements of silver and sulfur in the electron-dense granules and cytoplasm detected by X-ray microanalysis suggested the antibacterial mechanism of silver: DNA lost its replication ability and the protein became inactivated after Ag(+) treatment. The slighter morphological changes of S. aureus compared with E. coli recommended a defense system of S. aureus against the inhibitory effects of Ag(+) ions. Copyright 2000 John Wiley & Sons, Inc.

Fenollar F. et al. *Comparison of a commercial disk test with vancomycin and colimycin susceptibility testing for identification of bacteria with abnormal gram staining reactions.* Eur J Clin Microbiol Infect Dis. 2000; 19(1) : 33-8.p Abstract: In an effort to identify bacteria that fail to give the expected Gram reaction, thus leading to misidentification, two nonstaining tests for Gram reaction, vancomycin and colimycin susceptibility testing and the Gram-Sure test (Remel, USA), were employed on 145 strains from 42 gram-negative and gram-positive genera with contradictory Gram stain results. The Gram-Sure test is a commercially available disk that detects the presence of L-alanine-aminopeptidase, an enzyme usually found only in the cell wall of gram-negative bacteria. In this test, aminopeptidase activity is detected using a substrate that can be hydrolyzed to produce a fluorescent compound under long-wave UV light. The commercial disk test and vancomycin plus colimycin susceptibility testing appeared to perform equally well except in the identification of Erysipelothrix and Lactobacillus, for which the commercial disk test was better, and Moraxella, for which vancomycin and colimycin susceptibility testing was more helpful. An advantage of the commercial disk test is that it can be performed in 10 min, whereas vancomycin and colimycin susceptibility testing requires at least 18 h. The commercial disk test is also less expensive than vancomycin and colimycin susceptibility testing. However, since the same results can be obtained with the 5 microg and 30 microg vancomycin disks, it is possible to use only one vancomycin disk, with the cost then being equivalent to that of the commercial disk test. The major inconvenience of the commercial disk test is the requirement of a UV ray. However, this test could be a useful tool for the identification of unusual organisms.

Fernandes C.J. et al. *Multi-centre collaborative study for the in vitro evaluation of new macrolides dirithromycin and erythromycylamine. Australian Group for Antimicrobial Resistance (AGAR).* Pathology. 1995; 27(1) : 74-8.p Abstract: A national study was conducted to determine the in vitro activity of 2 newer macrolides, dirithromycin and erythromycylamine compared with that of erythromycin, tetracycline and penicillin. Nineteen major teaching hospitals participated in the study. Minimal Inhibitory Concentrations (MICs) were determined by agar dilution, mostly using Iso-Sensitest Agar and an inoculum of 10(4) cells per spot. 2284 clinically significant strains were isolated in late 1991 and early 1992, comprising 1736 Gram-positive cocci, 355 Haemophilus influenzae, 97 Moraxella catarrhalis, 32 Listeria monocytogenes, 25 Neisseria meningitidis and 39 Neisseria gonorrhoeae were tested. The study indicates that dirithromycin and erythromycylamine possess antibacterial activity equivalent to that of erythromycin against most Gram-positive cocci and M. catarrhalis. Strains resistant to erythromycin were also resistant to dirithromycin and to erythromycylamine. Tetracycline was as active as the macrolides against both penicillin-resistant and penicillin-susceptible strains of Staphylococcus aureus. Coagulase-negative penicillin-resistant staphylococci, compared with tetracycline, were relatively resistant to the macrolides. H. influenzae was less susceptible than the Gram-positive cocci.

Fernandes S.A. et al. *Characterization of lactose-fermenting Salmonella agona strains isolated in a pediatric unit.* Rev. microbiol. 1997; 28(4) : 273-8.p Abstract: Eight lactose-fermenting Salmonella agona strains isolated in a pediatric unit were characterized by classic and molecular methods. The strains were classified as biotypes 1a, corresponding to the most frequen one in Brazil. None of the strains produced colicin. Multiple resistence to antimicrobials was observed among the strains studied, It was demonstrated that the lactose-fermenting character was encoded by a plasmid with spontaneous segregaton at a frequency of 1 percer center. This plasmid was transferable by conjugation at a frequency between 4x10(-8) and 5x10(-10). The lac+ plasmid, which molecular weight was approximately 90 MDa, encoded both lactose fermentation and multiple resistance to antimicrobials. Replicon typing showed that this plasmid did not belong to the known types, suggesting the present of a new replicon

type. Classic methods showed that the studied strains had the same characteristics as the clone widely occurring in our area, differing only by lactose-fermenting ability. This conclusion was supported by the results of ribotyping study. (AU).

Fernandez Cobo M. et al. *Characterization of an outbreak of tetM-containing Neisseria gonorrhoeae in Argentina.* Int J STD AIDS. 1999; 10(3) : 169-73.p Abstract: Phenotypic and molecular characterization of an outbreak of 9 Neisseria gonorrhoeae (NG) isolates exhibiting high-level plasmid mediated resistance to penicillin and tetracycline (PP-TRNG) that took place in Tandil, Argentina between February and April 1995. Comparison with the patterns of the 3 PP-TRNG strains previously isolated were made. We determined the following markers for each strain: antimicrobial susceptibility, serogroup, auxotype, plasmid profile, presence of tetM determinant and restriction pattern of the tetM-containing plasmid. Antimicrobial tests values were: tetracycline disk diameter 12-14 mm, minimum inhibitory concentration (MIC) 32 micrograms/ml; penicillin disk diameter 6 mm, MIC 32 micrograms/ml and sensitive by both methods to spectinomycin, cefuroxime, ceftriaxone and ciprofloxacin. All isolates were of the same serogroup (WI). Ten of the strains, including the 9 from Tandil outbreak, were arginine-requiring, while the other 2 were methionine and arginine-requiring. All of them demonstrate the same plasmid profile (2.6, 3.2, 25.2 MDa). They were positive for the tetM determinant and the restriction analysis identified it is a Dutch-type plasmid. In spite of the temporal and geographical dispersion, PP-TRNG strains in Argentina seem to be highly homogeneous in terms of antimicrobial susceptibility, serogroup, plasmid profiles and even auxotype.

Fernandez Guerrero M.L. et al. *Treatment of experimental endocarditis due to ampicillin-susceptible or ampicillin-resistant Salmonella enteritidis.* Antimicrob Agents Chemother. 1996; 40(7) : 1589-93.p Abstract: Using two strains of Salmonella enteritidis, one susceptible and one resistant to ampicillin, we studied the efficacies of ampicillin, gentamicin, ampicillin plus gentamicin, ofloxacin, and cefotaxime for the treatment of experimental salmonella endocarditis. Rabbits were treated for 3 days with dosages of antibiotic selected to achieve concentrations in serum equivalent to those obtained in humans during therapy. Aortic salmonella endocarditis seemed to be very difficult to treat, and all antimicrobial regimens failed to achieve the complete sterilization of cardiac vegetations. In vitro studies did not accurately predict the in vivo response to therapy, and no correlations regarding the synergistic activity of the combination of ampicillin plus gentamicin were observed. For the ampicillin-susceptible S. enteritidis isolate, ampicillin and cefotaxime produced the greatest reduction in the number of organisms in vegetations, with no significant differences between them. For the ampicillin-resistant strain, the combination of ampicillin with gentamicin produced a synergistic effect that was not anticipated by the in vitro studies. Both cefotaxime and ofloxacin were effective in reducing the number of microorganisms in the vegetations, although the reduction produced by cefotaxime was less that that produced against the ampicillin-susceptible strain. Monotherapy with gentamicin exhibited only modest activity against the ampicillin-susceptible S. enteritidis strain.

Fernandez H. et al. *Antimicrobial susceptibility of Campylobacter jejuni subsp. jejuni assessed by E-test and double dilution agar method in Southern Chile.* Mem Inst Oswaldo Cruz. 2000; 95(2) : 247-9.p Abstract: The susceptibility patterns of 108 Campylobacter jejuni subsp. jejuni clinical strains, to six antimicrobial agents was determined by using the E-test and the double dilution agar methods. Using both methods, no strain was found to be resistant to ciprofloxacin, erythromycin and gentamicin, but two (1.8%) were resistant to tetracycline and all to aztreonam. Seven (6.5%) strains were resistant to ampicillin by the E-test and five (4.6%) by the double dilution agar method and by both methods. No great discrepancies were observed between both methods.

Fernandez M. et al. *Antimicrobial susceptibilities of group B streptococci isolated between 1992 and 1996 from patients with bacteremia or meningitis.* Antimicrob Agents Chemother. 1998; 42(6) : 1517-9.p Abstract: In vitro testing of 229 group B streptococcal isolates from a variety of patients with invasive infections indicated uniform penicillin G susceptibility. However, 17 (7.4%) isolates were resistant to erythromycin and 8 (3.4%) were resistant to clindamycin. These results support the continued use of penicillin G as the drug of choice for the treatment and prevention of group B streptococcal disease.

Fernandez-Roblas R. et al. *In vitro activity of gemifloxacin (SB-265805) compared with 14 other antimicrobials against intestinal pathogens.* J Antimicrob Chemother. 2000; 46(6) : 1023-1027.p Abstract: We studied the in vitro activity of gemifloxacin (SB-265805) and 14 comparator antimicrobials against 288 recent isolates of enteropathogenic bacteria (106 SALMONELLA: spp., 32 Hafnia alvei, 22 Yersinia enterocolitica, 21 SHIGELLA: spp., 16 AEROMONAS: spp. and 91 Campylobacter jejuni). Gemifloxacin, the other fluoroquinolones and cefotaxime were very active against all microorganisms tested except for C. jejuni. Seventy-seven per cent of isolates of C. jejuni were inhibited by erythromycin </=0.5 mg/L. Only one strain of C. jejuni was highly resistant to this antimicrobial agent. Of the compounds tested, gentamicin was the most active in vitro. The in vitro activity of the other antibiotics tested was variable. A quinolone could be a good choice for treating gastrointestinal infections when antimicrobial therapy is indicated. For C. jejuni, another antibiotic such as erythromycin should be considered.

Fernbach S.K. et al. *Pediatric voiding cystourethrography: a pictorial guide.* Radiographics. 2000; 20(1) : 155-68; discussion 168-71.p Abstract: Voiding cystourethrography is commonly performed in children with prenatally diagnosed hydronephrosis, urinary tract infections, and voiding abnormalities. Voiding cystourethrography can be performed with many variations designed to optimize visualization of disease and minimize radiation exposure. The procedure should include assessment of the spine and pelvis; masses or opaque calculi; bladder capacity, contour, and emptying capability; presence and grade of reflux; and urethral appearance. Radiologists differ as to whether the patient should void prior to catheterization. Anteroposterior imaging of the bladder is performed during early filling; little or no imaging is necessary during intermediate filling. When bladder filling is complete, steep oblique images that are centered on the ureterovesical junction should be obtained. If reflux is observed, the ipsilateral renal fossa may be imaged prior to voiding. With a smaller than expected voiding volume, bladder refilling is recommended. Voiding around the catheter is also strongly recommended. In girls, one anteroposterior image of the urethra is usually sufficient; in boys, the entire urethra must be imaged. Steep oblique imaging is optimal. At the conclusion of voiding, each renal fossa should be imaged to detect reflux missed at fluoroscopy as well as other anomalies. Familiarity with these abnormalities and use of proper techniques will allow detection of most common pathologic conditions with very low radiation exposure.

Ferrara A. et al. *Effect of different beta-lactams in combination with beta-lactamase inhibitors in the presence or absence of tobramycin against some enterobacteriaceae producing extended-spectrum beta-lactamases.* Chemotherapy. 1998; 44(5) : 313-7.p Abstract: Extended-spectrum beta-lactamase (ESBL) production among members of the family Enterobacteriaceae generally involves resistance to oxyiminocephalosporins and monobactams, while implying different susceptibility profiles with other antimicrobial agents. We have investigated the activity of some beta-lactam antibiotics, alone or in double and triple combinations with beta-lactamase inhibitors, in the presence or absence of tobramycin (TOB), against some Enterobacteriaceae producing ESBL by means of time-kill curves. Antimicrobials employed were ceftazidime (CAZ), cefotaxime (CTX), TOB, ampicillin (AMP), ampicillin-sulbactam (ASL), amoxicillin (AML), amoxicillin-clavulanic acid (AMC), piperacillin (PIP) and piperacillin-tazobactam

(TZP), at 1/4 minimum inhibitory concentration for susceptible strains and at achievable serum concentrations for resistant strains. Only the combinations CTX-ASL, CAZ-ASL and PIP-ASL were synergistic, both at 6 and 24 h, on some strains of Klebsiella species.

Ferrara A. et al. *High-level gentamicin-resistant enterococci: in vitro activity of double and triple combinations of antimicrobial drugs.* Chemotherapy. 1996; 42(1) : 37-46.p Abstract: The ability of double and triple combinations of antimicrobials with different mechanisms of action, such as teicoplanin, meropenem, gentamicin and sparfloxacin, to achieve synergisms was investigated in vitro on some moderate-level gentamicin-resistant (MLGR: 8 < or = MIC < or = 256 mg/l) and high-level gentamicin-resistant (HLGR: MIC > 500 mg/l) enterococci. On MLGR strains, a constant synergistic effect was achieved by a combination of teicoplanin with gentamicin or with meropenem, while generally addition, sometimes close to synergism, was exhibited by gentamicin-meropenem, gentamicin-sparfloxacin and teicoplanin-sparfloxacin associations. Triple combinations of teicoplanin, meropenem and gentamicin, or teicoplanin, sparfloxacin and gentamicin, always showed a remarkable advantage in terms of synergism over double combinations. On HLGR enterococci, the only double association showing an additive effect, sometimes close to synergism, was teicoplanin plus meropenem, while the triple combination of teicoplanin with gentamicin and meropenem always showed a marked synergistic effect. An effect very close to synergism was also shown by the combination of teicoplanin with sparfloxacin and gentamicin.

Ferrucci P.F. et al. *Evaluation of acute toxicities associated with autologous peripheral blood progenitor cell reinfusion in patients undergoing high-dose chemotherapy.* Bone Marrow Transplant. 2000; 25(2) : 173-7.p Abstract: Peripheral blood progenitor cell reinfusion (PBPC) in patients undergoing high-dose chemotherapy (HDC) for poor prognosis malignancies, has been described as causing possible acute gastrointestinal (nausea, vomiting), allergic (oedema, bronchospasm, anaphyl- axis), renal (proteinuria, haematuria) and/or cardiovascular (hypotension, arrhythmia, conduction disturbances, transient ischaemic phenomena) toxicities. To establish the clinical relevance of these observations and the possible relationship with different HDC regimens used, we performed a clinical and instrumental evaluation on 33 patients with advanced breast cancer, non-Hodgkin's lymphoma, Hodgkin's disease, relapsed ovarian cancer, Ewing's sarcoma, extragonadal germinal tumour and small cell lung cancer. They underwent at least one reinfusion each for a total of 51 studied procedures. No patient had a previous history of cardiovascular disease or significant intercurrent illness such as diabetes or liver, renal or neurologic impairment. All patients had totally implanted central venous catheters, through which the transplants had been collected and reinfused without technical consequences. To evaluate cardiovascular function, we continuously monitored 12-lead ECGs, with arterial pressure (AP) measurements every 5 min from the beginning of the procedure to 15 min after the reinfusion ended. We did not observe any significant differences between basal and subsequent steps in AP, heart rate, PQ and QTc time, P wave and QRS complex duration or P wave and QRS electrical axes. No patient showed any ST-T tract pathological abnormality, but one patient developed a transient ectopic atrial rhythm, without any haemodynamic disfunction and with spontaneous reversion to sinus rhythm. No patient complained of symptoms of haemodynamic failure. Gastrointestinal side-effects appeared to be strictly related to speed of reinfusion and to the number of packs reinfused, probably reflecting on the amount of dimethylsulphoxide infused. In one patient a tonic-clonic seizure occurred during a vomiting episode, but no patient developed allergic or renal toxicities. We conclude that PBPC reinfusion, if managed according to the procedure we propose in patients without organic impairment, is a safe procedure not associated either with increased risk of acute arrhythmias or ischaemic or significant systemic acute toxicities. Bone Marrow Transplantation (2000) 25, 173-177.

Fey P.D. et al. *Ceftriaxone-resistant salmonella infection acquired by a child from cattle.* N Engl J Med. 2000; 342(17) : 1242-9.p Abstract: BACKGROUND: The emergence of resistance to antimicrobial agents within the salmonellae is a worldwide problem that has been associated with the use of antibiotics in livestock. Resistance to ceftriaxone and the fluoroquinolones, which are used to treat invasive salmonella infections, is rare in the United States. We analyzed the molecular characteristics of a ceftriaxone-resistant strain of Salmonella enterica serotype typhimurium isolated from a 12-year-old boy with fever, abdominal pain, and diarrhea. METHODS: We used pulsed-field gel electrophoresis and analysis of plasmids and beta-lactamases to compare the ceftriaxone-resistant S. enterica serotype typhimurium from the child with four isolates of this strain obtained from cattle during a local outbreak of salmonellosis. RESULTS: The ceftriaxone-resistant isolate from the child was indistinguishable from one of the isolates from cattle, which was also resistant to ceftriaxone. Both ceftriaxone-resistant isolates were resistant to 13 antimicrobial agents; all but one of the resistance determinants were on a conjugative plasmid of 160 kb that encoded the functional group 1 beta-lactamase CMY-2. Both ceftriaxone-resistant isolates were closely related to the three other salmonella isolates obtained from cattle, all of which were susceptible to ceftriaxone. CONCLUSIONS: This study provides additional evidence that antibiotic-resistant strains of salmonella in the United States evolve primarily in livestock. Resistance to ceftriaxone, the drug of choice for invasive salmonella disease, is a public health concern, especially with respect to children, since fluoroquinolones, which can also be used to treat this disease, are not approved for use in children.

Fica C. A. et al. *Altos niveles de resistencia en escherichia coli causante de infecciones urinarias en una comunidad rural del Area Metropolitana: Til-Til.* Rev. chil. infectología. 1999; 16(2) : 120-6.p Abstract: La resistencia antimicrobiana en aislamientos de E. coli asociados a infecciones del tracto urinario (ITU) es desconocida en comunidades rurales en nuestro país. Para explorar la magnitud de este problema se analizaron los registros de ITU causadas por E. coli en la localidad rural de Til-Til cerca de Santiago, acumulados entre enero y octubre de 1997. Veintiocho aislamientos pertenecientes a diferentes pacientes fueron identificados. Se detectó un alto porcentaje de resistencia a ampicilina y cotrimoxazol (sobre el 70%). La resistencia ante cefalosporinas de primera generación fue superior al 18% y sobre el 10% de los aislamientos fueron resistentes a ciprofloxacina. Más del 70% de las cepas fueron multiresistentes y sólo un 17% fue multisensible. Este estudio demuestra que, incluso en lugares donde la entrega de antibióticos es restringida, la resistencia antimicrobiana es elevada y limita las opciones terapéuticas además de aumentar el costo del tratamiento de las ITU causadas por E. coli (AU).

Fik E. et al. *New plant glycoprotein against methicillin resistant staphylococci and enterococci.* Acta Microbiol Pol. 1997; 46(3) : 325-7.p Abstract: New glycoprotein (CML) isolated from Chelidonium maius exhibits good antibacterial activity against methicillin resistant staphylococci and enterococci. It may constitute new antimicrobial agent against methicillin and vancomycin-resistant staphylococci as well as multiresistant enterococci.

Filali B.K. et al. *Waste water bacterial isolates resistant to heavy metals and antibiotics.* Curr Microbiol. 2000; 41(3) : 151-6.p Abstract: Sewage water of Casablanca, an industrial city in Morocco, was studied for microorganisms resistant to heavy metals. Isolates were purified and collected on agar slants to be screened for resistance to heavy metals, including mercury in vitro. The strains that showed high resistance to heavy metals were also studied for their resistance to antibiotics and aromatic hydrocarbons. Results indicated that the strains most resistant to all tested products belonged to Ps. fluorescens, Ps. aeruginosa, Klebsiella pneumoniae, Proteus mirabilis, and Staphylococcus sp. These strains exhibit high minimal inhibitory concentrations for heavy metals such as cadmium (2 mm) or mer-

cury (1.2 mm). Growth of Ps. fluorescens and Klebsiella pneumoniae in the presence of heavy metals was also determined, and the growth curves indicated that mercury, copper, and zinc present a slight inhibitory action, while cadmium and silver could have a potent inhibitory action on growth compared with the controls. These studies also investigated growth in media containing aromatic compounds as the sole source of carbon. The results demonstrate that these strains could be good candidates for remediation of some heavy metals and aromatic compounds in heavily polluted sites.

Finch R.G. *A review of worldwide experience with sparfloxacin in the treatment of community-acquired pneumonia and acute bacterial exacerbations of chronic bronchitis.* Int J Antimicrob Agents. 1999; 12(1) : 5-17.p Abstract: The worldwide occurrence of community-acquired pneumonia (CAP) shows an undiminished prevalence of this serious illness and hospitalisation is common in those patients with severe illness. The diversity of bacterial pathogens that can act as aetiologic agents presents a challenge to initial empiric antimicrobial management. In recent years, treatment has been further complicated by an increased incidence of antibiotic resistance in pathogens such as Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis. The newly available fluoroquinolones including sparfloxacin offer an alternative approach to empiric management. Sparfloxacin is active against many typical and atypical pathogens, as well as strains resistant to conventional agents. In comparative studies, the in vitro potency of sparfloxacin and its pharmacokinetic profile have been confirmed. The clinical trial efficacy and safety data suggest it might be a useful empiric therapy for both CAP and acute bacterial exacerbation of chronic bronchitis.

Fine D.H. et al. *Effects of sublethal exposure to an antiseptic mouthrinse on representative plaque bacteria.* J Clin Periodontol. 1996; 23(5) : 444-51.p Abstract: Although the mechanism responsible for the clinical antiplaque efficacy of oral antiseptics is generally considered to be primarily one of bactericidal activity, it has been suggested that oral antiseptics may have additional effects on bacteria exposed to sublethal levels. Studies reported herein, investigated the effects of sublethal levels of an essential oil-containing antiseptic mouthrinse (Listerine Antiseptic, Warner-Lambert Co., Morris Plains, NJ) on selected activities of representative plaque microorganisms using in vitro models. These studies demonstrated that sublethal exposure to the tested oral antiseptic can have significant effects in reducing intergeneric coaggregation, increasing bacterial generation time, and extracting endotoxin from Gram-negative bacteria. These in vitro activities can be correlated with features of plaque formation and pathogenicity seen in vivo; however, additional studies will be necessary to confirm that these mechanisms are, in fact, operative clinically.

Finegold S.M. *Perspective on susceptibility testing of anaerobic bacteria.* Clin Infect Dis. 1997; 25 Suppl 2 : S251-3.p Abstract: Physicians must use empirical treatment initially for anaerobic infections. However, such treatment can be targeted if clinicians establish the nature of the infection and know the usual infecting flora of that type of infection and how the flora may have been modified by the use of antimicrobials. Physicians must also be aware of the usual susceptibility patterns of various anaerobes and nonanaerobes in the hospitals in which they work. Despite cost containment, it is still important to isolate all anaerobes present, to provide at least general identification (and specific identification of key organisms such as the Bacteroides fragilis group), and to keep the organisms alive so that they may be referred elsewhere for definitive identification and susceptibility testing, if indicated. Because resistance is increasing among anaerobes, susceptibility testing is very important. Susceptibility testing should be done when patients are seriously ill, when patients do not respond to therapy or relapse, when there are few data available on a species, when the organisms isolated are frequently resistant, and when patients require prolonged therapy. Periodic surveys of susceptibility patterns should be done on isolates from individual hospitals. Tests most useful for individual patient isolates are the Etest (AB BIODISK, Solna, Sweden), an expensive test, and the microbroth dilution test. Testing should be done on organisms that are the most virulent and most resistant to antimicrobial agents.

Finkelstein J.A. et al. *Antimicrobial use in defined populations of infants and young children.* Arch Pediatr Adolesc Med. 2000; 154(4) : 395-400.p Abstract: BACKGROUND: Antimicrobial overprescribing contributes to bacterial resistance, but data on use in infants and young children are limited. OBJECTIVES: To assess antimicrobial use in a defined population of infants and young children and to determine diagnosis-specific prescribing rates for common infections. DESIGN AND SETTING: Retrospective cohort study of children served by 44 practices affiliated with 2 managed care organizations. PATIENTS: Children aged 3 months to 72 months enrolled in either health plan between September 1, 1994, and August 31, 1996. ANALYSIS: Rates of antimicrobial use were calculated as the number of pharmacy dispensings divided by the number of person-years of observation contributed to the cohort in 2 age groups (3 to <36 months and 36 to <72 months). Other outcomes included the distribution of diagnoses associated with antimicrobial dispensing and population-based rates of diagnosis of common acute respiratory tract illnesses. RESULTS: A total of 46477 children contributed 59710 person-years of observation across the 2 health plans. Rates of antimicrobial dispensing for children aged 3 to 36 months were 3.2 and 2.1 dispensings per person-year in the 2 populations. A substantial fraction of younger children (35% in population A and 23% in population B) received 4 or more antimicrobial prescriptions in a single year. For children aged 36 to 72 months, the dispensing rates for the 2 populations were 2.0 and 1.5 antimicrobials per person-year. We found significant differences in rates between the populations studied and a decrease in use at all sites from 1995 to 1996. The diagnosis of otitis media accounted for 56% of antimicrobial drugs dispensed to children aged 3 to 36 months and 40% of those dispensed to children aged 36 to 72 months. Antimicrobial prescribing for colds and upper respiratory tract infections, bronchitis, and sinusitis was less frequent than previously reported but accounted for 10% to 14% of antimicrobial drugs dispensed. CONCLUSIONS: In these populations, otitis media accounted for the largest number of antimicrobial agents dispensed to children younger than 6 years. Clearly inappropriate indications such as cold, upper respiratory tract infection, and bronchitis accounted for smaller fractions of antimicrobial use but may be most amenable to change. However, interventions that encourage use of strict criteria for diagnosis and treatment of otitis media will likely have the greatest impact on overall antimicrobial exposure. Monitoring defined populations longitudinally will allow assessment of the effectiveness of such national and local initiatives.

Finkelstein R. et al. *Device-associated, device-day infection rates in an Israeli adult general intensive care unit.* J Hosp Infect. 2000; 44(3) : 200-5.p Abstract: Surveillance is an essential element of hospital infection control programs. Previous studies have shown that interhospital comparison of intensive care unit (ICU) nosocomial infections (NI) may be best made by comparing ICU-type-specific, device-associated infection rates and that these adjusted rates vary by ICU type. The aim of this study was to evaluate whether significant structural improvements introduced in an adult general ICU were associated with changes in the NI rates in this unit. In addition, we compared these rates with those of ICUs reported by the National Nosocomial Infections Surveillance (NNIS) System of the Centers for Diseases Control and Prevention. During a 12-month period 337 patients were surveyed. There were 20 ventilator-associated pneumonias (VAP)/1000 ventilator (VEN)-days, 12 bloodstream infections (BSI)/1000 central vascular catheter (CVC)-days and 14 urinary tract infection (UTI)/1000 indwelling urinary catheter (IUC)-days. Structural changes and reduction in device utilization ratios were not followed by change in NI rates in this unit. VAP and BSI rates were comparable to those reported for neurosurgical and burn

ICUs, respectively, in the NNIS System, despite a much higher device utilization ratios. The present study provides specific surveillance data for further interhospital comparison with similar types of ICUs. Copyright 2000 The Hospital Infection Society.

Fiori P.L. et al. *A pre-existing infection by Mycobacterium avium subsp. avium modulates anti-Cryptococcus neoformans and anti-Candida albicans activities in human macrophages.* Microb Pathog. 2000; 29(2) : 93-100.p Abstract: Mycobacterium avium is a facultative intracellular microorganism, able to survive and multiply within mammalian macrophages by circumventing antimicrobial mechanisms. In this study we hypothesize that pre-existing M. avium infection could result in macrophage superinfections by other microorganisms. We found that 24 h after ingestion of M. avium at a low multiplicity of infection, macrophages are unable to efficiently produce superoxide anions when over-stimulated with phorbol esters, and that the generation of oxidative burst is only partially restored 72 h after bacteria ingestion. We also demonstrate that intracellular killing of Cryptococcus neoformans is markedly impaired in human macrophages that have previously ingested M. avium (but not other bacteria such as Escherichia coli). This inhibitory effect is observed with live mycobacteria, but not when heat-inactivated bacteria are ingested. In contrast, when Candida albicans is given to macrophages instead of C. neoformans, an enhancement of intracellular killing is observed, suggesting that cytocidal mechanisms other than respiratory burst are involved in the anti- Candidacidal activity of macrophages. Copyright 2000 Academic Press.

Firsov A.A. et al. *Prediction of the antimicrobial effects of trovafloxacin and ciprofloxacin on staphylococci using an in-vitro dynamic model.* J Antimicrob Chemother. 1999; 43(4) : 483-90.p Abstract: To compare the pharmacodynamics of trovafloxacin and ciprofloxacin, three clinical isolates of Staphylococcus aureus with different MICs (0.03, 0.15, 0.6 and 0.1, 0.25, 1.25 mg/L, respectively) were exposed to decreasing concentrations of the quinolones according to their half-lives of 9.25 and 4 h, respectively. With each organism, single doses of trovafloxacin and twice-daily doses of ciprofloxacin were designed to provide 8-fold ranges of the ratio of area under the concentration-time curve (AUC) to the MIC, 58-466 and 116-932 (mg x h/L)/(mg/L), respectively. The antimicrobial effect was expressed by its intensity: the area between the control growth in the absence of antibiotics and the antibiotic-induced time-kill/regrowth curves (I(E)). Linear relationships established between I(E) and log AUC/MIC were bacterial strain-independent but specific for the quinolones (r2 = 0.99 in both cases). At a given AUC/MIC ratio, the I(E)s of trovafloxacin were greater than those of ciprofloxacin, suggesting that the antimicrobial effect of trovafloxacin compared with ciprofloxacin against staphylococci may be even greater than might be expected from the difference in their MICs. These data were combined with previous results obtained with three Gram-negative bacteria. Again, I(E) correlated well with the log AUC/MIC of trovafloxacin and ciprofloxacin in a strain- and species-independent fashion (r2 = 0.94 and 0.96, respectively). On this basis, a value of the AUC/MIC of trovafloxacin which might be equivalent to Schentag's AUC/MIC = 125 (mg x h/L)/(mg/L) reported as the breakpoint value for ciprofloxacin was estimated at 71 (mg x h/L)/(mg/L) with the respective MIC breakpoint of 0.27 mg/L. Based on the I(E)-log AUC/MIC relationships, the I(E)s were plotted against the logarithm of trovafloxacin and ciprofloxacin dose (D) for hypothetical representatives of S. aureus, Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa with MICs corresponding to the MIC50s. These I(E)-log D relationships allow prediction of the effect of a given quinolone on a representative strain of the bacterial species.

Fischer S. et al. *Activation of human gamma delta T-cells by heat-treated mistletoe plant extracts.* Immunol Lett. 1996; 52(2-3) : 69-72.p Abstract: Various microorganisms including mycobacteria, other bacteria and parasites such as Plasmodium falciparum are known to activate human gamma delta T-cells in vitro. In this study, we demonstrate that heat-treated (but not untreated) mistletoe extracts similarly stimulate human gamma delta T-cells during in vitro culture. The responding T-cells express the variable T-cell receptor elements V gamma 9 and V delta 2. The gamma delta-stimulating activity of heat-treated mistletoe extracts is sensitive to treatment with alkaline phosphatase but not with proteinase K, indicating that the ligands are non-proteinaceous phosphate-containing compounds. Mistletoe-derived ligands share these features with the previously defined mycobacteria-derived ligands for gamma delta T-cells.

Fish D.N. et al. *Development of resistance during antimicrobial therapy: a review of antibiotic classes and patient characteristics in 173 studies.* Pharmacotherapy. 1995; 15(3) : 279-91.p Abstract: The incidence of emergent resistance and clinical factors affecting its development were evaluated by retrospective review of 173 studies encompassing over 14,000 patients. Eight antibiotic classes and 225 individual treatment regimens were evaluated. Emergent resistance occurred among 4.0% of all organisms and 5.6% of all infections treated. It appeared to be significantly more frequent with penicillin and aminoglycoside monotherapy, with significantly lower rates associated with imipenem-cilastatin, aztreonam, and combination therapy. Clinical failure also appeared to be significantly more likely to occur after emergence of resistance among organisms treated with fluoroquinolones or aminoglycosides. Infections associated with higher resistance rates were cystic fibrosis, osteomyelitis, and lower respiratory tract infections. Resistance was most common in patients in intensive care units or receiving mechanical ventilation. It was also significantly frequent among studies performed in university or teaching hospitals. Organisms associated with high resistance rates were Pseudomonas aeruginosa, Serratia, Enterobacter, and Acinetobacter sp. Factors such as infection type, underlying diseases, type of institution, and specific pathogens warrant consideration when examining emergent resistance.

Fitzgerald M.A. *Acute otitis media in an era of drug resistance: implications for NP practice.* Nurse Pract. 1999; 24(10 Suppl) : 10-4.p Abstract: Nearly two-thirds of all children will have at least one episode of acute otitis media (AOM) by age 2 years. Acute otitis media is the most common indication for pediatric outpatient and antibiotic therapy. Minimizing AOM risk factors, prescribing the most appropriate and effective AOM therapy while limiting inappropriate antimicrobial use is an important part of the pediatric primary care.

Fitzgerald M.A. et al. *Measurement of antimicrobial susceptibility among invasive isolates of Streptococcus pneumoniae: comparison of the Etest with the standard agar dilution method.* Alaska Med. 1997; 39(1) : 3-7.p Abstract: High rates of invasive disease caused by Streptococcus pneumoniae occur in the Alaska Native population. Because of the wide use of empiric antibiotics to treat infection in rural regions of Alaska and concern over the emergence of pneumococcal strains now resistant to an increasing number of antibiotics we compared a simple strip system (Etest) for the measurement of antibiotic susceptibilities to the standard agar dilution method. Eighty-two pneumococcal isolates were tested by both methods. Overall, the Etest MICs of 91% of the isolates agreed within one log2 of the agar dilution, and 99.3% agreed within 2 log2 dilutions. There were no very major or major interpretative category discrepancies with the Etest for any antibiotic tested. There were 4.1% minor interpretative errors with the Etest, which generally occurred at the breakpoint between susceptible and intermediate resistance. The results indicated that the Etest was comparable to the agar dilution method for the measurement of antibiotic MICs for Streptococcus pneumoniae.

Flaherty J.P. et al. *Nosocomial infection caused by antibiotic-resistant organisms in the intensive-care unit.* Infect Control Hosp Epidemiol. 1996; 17(4) : 236-48.p Abstract: Resistance to antimicrobial agents is an evolving process, driven by the selective pressure of heavy antibiotic use in individuals living in close proximity to others. The intensive care

unit (ICU), crowded with debilitated patients who are receiving broad-spectrum antibiotics and being cared for by busy physicians, nurses, and technicians, serves as an ideal environment for the emergence of antibiotic resistance. Problem pathogens presently include multiply resistant gram-negative bacilli, methicillin-resistant Staphylococcus aureus, and the recently emerged vancomycin-resistant enterococci. The prevention of antimicrobial resistance in ICUs should focus on recognition via routine unit-based surveillance, improved compliance with handwashing and barrier precautions, and antibiotic-use policies tailored to individual units within hospitals.

Flamini G. et al. *Antimicrobial activity of the essential oil of Calamintha nepeta and its constituent pulegone against bacteria and fungi.* Phytother Res. 1999; 13(4) : 349-51.p Abstract: The chemical composition of the essential oil of Calamintha nepeta and its antimicrobial activity against Listeria monocytogenes, Bacillus cereus, Salmonella veneziana, S. paratyphi B. S. typhimurium, Fusarium moniliforme, Botrytis cinerea, Aspergillus niger and Pyricularia oryzae have been studied. Moreover the main constituents of the oil (limonene, menthone, pulegone, menthol) have been tested against the same microorganisms. Only pulegone showed antimicrobial activity, particularly against all the Salmonella species.

Flanagan D.A. et al. *Antimicrobial activities of dental impression materials.* Dent Mater. 1998; 14(6) : 399-404.p Abstract: OBJECTIVE: The aim of this study was to measure the in vitro killing effects five commercial alginate impression materials had on five test microorganisms. METHODS: Two alginates with no added disinfectant, one supplemented with chlorhexidine and two others containing quaternary ammonium compounds were tested. Challenge microbes included two gram-positive cocci, two gram-negative bacilli and a yeast. Saline solutions containing standardized concentrations of test microbes were used to mix the alginates. Some set specimens were immediately homogenized and the resulting fluids diluted and spread plated. Other specimens were processed 30 or 60 min after setting. After culturing, the numbers of colonies were counted and the levels of microbial reductions determined. RESULTS: Unsupplemented alginates had no antimicrobial effects. The quaternary-ammonium-containing alginates were completely effective against all five test microorganisms. The alginate with chlorhexidine killed all the gram-negative bacilli and the majority (95-99%) of the gram-positive cocci and yeast. SIGNIFICANCE: Results indicated that disinfectant-containing alginate impression materials could reduce the number of soiling microorganisms present on and within test specimens.

Fleischer W. et al. *Povidone-iodine in antisepsis—state of the art.* Dermatology. 1997; 195 Suppl 2 : 3-9.p Abstract: The natural element iodine has been used for more than 150 years to prevent infection and treat wounds. Yet only due to the development of iodophors has it become possible to use this highly efficient microbicide in a wide range of medical applications. The antimicrobial spectrum is universal. Its efficiency against clinically and epidemiologically significant new pathogens, such as methicillin-resistant Staphylococcus aureus and Enterococcus sp. has also been validated. No development of resistance has been determined. New data are also available on the excellent local tolerability of Betaisodona (povidone-iodine) preparations. On these grounds, a number of clinical fields exist in prophylaxis and therapy, for either once only or repeated applications: the disinfection of hands and skin, mucosa antisepsis, intra- and postoperative wound treatment, therapy of skin infections, burns and chronic wounds.

Flores A. et al. *Multiresistant Shigella species isolated from pediatric patients with acute diarrheal disease.* Am J Med Sci. 1998; 316(6) : 379-84.p Abstract: A total of 57 strains of Shigella (36 S sonnei, 21 S flexneri), isolated from children with acute diarrheal disease who presented for treatment at the Andes University Hospital, Merida, Venezuela, from June 1993 to June 1995, were tested for their susceptibility to trimethoprim, sulfamethoxazole, ampicillin, cefamandole, ceftriaxone, streptomycin, fleroxacin, and nalidixic acid, by the agar dilution method. Twenty-seven strains (75%) of S sonnei and eight strains of S flexneri (38.1%) isolates showed high-level resistance to trimethoprim (MIC90 > 1024 microg/mL), which was also associated with other resistance patterns. The most common resistant phenotype associated with trimethoprim-resistance among S sonnei isolates was sulfamethoxazole-streptomycin (63%); among S flexneri isolates, it was sulfamethoxazole-ampicillin-streptomycin (87.5%). Individual resistance was only observed for ampicillin, mainly in four isolates of S flexneri, and in one isolate of S sonnei. Most Shigella strains were resistant to three or more antimicrobial agents. These results confirmed that multiresistant strains of Shigella are present in Merida, and emphasize the importance to maintain these under surveillance in order to assess local susceptibility patterns and empiric therapy.

Flournoy D.J. et al. *Increasing antimicrobial resistance in gram-negative bacilli isolated from patients in intensive care units.* Am J Infect Control. 2000; 28(3) : 244-50.p Abstract: BACKGROUND: We investigated gram-negative bacilli from patients in intensive care units to determine whether antimicrobial resistance was increasing. METHODS: Minimal inhibitory concentrations were determined by broth microdilution on 334 gram-negative bacilli collected in 1990, 1995, and 1998. RESULTS: During the 3 study years, the types of gram-negative bacilli encountered in our intensive care units changed with proportional increases of Pseudomonas sp and decreases of inducible enterics. Dramatic increases in resistance for ceftazidime, cefotaxime, and piperacillin were paralleled between respiratory-tract isolates and inducible enterics. By 1998, ticarcillin was more active than piperacillin against most isolates except Escherichia coli and Klebsiella sp, and most isolates became more resistant to gentamicin and tobramycin. CONCLUSIONS: Continuous changes in the types of gram-negative bacilli and antimicrobial resistance complicate empirical selection of antimicrobials in the intensive care units. These complications will place more emphasis on communication and strategy formations among health care workers (nurses, physicians, laboratorians, and pharmacists) in an effort to treat infections in a timely and effective manner.

Fluhr J.W. et al. *In-vitro and in-vivo efficacy of zinc acetate against propionibacteria alone and in combination with erythromycin.* Zentralbl Bakteriol. 1999; 289(4) : 445-56.p Abstract: Some studies have been published about the in vitro activity of zinc acetate (ZA), erythromycin (E) and their combination (ZA/E) against Propionibacterium spp., especially erythromycin resistant strains. The efficacy of topical ZA/E combination has been reported as well, but a comparison to ZA monotherapy is missing. Therefore, the MIC values of ZA, E and the ZA/E combination were determined for 15 erythromycin-resistant and 12 erythromycin-sensitive Propionibacterium strains using the agar dilution method and the checkerboard technique. Furthermore, the antimicrobial efficacy of ZA (1.2%) vs. the ZA/E (1.2%/4%) combination in an alcoholic solution was tested in a 7-day treatment administered to 32 acne patients. The MIC 100 for ZA was 1024 micrograms ZA/ml for both, erythromycin resistant and erythromycin sensitive Propionibacterium strains. The ZA, as well as the ZA/E solution showed efficacy reducing both the Propionibacterium spp., and the Micrococcaceae in the sebaceous gland infundibula of acne patients. There was no significant difference between the two treatments. As the MIC 100 of ZA/E was equal to the MIC 100 of ZA, the decrease of the erythromycin MIC of the ZA/E combination in erythromycin-resistant strains may be partly attributed to the addition of ZA to E. The in vivo antibacterial efficacy on 32 acne patients supports the hypothesis that the antibacterial effect of ZA/E in short-term treatment can be mostly attributed to ZA.

Fluit A.C. et al. *Antimicrobial susceptibility and frequency of occurrence of clinical blood isolates in Europe from the SENTRY antimicrobial surveillance*

program, 1997 and 1998. Clin Infect Dis. 2000; 30(3) : 454-60.p Abstract: As part of the European arm of the SENTRY Antimicrobial Surveillance Program, 25 European university hospitals referred 9613 blood isolates for in vitro testing against >20 antimicrobial agents. Escherichia coli, Staphylococcus aureus, coagulase-negative Staphylococcus, Pseudomonas aeruginosa, and Klebsiella pneumoniae were the 5 most frequent isolates and accounted for two-thirds of all referrals, with minor regional variation. Of these, approximately 0.36% of E. coli and 16.7% of K. pneumoniae isolates proved to be potential extended-spectrum beta-lactamase producers, and their incidence clearly varied regionally. Quinolone resistance was detected among gram-negative species; in particular, P. aeruginosa and Acinetobacter species. Considerable regional variation was observed in the incidences of methicillin resistance in S. aureus and penicillin resistance in Streptococcus pneumoniae. The incidence of vancomycin resistance in enterococci was relatively low overall and primarily associated with Enterococcus faecium. However, extrapolation of these data to smaller and nonteaching hospitals should be undertaken with caution, since resistance rates may be lower in these facilities.

Fluit A.C. et al. *Antimicrobial resistance among community-acquired pneumonia isolates in Europe: first results from the SENTRY antimicrobial surveillance program 1997. SENTRY Participants Group.* Int J Infect Dis. 1999; 3(3) : 153-6.p Abstract : OBJECTIVE: The SENTRY antimicrobial surveillance program was established to monitor the occurrence and antimicrobial susceptibility of bacterial pathogens via an international network of sentinel hospitals. MATERIAL AND METHODS: Microorganisms were forwarded to the reference laboratory for testing against various antimicrobial agents using broth microdilution. Twenty European hospitals referred 286 Streptococcus pneumoniae, 309 Haemophilus influenzae, and 167 Moraxella catarrhalis isolates during the first 10 months of the study, starting in April 1997. RESULTS: Seven percent of the S. pneumoniae isolates were highly resistant to penicillin, and 21% showed intermediate resistance. The highly resistant pneumococcal isolates came from Coimbra, Barcelona, Athens, and London, whereas the intermediate penicillin-resistant isolates were received from all participating countries. The incidence of intermediate penicillin-resistant pneumococci was lowest in Lausanne, Freiburg and Duesseldorf, London, and Utrecht and highest in southern European countries. Fifty-five percent of the penicillin-resistant S. pneumoniae were also resistant to erythromycin, and 35% to clindamycin. Sparfloxacin, trovafloxacin, levofloxacin, and vancomycin were fully active against pneumococcal isolates. Haemophilus influenzae isolates were generally highly susceptible to most of the antibiotics tested, and 92% of the M. catarrhalis isolates were resistant to penicillin. Susceptibility to cephalosporins, ciprofloxacin, levofloxacin, and rifampicin was 100%. CONCLUSION: Penicillin may no longer be the first-choice drug for empirical treatment of pneumococcal infections. The newer fluoroquinolones may play a role in the empirical treatment of community-acquired pneumonia.

Flynn C.M. et al. *In vitro efficacy of levofloxacin alone or in combination tested against multi-resistant Pseudomonas aeruginosa strains.* J Chemother. 1996; 8(6) : 411-5.p Abstract: Levofloxacin, the S(-) isomer of ofloxacin, demonstrates in vitro activity against Pseudomonas aeruginosa. To further characterize this activity, levofloxacin was tested against three populations of recent clinical isolates categorized by their resistance patterns to several other anti-pseudomonal agents. Results demonstrate the minimum inhibitory concentrations (MICs) for levofloxacin were generally two- to fourfold higher than for ciprofloxacin. Higher fluoroquinolone MICs were associated with MIC increases in other drugs. Levofloxacin demonstrated cross resistance against ciprofloxacin-resistant strains. Combinations of levofloxacin and several codrugs revealed that the majority of evaluable interactions demonstrated indifferent action. Levofloxacin exhibited enhanced activity (additive or degrees of synergy) principally with piperacillin, aztreonam, or ceftazidime. The synergy and additive rate (21 to 30%) compared favorably with the enhanced interactions observed with gentamicin combined with piperacillin or ceftazidime (27 to 30%). Levofloxacin activity against P. aeruginosa was most comparable to that of ciprofloxacin, which was applicable against > 90% of strains found to be resistant to other classes of antimicrobial agents.

Flynn E.R. *Management of antibiotic-resistant organisms in the rehabilitation setting.* Rehabil Nurs. 1999; 24(6) : 232-3.p Abstract: Preventing the spread of infection is a team effort. Development and use of rehabilitation-based infection control practices for control of ARO nosocomial infections must be a priority for rehabilitation research. Ongoing infection control surveillance of ARO presence, along with monitoring of resistance patterns, equips infection control practitioners with scientific data to identify appropriate barriers for use in the rehabilitation setting. Modification of antimicrobial usage may offer hope for reversing some of the damage done. With the assistance of physicians, infection control practitioners, laboratory personnel and others, we can prevent the spread of these dangerous organisms.

Focht J. et al. *[1996 pathogen incidence and resistance status in peritonitis].* Langenbecks Arch Chir. 1997; 382(4 Suppl 1) : S1-4.p Abstract: Severe intra-abdominal infection is associated with a high mortality rate. In addition to risk factors in the patients, the causal pathogens and the selection of appropriate therapeutic procedures play an essential part in the course of these conditions. In the majority of intra-abdominal infections mixed aerobic/anaerobic infections, mostly with some involvement of enterobacteria and also of enterococci and staphylococci can be demonstrated. In addition to surgical intervention a calculated antimicrobial initial treatment of intra-abdominal infections with an antibiotic with an adequate effect to combat the pathogen concerned can contribute to improving the patient's prognosis. A calculated antibiotic treatment can only be effectively and reliably carried through if the frequency of the pathogen and the resistance situation are known. Retrospective evaluations of data on the sensitivity and frequency of pathogens from a defined group of subjects allow conclusions on the epidemiological situation in a particular catchment area or in a medical sector and thus make it possible to calculate the appropriate therapy for infections. In 1996 a total of 2,779 bacterial isolates from the intra-abdominal infection sector were examined: 935 Enterobacteriaceae, 83 nonfermenters, 177 Staphylococcus spp., 211 Enterococcus spp., 39 Streptococcus spp., and 1334 different anaerobic bacteria. Fresh clinical isolates were available for all pathogens tested. The most frequent gram-negative pathogen was E. coli (60%) and the most frequent gram-positive pathogen, E. faecalis (44%); the most frequent anaerobic pathogen was B. fragilis (39%). Taurolodine had the lowest resistance rate against gram-negative and anaerobic pathogens. Teicoplanin had the highest activity against gram-positive pathogens.

Foley D.S. et al. *Percutaneous cannulation for pediatric venovenous extracorporeal life support.* J Pediatr Surg. 2000; 35(6) : 943-7.p Abstract: BACKGROUND/PURPOSE: The objective of this study was to show the safety and efficacy of a method of percutaneous cannulation for venovenous extracorporeal life support (ECLS) access in nonneonatal (>10 kg) pediatric patients. METHODS: Between June 1992 and October 1998, 26 pediatric patients (age range, 3 to 17 years; weight range, 19 to 100 kg) underwent attempted percutaneous cannulation for venovenous ECLS at our institution. Venous drainage access was attempted using a modified Seldinger technique via the right internal jugular vein (RIJ, n = 22) or right femoral vein (RFV, n = 4). Reinfusion access was attempted via the RFV (n = 19), RIJ (n = 4), or left femoral vein (n = 3). RESULTS: The percutaneous technique was successful in 24 of 26 patients (92.3%). Maximum blood flow during ECLS was 80.1 +/- 30.0 mL/kg/min, generating a postmembrane lung outlet pressure of 138 +/- 54.8 mm Hg. Adequate gas exchange was achieved in all patients, and survival to discharge was 79.2%. There was no procedure-related mor-

tality. Complications potentially related to the percutaneous technique included RIJ thrombosis (n = 1) detected after decannulation and cannula site bleeding (n = 3). CONCLUSION: Percutaneous access may be used safely and effectively for venovenous ECLS in pediatric patients.

Font C. et al. *[A study of 30 patients with bacteremia due to Campylobacter spp.].* Med Clin (Barc). 1997; 108(9) : 336-40.p Abstract: BACKGROUND: To get better knowledge about clinical and bacteriological features in Campylobacter spp. bacteremia. PATIENTS AND METHODS: Over a period of 8 years (1987-1994) we prospectively analyzed underlying diseases, predisposing factors, clinical manifestations, complications and outcome of patients with Campylobacter spp. bacteremia. The study took place in an urban third-level teaching hospital. Antibiogram was tested in all the strains isolated. RESULTS: We identified 30 cases of Campylobacter spp. bacteremia (26 due to C. jejuni and 4 due to C. fetus). Seventy-three percent of the patients were male and the mean age +/- SD of all the patients was 52 +/- 19 years. Ninety percent of patients had some kind of immunodepression related to immunosuppressive therapy or to underlying diseases, especially liver cirrhosis and HIV infection. All patients had fever and 40% complained of intestinal symptoms before bacteremia. Mortality rate in patients with C. jejuni bacteremia was 30.8% (8 patients) during the admission, the death was directly related to bacteremia in 11.5% (3 patients). In all the fatal cases C. jejuni was resistant to empirical antibiotherapy instituted. In contrast, none of the patients with C. fetus bacteremia died. We detected an increasing ciproflaxin resistance in C. jejuni strains during this period which reached to 75% in the last years. Antimicrobial susceptibility to erythromycin and aminoglucosids was kept in all the strains. CONCLUSIONS: Campylobacter spp. bacteremia has a remarkable mortality rate, probably related to immunosuppressive underlying diseases in affective patients. In our institution we detected an increasing fluoroquinolone resistance over the years while susceptibility to erythromycin and aminoglucosids was maintained.

Forauer A.R. et al. *Importance of US findings in access planning during jugular vein hemodialysis catheter placements.* J Vasc Interv Radiol. 2000; 11(2 Pt 1) : 233-8.p Abstract: PURPOSE: To evaluate the significance of internal jugular vein ultrasound (US) findings in long-term hemodialysis patients and to assess how frequently these findings lead to a change in access approach. MATERIALS AND METHODS: One hundred consecutive hemodialysis catheter placements in 79 patients were retrospectively analyzed. Prior to catheter insertion, each patient underwent an US examination of the proposed access site by an interventional radiologist or interventional radiology fellow. The examinations were recorded on VHS tapes. The procedure notes, dictated radiology reports, and VHS tapes were reviewed for evidence of total occlusion, non-occlusive thrombus, presence of venous collaterals, stenosis, or variation in normal anatomy. The number of months that the patient required hemodialysis prior to catheter placement was also noted. RESULTS: Significant US findings were present in 28 patients (35%). Findings included total occlusion (n = 18), non-occlusive thrombus (n = 11), stenosis (n = 5), and anatomic variation (n = 1). These required a change in access approach in 21 patients. Unexpectedly, 54% of the patients with US findings had been undergoing dialysis for 12 months or less. CONCLUSION: These results underscore the importance of sonography in planning and performing vascular access procedures. A thorough US examination of the internal jugular veins is warranted prior to hemodialysis catheter placement, especially in patients with previous temporary or tunneled catheters. Three-quarters of patients with sonographic abnormalities required a change in access approach.

Forchielli M.L. et al. *Success rates and cost-effectiveness of antibiotic combinations for initial treatment of central-venous-line infections during total parenteral nutrition.* JPEN J Parenter Enteral Nutr. 2000; 24(2) : 119-25.p Abstract: BACKGROUND: Central-venous-line infections can be successfully treated with appropriate antibiotics, thus avoiding the need for catheter removal. Based on our experience, vancomycin, gentamicin, piperacillin, ceftazidime, and amphotericin, alone or in combination, are usually administered, pending sensitivity results. This empirical list, however, has never been verified against actual sensitivity results nor has it been tested for cost or efficacy. METHODS: Medical records of inpatients on hyperalimentation over 1 year were reviewed. Success rate, therapy duration, and drug acquisition cost and charge were assessed for central-venous-line infections. Antibiotics then were paired and evaluated in terms of charge and efficacy against all microorganisms as determined by sensitivity results. RESULTS: In 500 inpatients receiving hyperalimentation for 9,698 patient-days, 8.4 central-venous-line infections/1,000 patient-days occurred. Staphylococcus non-aureus, Candida species, Enterococcus faecium, and Staphylococcus aureus predominantly were isolated. Of the infections, 51 (67%) were sensitive to one or more of the initial antibiotics. A 2-week course of antibiotics successfully treated 50 (66%) catheter infections without line removal. Appropriate initial therapy on average reduced treatment duration by 8 to 10 days and drug charges by $400 to $700. CONCLUSIONS: Amikacin-vancomycin appears to be the most cost-effective selection for presumed central-venous-line infections, pending sensitivity results, followed by valid alternatives. Lower failure rates are well worth the extra cost in pharmaceutical charges.

Ford C.W. et al. *Oxazolidinones: new antibacterial agents.* Trends Microbiol. 1997; 5(5) : 196-200.p Abstract: The oxazolidinones are a new chemical class of synthetic antibacterial agents that are active orally or intravenously against multidrug-resistant Gram-positive bacteria. Their unique mechanism of action and activity against bacteria that pose therapeutic problems in hospital and community treatments make them promising candidates for antimicrobial agents.

Forrest J.M. et al. *Pneumococcal disease in Australia.* Commun Dis Intell. 2000; 24(4) : 89-92.p Abstract: The proceedings of the Pneumococcal Disease in Australia Workshop, held on 26-27 March 1999 are presented in this report. The world-wide epidemiology of the pneumococcus, with its predilection for the very young and the very old, differs between the developing and the developed world, and between indigenous and non-indigenous populations. Sources of data on pneumococcal disease in each of the Australian States, clinical aspects of invasive and non-invasive disease, and the role of the public health laboratory in surveillance of serotypes and antimicrobial sensitivity, both nationally and over time, were discussed at the Workshop. Polysaccharide pneumococcal vaccines are recommended for those over 65 years of age and for at-risk groups, but are supplied free of charge only in Victoria and for indigenous Australians over 50 years of age. Children will require conjugate vaccines, which are likely to be licensed in the United States of America early in 2000. In Australia indigenous children, especially in rural areas, will be the priority group for conjugate vaccines.

Fortis A.A. et al. *Adherence of Staphylococcus aureus, Klebsiella pneumoniae and Candida albicans to human buccal epithelial cells, from healthy persons and HIV carriers, under the influence of Broncho Vaxom in vitro and ascorbic acid in vivo.* APMIS. 1998; 106(4) : 441-8.p Abstract: We examined the in vitro effect of Broncho Vaxom (BV) (an immunobiotherapeutic preparation containing a lysate made from bacteria often involved in respiratory tract infections) on adherence of Staphylococcus aureus, Klebsiella pneumoniae and Candida albicans to human buccal epithelial cells (BEC) of healthy volunteers and HIV carriers. We also examined the ex vivo effect of ascorbic acid on the adherence of the same microorganisms to BEC of HIV carriers. The study reached the following conclusions: The presence of BV in vitro significantly reduces the adherence of the tested strains to BEC from healthy persons and HIV carriers. No significant difference was observed between healthy persons and HIV carriers regarding the adherence of the tested strains to BEC. Significant difference in the adherence of the tested strains to BEC was observed

between HIV carriers who had been taking ascorbic acid over a 3-month period and those who had not. There was no further reduction in the adherence of the tested strains to BEC from HIV carriers who had been taking ascorbic acid in the presence of BV in vitro.

Fortun Abete J. et al. *[The risk factors associated with colonization and bacteremia in non-tunnelled central venous catheters].* Rev Clin Esp. 2000; 200(3) : 126-32.p Abstract: OBJECTIVE: To identify risk factors for colonization and bacteremia among patients with non-tunnelled central venous catheters. MATERIALS AND METHODS: A prospective study was conducted of a cohort of patients carrying non-tunnelled central venous catheters. Different parameters were obtained and the degree of its association with colonization of the distal portion of the catheter or with bacteremia associated with colonization was estimated. The CDC (centers for Disease Control) diagnostic criteria of colonization and catheter-related bacteremia were used. RESULTS: A total of 118 catheters were eventually analyzed, corresponding to 114 patients, with a catheterization mean time of 14 +/- 8 days (mean +/- SD); out of these 114 patients, 51 were colonized and in 22 the presence of associated bacteremia was confirmed. The parameters associated with a higher risk for catheter colonization included length of colonization, femoral location, number of lumina and a vital prognosis lower than one month. All these factors, with the exception of the increase in the number of lumina, showed an independent association with colonization on the multivariate analysis [catheterization length (in weeks): OR 1.46; 95% CI: 1.0-2.11; femoral location: OR 3.73; 95% CI: 1.16-11.9; vital prognosis lower than one month: OR 12.7; 95% CI: 1.4-112.7]. As for risk for catheter-related bacteremia, the univariate analysis showed an association with catheterization length and a vital prognosis lower than one month; the latter was the only factor that maintained an independent association in the multivariate analysis (OR 5.75; 95% CI: 1.17-28.27). CONCLUSION: The present study documents the relevance of prolonged catheterization as a consistent risk for colonization of non-tunnelled central venous catheters. This risk increases independently in canalization at femoral site and particularly among severely ill patients. The presence of these factors allows the identification of a high risk population for the development of catheter related bacteremia.

Foster J.W. *When protons attack: microbial strategies of acid adaptation.* Curr Opin Microbiol. 1999; 2(2) : 170-4.p Abstract: Inducible tolerance to acidic and alkaline environments is recognized as an important survival strategy for many prokaryotic and eukaryotic microorganisms. Recent developments in understanding this phenomenon include the identification of regulatory genes, specific tolerance mechanisms and genes associated with tolerance. In addition, there is significant evidence linking pH responses with virulence.

Fowler V.G. Jr et al. *Infective endocarditis due to Staphylococcus aureus: 59 prospectively identified cases with follow-up.* Clin Infect Dis. 1999; 28(1) : 106-14.p Abstract: Fifty-nine consecutive patients with definite Staphylococcus aureus infective endocarditis (IE) by the Duke criteria were prospectively identified at our hospital over a 3-year period. Twenty-seven (45.8%) of the 59 patients had hospital-acquired S. aureus bacteremia. The presumed source of infection was an intravascular device in 50.8% of patients. Transthoracic echocardiography (TTE) revealed evidence of IE in 20 patients (33.9%), whereas transesophageal echocardiography (TEE) revealed evidence of IE in 48 patients (81.4%). The outcome for patients was strongly associated with echocardiographic findings: 13 (68.4%) of 19 patients with vegetations visualized by TTE had an embolic event or died of their infection vs. five (16.7%) of 30 patients whose vegetations were visualized only by TEE (P <.01). Most patients with S. aureus IE developed their infection as a consequence of a nosocomial or intravascular device-related infection. TEE established the diagnosis of S. aureus IE in many instances when TTE was nondiagnostic. Visualization of vegetations by TTE may provide prognostic information for patients with S. aureus IE.

Fox K.K. et al. *Antimicrobial resistance in Neisseria gonorrhoeae in the United States, 1988-1994: the emergence of decreased susceptibility to the fluoroquinolones.* J Infect Dis. 1997; 175(6) : 1396-403.p Abstract: Antimicrobial susceptibilities of Neisseria gonorrhoeae have been prospectively determined in the Gonococcal Isolate Surveillance Project of the Centers for Disease Control and Prevention. From 1988 through 1994, susceptibilities were determined for 35,263 isolates from 27 clinics. Patients were demographically similar to those in nationally reported gonorrhea cases. In 1994, 30.5% of isolates had chromosomally or plasmid-mediated resistance to penicillin or tetracycline. Penicillin resistance increased from 1988 (8.4%) to 1991 (19.5%) and then decreased in 1994 (15.6%). Tetracycline resistance decreased from 1988 (23.4%) to 1989 (17.3%) and then increased in 1994 (21.7%). Most isolates (99.9%) were highly susceptible to broad-spectrum cephalosporins. Isolates with decreased susceptibility to ciprofloxacin increased from 1991 (0.4%) to 1994 (1.3%); 4 isolates were ciprofloxacin-resistant. Ciprofloxacin-resistant strains may not respond to therapy with recommended doses of fluoroquinolones, and the clinical importance of strains with decreased susceptibility is unknown. The emergence of fluoroquinolone resistance in N. gonorrhoeae in the United States threatens the future utility of this class of antimicrobials for gonorrhea therapy.

Frank K.E. et al. *A simple, inexpensive apparatus for performance of preparative scale solution phase multiple parallel synthesis of drug analogs. II. Biological evaluation of a retrospective library of quinolone antiinfective agents.* Comb Chem High Throughput Screen. 1998; 1(2) : 89-99.p Abstract: A series of pure fluoroquinolone antiinfective agents was prepared by multiple parallel synthesis using a simple new apparatus. These compounds were evaluated biologically against Gram-positive and Gram-negative microorganisms and against a BCG strain transfected with luciferase in a fluorescence-based antitubercular assay. Activity against relatively fast growing, acid-fast Mycobacterium smegmatis was determined in part by agar-dilution streak assays. Data obtained against Escherichia coli-derived DNA gyrase does not correlate well with whole cell assays against E. coli. These compounds were assayed by a convenient glass-fiber filter binding method modified for high throughput screening. In these analogs, the results with a N-1 cyclopropyl substituent were often inferior to those obtained with a N-1 2',4'-difluorophenyl substituent. None of the new compounds prepared was superior in its antimycobacterial potency to ciprofloxacin or temafloxacin.

Frankel R.E. et al. *Invasive pneumococcal disease: clinical features, serotypes, and antimicrobial resistance patterns in cases involving patients with and without human immunodeficiency virus infection.* Clin Infect Dis. 1996; 23(3) : 577-84.p Abstract: We reviewed 153 episodes of invasive pneumococcal disease involving 147 hospitalized patients with and without human immunodeficiency virus (HIV) disease to examine and compare epidemiologic and clinical features, capsular serotypes, and antibiotic susceptibility patterns. HIV infection was the most common risk factor for invasive pneumococcal disease. Pneumococcal disease in HIV-infected individuals was characterized by the greater frequency with which pneumonia was the source of bacteremia (90% vs. 63%) (P <.01) and an increased recurrence rate (15% vs. < 1%) (P <.01). The overall mortality rate was 12% and did not vary by HIV serostatus. Capsular-type data were available for 149 episodes; 90% of the types were among those found in the polyvalent pneumococcal vaccine. The four most common capsular types causing invasive disease were 14, 6b, 9v, and 22f; capsular type 9v was significantly more common among HIV-infected patients (P <.01). Penicillin-resistant isolates were identified in 7.2% of all cases, and their presence did not vary by HIV status; 20% of isolates from cerebrospinal fluid were resistant. The majority of the resistant isolates were of capsular type 9v. Given the worldwide increase in both HIV and penicillin-resistant pneumococcal infections, better preventative and therapeutic strategies are greatly needed.

Franzin L. et al. *Clarithromycin and amoxicillin susceptibility of Helicobacter*

pylori strains isolated from adult patients with gastric or duodenal ulcer in Italy. Curr Microbiol. 2000; 40(2) : 96-100.p Abstract: Helicobacter pylori strains, isolated from 100 gastric biopsies from 49 previously untreated adult patients with endoscopy and histology-confirmed gastric or duodenal ulcer, were tested for in vitro antimicrobial susceptibility. Strains were isolated from biopsies of 75.5% (37 of 49) patients before therapy and of 13.5% after therapy. Clarithromycin and amoxicillin susceptibility testing was performed on pretreatment and posttreatment strains by using the agar disk diffusion method and E-test, a quantitative technique for the minimal inhibitory concentration (MIC) determination. All strains (n = 53) were susceptible to amoxicillin by the two methods. Three strains of 34 (8.8%) patients were resistant to clarithromycin: two by both methods and one by E-test (MIC > 2 microg/ml). E-test, although more expensive than the disk diffusion method, is easy to perform and is a reliable method for testing H. pylori susceptibility to antimicrobial agents in the clinical microbiology laboratory.

Frebourg N.B. et al. *PCR-Based assay for discrimination between invasive and contaminating Staphylococcus epidermidis strains.* J Clin Microbiol. 2000; 38(2) : 877-80.p Abstract: The discrimination between Staphylococcus epidermidis strains that contaminate and infect blood cultures is a daily challenge for clinical laboratories. The results of PCR detection of putative virulence genes were compared for contaminating strains, sepsis-related strains, catheter strains, and saprophytic strains. Multiplex PCR was used to explore the atlE gene, which is involved in initial adherence, the intercellular adhesion gene cluster (ica), which mediates the formation of the biofilm, and the agrA, sarA, and mecA genes, which might contribute to the pathogenicity of S. epidermidis. Whereas the atlE, agrA, and sarA genes were almost ubiquitously amplified, the ica and mecA genes were detected significantly more in infecting strains than in contaminating strains (P </= 0.02) and thus appeared to be related to the potential virulence of S. epidermidis.

Fredriksen F. et al. *In situ localization of Streptococcus pyogenes during acute tonsillitis: an immunocytochemical study with gold markers.* Acta Otolaryngol. 1996; 116(6) : 892-5.p Abstract: Epithelial cells were harvested from the surface of the palatine tonsils of seven patients with current acute tonsillitis, proven culture-positive for Streptococcus pyogenes. The epithelial cells harboured attached bacteria, which expressed positive affinity to gold-labelled antiserum to S. pyogenes. The gold particles adhered selectively to the bacterial capsules. The microorganisms were held in place by projections protruding from the epithelial cells, which were in close contact with the pili of the bacteria. In some areas, positive immunogold-labelled bacteria intermingled with bacteria lacking such labelling. None of the culture-negative controls harboured epithelial cells with positive immunogold-labelled bacteria. Orally administered phenoxymethylpenicillin caused a significant reduction in both culture-positive S. pyogenes and bacteria displaying positive coating with specific gold-labelled antiserum to S. pyogenes.

Freeman C.D. et al. *Metronidazole. A therapeutic review and update.* Drugs. 1997; 54(5) : 679-708.p Abstract: The nitroimidazole antibiotic metronidazole has a limited spectrum of activity that encompasses various protozoans and most Gram-negative and Gram-positive anaerobic bacteria. Metronidazole has activity against protozoans like Entamoeba histolytica, Giardia lamblia and Trichomonas vaginalis, for which the drug was first approved as an effective treatment. Anaerobic bacteria which are typically sensitive are primarily Gram-negative anaerobes belonging to the Bacteroides and Fusobacterium spp. Gram-positive anaerobes such as peptostreptococci and Clostridia spp. are likely to test sensitive to metronidazole, but resistant isolates are probably encountered with greater frequency than with the Gram-negative anaerobes. Gardnerella vaginalis is a pleomorphic Gram-variable bacterial bacillus that is also susceptible to metronidazole. Helicobacter pylori has been strongly associated with gastritis and duodenal ulcers. Classic regimens for eradicating this pathogen have included metronidazole, usually with acid suppression medication plus bismuth and amoxicillin. The activity of metronidazole against anaerobic bowel flora has been used for prophylaxis and treatment of patients with Crohn's disease who might develop an infectious complication. Treatment of Clostridium difficile-induced pseudomembraneous colitis has usually been with oral metronidazole or vancomycin, but the lower cost and similar efficacy of metronidazole, coupled with the increased concern about imprudent use of vancomycin leading to increased resistance in enterococci, have made metronidazole the preferred agent here. Metronidazole has played an important role in anaerobic-related infections. Advantages to using metronidazole are the percentage of sensitive Gram-negative anaerobes, its availability as oral and intravenous dosage forms, its rapid bacterial killing, its good tissue penetration, its considerably lower chance of inducing C. difficile colitis, and expense. Metronidazole has notable effectiveness in treating anaerobic brain abscesses. Metronidazole is a cost-effective agent due to its low acquisition cost, its pharmacokinetics and pharmacodynamics, an acceptable adverse effect profile, and its undiminished antimicrobial activity. While its role as part of a therapeutic regimen for treating mixed aerobic/anaerobic infections has been reduced by newer, more expensive combination therapies, these new combinations have not been shown to have any therapeutic advantage over metronidazole. Although the use of metronidazole on a global scale has been curtailed by newer agents for various infections, metronidazole still has a role for these and other therapeutic uses. Many clinicians still consider metronidazole to be the 'gold standard' antibiotic against which all other antibiotics with anaerobic activity should be compared.

Freitas C.C.de. *Resistência aos antibióticos em Neisseria gonorrhoeae: dos mecanismos ao monitoramento.* DST j. bras. doenças sex. transm. 1999; 11(2) : 26-33.p Abstract: Gonorréia continua sendo uma infecção clinicamente importante, no mundo inteiro cerca de 60 milhöes de casos/ano, mas com uma distribuição geográfica diferente entre os países desenvolvidos e aqueles em desenvolvimento. Embora nos primeiros a doença tenha declinado nos ltimos 10 anos, a N. gonorrhoeae permanece como a principal causa de infecção e, consequentemente, um sério problema de saúde pública. Nos países subdesenvolvidos, portanto, a gonorréia ainda é motivo de muita preocupacao para os estudiosos das doenças sexualmente transmissíveis - DSTs especialmente, em virtude das complicacoes clínicas que pode causar e pela capacidade que tem de favorecer a transmissão do vírus da imunodeficiência humana -VIH.

Frick P.A. et al. *Prevalence of antimicrobial drug-resistant Streptococcus pneumoniae in Washington State.* West J Med. 1998; 169(6) : 364-9.p Abstract: We conducted a survey to assess the prevalence and geographic distribution of antimicrobial drug resistance among invasive isolates of Streptococcus pneumoniae in Washington State. Sequential sterile-site pneumococcal isolates were submitted from 13 hospital laboratories between 1 October 1995 and 30 January 1997. We serotyped 275 isolates from adults and children and determined minimum inhibitory concentrations (MIC) for commonly used antimicrobial drugs. Data were abstracted from medical records to compare differences in outcome and risk factors for infection. Of the 275 isolates, 73 (26.5%) were nonsusceptible to one or more antimicrobial drugs. Penicillin-nonsusceptible pneumococci (PNSP, MIC > or = 0.1 microgram/ml) accounted for 42 (15.3%) of the 275 isolates including 4 (1.5%) resistant strains (MIC > or = 2 micrograms/ml). The 42 PNSP included serogroups 6, 9, 14, 19, and 23, all of which are represented in the 23-valent pneumococcal vaccine. PNSP were also nonsusceptible to trimethoprim/sulfamethoxazole (92.9%), erythromycin (38.1%), imipenem (28.6%), and ceftriaxone (23.8%). Forty-seven (17.1%) of the 275 isolates were multiple drug-nonsusceptible pneumococci (MDNSP). A significantly greater number of patients < or = 12 years of age were infected with MDNSP compared with those > 12 years. Prior use of antimicrobial drugs and an immunosuppressive disorder were risk factors for infection with PNSP. In summary, pneumococci nonsusceptible to penicillin and other antimicrobial drugs are prevalent among adults

with invasive pneumococcal disease in Washington State. A large proportion of PNSP are resistant to other commonly used antimicrobial drugs. Local antibiotic susceptibility data should be considered when designing empiric treatment regimens.

Fridkin S.K. et al. *Surveillance of antimicrobial use and antimicrobial resistance in United States hospitals: project ICARE phase 2. Project Intensive Care Antimicrobial Resistance Epidemiology (ICARE) hospitals.* Clin Infect Dis. 1999; 29(2) : 245-52.p Abstract: The search for the means to understand and control the emergence and spread of antimicrobial resistance has become a public health priority. Project ICARE (Intensive Care Antimicrobial Resistance Epidemiology) has established laboratory-based surveillance for antimicrobial resistance and antimicrobial use at a subset of hospitals participating in the National Nosocomial Infection Surveillance system. These data illustrate that for most antimicrobial-resistant organisms studied, rates of resistance were highest in the intensive care unit (ICU) areas and lowest in the outpatient areas. A notable exception was ciprofloxacin- or ofloxacin-resistant Pseudomonas aeruginosa, for which resistance rates were highest in the outpatient areas. For most of the antimicrobial agents associated with this resistance, the rate of use was highest in the ICU areas, in parallel to the pattern seen for resistance. These comparative data on use and resistance among similar areas (i.e., ICU or other inpatient areas) can be used as a benchmark by participating hospitals to focus their efforts at addressing antimicrobial resistance.

Friedberg D. et al. *The amino acid sequence of Lrp is highly conserved in four enteric microorganisms.* J Bacteriol. 1995; 177(6) : 1624-6.p Abstract: Lrp (leucine-responsive regulatory protein) is a global regulator of metabolism in Escherichia coli (J. M. Calvo and R. G. Matthews, Microbiol. Rev. 58:466-490, 1994). The lrp genes from three other enteric microorganisms, Enterobacter aerogenes, Klebsiella aerogenes, and Salmonella typhimurium, were cloned and sequenced. An analysis of these sequences and of the previously determined sequence from E. coli indicated that the vast majority of changes were synonymous rather than nonsynonymous changes. Nucleotide changes occurred at 89 of 492 positions but resulted in amino acid changes at only 2 of 164 positions. This analysis suggests that the Lrp amino acid sequence is highly adapted for function and that almost all amino acid changes lead to a protein that functions less well than the wild-type protein.

Friedland I.R. *Comparison of the response to antimicrobial therapy of penicillin-resistant and penicillin-susceptible pneumococcal disease.* Pediatr Infect Dis J. 1995; 14(10) : 885-90.p Abstract: The continued spread of penicillin-resistant pneumococci raises therapeutic concerns. Optimal therapy for resistant infections is unknown and it is not clear whether the efficacy of penicillin or equally active beta-lactam agents is compromised in non-meningeal-resistant infections. A prospective nonintervention study was undertaken to compare the clinical response in penicillin-resistant vs. penicillin-susceptible bacteremic pneumococcal infections, excluding meningitis. Of 108 children enrolled, 35 (32%) had penicillin-resistant (one highly resistant) isolates. Seventy-eight children had pneumonia, 21 had occult bacteremia (sepsis) and 9 had peritonitis. Children with resistant infections were more likely to have underlying disorders, especially human immunodeficiency virus infection, and to have received antimicrobial therapy in the previous month. After 48 hours of therapy 64% of penicillin-susceptible infections showed improvement vs. 60% of penicillin-resistant infections (odds ratio, 1.2; 95% confidence intervals, 0.5 to 3.0). In children with pneumonia treated with ampicillin or an equivalent beta-lactam agent, 93% with penicillin-susceptible infections had improved by Day 7 of therapy compared with 88% with resistant infections (odds ratio, 1.9; 95% confidence interval 0.3 to 15.9). The durations of respiratory distress, fever and oxygen requirement were similar in penicillin-susceptible and -resistant infections. These results suggest that intermediate penicillin resistance is of little significance in pneumococcal pneumonia or sepsis and that standard beta-lactam therapy is still highly effective. Further studies of highly penicillin-resistant infections are necessary.

Friedrich L.V. et al. *Impact of use of multiple antimicrobials on changes in susceptibility of gram-negative aerobes.* Clin Infect Dis. 1999; 28(5) : 1017-24.p Abstract: Evaluation of antimicrobial usage vs. susceptibility relationships typically involves single agents. However, susceptibility profiles may be affected by multiple drugs. From 1992 through 1996, we studied relationships between drug usage and the susceptibility (only susceptibility rates of > or = 70%) of Acinetobacter anitratus (baumannii), Enterobacter aerogenes, Escherichia coli, Enterobacter cloacae, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis, and Serratia marcescens to 22 agents. Linear regression was used to assess usage of each agent vs. susceptibility to it and to all agents. Only relationships with a coefficient of determination of > or = 0.5 and a negative slope were evaluated and classified as increasing drug use and decreasing susceptibility (increasing D, decreasing %S) or decreasing drug use and increasing susceptibility (decreasing D, increasing %S). The mean numbers (range) of drugs associated with a change in susceptibility were 1.7 (0-14) and 0.6 (0-7), respectively, for increasing D, decreasing %S and decreasing D, increasing %S relationships. Multiple antimicrobials are associated with susceptibility to other drugs; thus, surveillance of these relationships should not be limited to single drugs.

Fuchs T.M. *Molecular mechanisms of bacterial pathogenicity.* Naturwissenschaften. 1998; 85(3) : 99-108.p Abstract: Cautious optimism has arisen over recent decades with respect to the long struggle against bacteria, viruses, and parasites. This has been offset, however, by a fatal complacency stemming from previous successes such as the development of antimicrobial drugs, the eradication of smallpox, and global immunization programs. Infectious diseases nevertheless remain the world's leading cause of death, killing at least 17 million persons annually [61]. Diarrheal diseases caused by Vibrio cholerae or Shigella dysenteriae kill about 3 million persons every year, most of them young children: Another 4 million die of tuberculosis or tetanus. Outbreaks of diphtheria in Eastern Europe threatens the population with a disease that had previously seemed to be overcome. Efforts to control infectious diseases more comprehensively are undermined not only by socioeconomic conditions but also by the nature of the pathogenic organisms itself; some isolates of Staphylococcus aureus and Enterobacter have become so resistant to drugs by horizontal gene transfer that they are almost untreatable. In addition, the mechanism of genetic variability helps pathogens to evade the human immune system, thus compromising the development of powerful vaccines. Therefore detailed knowledge of the molecular mechanisms of microbial pathogenicity is absolutely necessary to develop new strategies against infectious diseases and thus to lower their impact on human health and social development.

Fujita N. et al. *[Infections with drug resistant bacteria and their treatment methods—VRE infections].* Rinsho Byori. 2000; Suppl 111 : 132-41.p Abstract: Vancomycin-resistant enterococci(VRE) is a worldwide threat now. Because we have lost a last resort vancomycin for enterococcal infections, and their resistant genes can be transferred to other more pathogenic gram-positive bacteria. We have only a few of optional therapeutic agents against VRE. VRE causes urinary tract infections, intra-abdominal infections, bacteremias, endocarditis and wound infections. Especially bacteremias caused by VRE result in high mortality. VRE infections including colonization and infectious diseases must be controlled by rapid detection of VRE, appropriate diagnosis of infections, followed by effective antimicrobial therapies and infection control measures.

Fujiue Y. et al. *[Results of antimicrobial susceptibilities of strains clinically isolated at 8 institutions in Hiroshima City to major oral antimicrobial drugs, mainly new quinolone drugs. Hiroshima Levofloxacin Susceptibility Surveillance Group].* Jpn J Antibiot. 2000; 53(6) : 409-21.p Abstract:

To evaluate the resistance for major oral antimicrobial agents, mainly new quinolones, we carried out a drug susceptibility surveillance of 3,050 strains of 11 microbial species clinically isolated at 8 institutions such as general hospitals and examination centers in Hiroshima city. 10 antimicrobial agents were used: 3 new quinolone drugs, 5 beta-lactam drugs, minocycline and clarithromycin. Among Gram-positive bacteria, methicillin resistant Staphylococcus aureus (MRSA) and Enterococcus faecalis showed low susceptibility to the new quinolone drugs, while methicillin susceptible Staphylococcus aureus (MSSA) and Streptococcus pneumoniae were highly sensitive to these drugs. Among Gram-negative bacteria, Pseudomonas aeruginosa showed high resistance for the new quinolone drugs, but enteric bacteria and Haemophilus influenzae did not show marked resistance, maintaining almost good sensitivity to these drugs. To reduce the appearance of resistant bacteria, appropriate antimicrobial agents should be selected. Drug susceptibility surveillance in the community will be also important in the future.

Fujiue Y. et al. *[The antimicrobial susceptibilities and serotypes of Pseudomonas aeruginosa isolated from sputum].* Jpn J Antibiot. 1998; 51(1) : 26-36.p Abstract: During the period of January 1992 and August 1995, 75 strains of Pseudomonas aeruginosa were isolated from sputum at the Hiroshima Prefectural Hiroshima Hospital. The antimicrobial susceptibilities and serotypes of those strains were investigated. The results are summarized as follows: 1. The analyses of antimicrobial susceptibilities revealed that meropenem (MEPM) was the most active among the carbapenems tested against those P. aeruginosa strains with MIC of < or = 6.25 micrograms/ml. All of the strains were thus found to be susceptible to MEPM, while 9 strains out of 75 (12%) were resistant to imipenem showing cross-resistance to biapenem. 2. The activities of the beta-lactams other than carbapenems were found to be the order of cefozopran > or = ceftazidime > aztreonam > piperacillin with MIC50 and MIC90 ranging of 3.13-6.25 micrograms/ml and 25- > or = 100 micrograms/ml, respectively. 3. Among aminoglycosides tested, 3 strains (4.0%) of the strains showed resistance to amikacin, however none of them were resistant to tobramycin. 4. Distribution of serotypes among the strains was; type G 22.7%, type M 21.3%, type A 16.0%, type B 13.3% and type E 8.0%. Strains of types M and E showed multiple resistance to beta-lactams except carbapenems. As documented in this study, the frequency of isolation of beta-lactam-resistant P. aeruginosa (including carbapenem-resistant) is steadily increasing. Continuous surveillance of antimicrobial susceptibility among clinically isolated P. aeruginosa seems to be necessary.

Fujiwara S. et al. *Effect of adherence on antimicrobial susceptibility of Pseudomonas aeruginosa, Serratia marcescens, and Proteus mirabilis.* Hiroshima J Med Sci. 1998; 47(1) : 1-5.p Abstract: A simple method was used for testing the antibiotic susceptibility of adherent bacteria to plastic surfaces. Pseudomonas aeruginosa, Serratia marcescens, and Proteus mirabilis cells adhering to the bottom of a plastic tissue culture plate were incubated in serially diluted antibiotic solutions. After 24-h incubation the solutions were removed and a fresh medium without antibiotics was added to each well. The viability of the cells was judged by their growth after a further 24-h incubation. In our assay system, we employed a short incubation time (1-h) involving adherence of bacteria to a surface for the purpose of minimizing the effect of the glycocalyx on antibiotic activity. Even if the bacteria did not form a biofilm, the minimal bactericidal concentrations for adherent bacteria (MBCADs) markedly elevated. The MBCADs of ofloxacin well correlated with the bacteriological eradication by ofloxacin treatment for urinary tract infections (UTIs) associated with indwelling urinary catheters, whereas the minimal inhibitory concentrations did not show a correlation. Kinetic studies showed that adherent Pseudomonas aeruginosa had a 2 h-lag time before logarithmically growing when these bacteria were incubated in Mueller-Hinton broth without antibiotics. The tolerance demonstrated by adherent cells is likely to play a role in the difficulties encountered in the antimicrobial chemotherapy of biofilm infections. Moreover, our assay system was considered to be useful in the therapeutic selection of antibiotics for these infections.

Fukatsu K. et al. *Influences of type and duration of antimicrobial prophylaxis on an outbreak of methicillin-resistant Staphylococcus aureus and on the incidence of wound infection.* Arch Surg. 1997; 132(12) : 1320-5.p Abstract: OBJECTIVE: To clarify how antibiotic prophylaxis influenced an outbreak of methicillin-resistant Staphylococcus aureus (MRSA) and postoperative infection. DESIGN: Retrospective review. SETTING: University-affiliated teaching hospital. PATIENTS: All patients (n=1824) undergoing subtotal esophagectomy, gastrectomy, or colorectal surgery during the period 1982 through 1995. MAIN OUTCOME MEASURES: Type, timing, and duration of prophylactic antibiotics. Postoperative infection by the Centers for Disease Control and Prevention definition and the organisms isolated. RESULTS: Third-generation cephalosporins were frequently administered for prophylaxis during the period 1982 through 1990. The rate of isolates of MRSA from the infected site increased, peaking in 1988 to 1990. Since 1991 to 1992, along with a marked decrease in third-generation cephalosporin use, the rates of MRSA isolated have declined dramatically. The timing of administration changed from postoperative to intraoperative. Although the duration was gradually decreased, coverage was still provided until about the fifth postoperative day, even during 1993 to 1995. Prolonged coverage did not reduce the rate of superficial incisional or organ/space surgical site infection or that of pneumonia. CONCLUSIONS: Overuse of third-generation cephalosporins for long periods caused an MRSA outbreak. Long-term prophylaxis did not lower infection rates. The briefest possible prophylaxis with first- or second-generation cephalosporins should be used in general surgery.

Fukui K. et al. *[Bacteriological study of oral open abscesses].* Kansenshogaku Zasshi. 1997; 71(12) : 1226-31.p Abstract: Although studies of bacteriology of closed oral abscesses have been extensively done, there are few studies on microorganisms involving open oral abscesses. We examined bacteriologically three open abscesses with precaution against bacterial contamination with oral normal flora and saliva, when sampling. The specimens were subjected to aerobic and anaerobic cultures within 2 hours after sampling. All three cases were infected with 5 to 14 species of aerobic and anaerobic bacteria; Streptococcus spp., Prevotella intermedia and other Prevotella spp. were predominant in all three cases. All six Prevotella spp. isolated were beta-lactamase producers, being resistant to beta-lactam antibiotics. These results emphasize the importance of prompt anaerobic culture for the bacteriological study of open oral abscess and the significance of nitrocefin test to detect beta-lactamase produced by oral isolates, especially Prevotella spp.

Fuller D.D. et al. *Comparison of BACTEC plus Aerobic/F, Anaerobic/F, Peds Plus/F, and Lytic/F media with and without fastidious organism supplement to conventional methods for culture of sterile body fluids.* Diagn Microbiol Infect Dis. 1997; 29(4) : 219-25.p Abstract: We compared the BACTEC 9240 continuous-read instrument using Peds Plus/F, Lytic/F, Aerobic/F, and Anaerobic/F media (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD) with and without fastidious organism supplement to conventional centrifugation preparation and plating for the recovery and speed of detection of microorganisms. A total of 908 sterile body fluid specimens were collected and processed, yielding 116 (13%) positive cultures. Of the 80 isolates considered clinically significant, 48 (60%) were recovered by both the BACTEC system and conventional culture, whereas 32 (40%) were recovered by BACTEC only. No clinically significant isolates were recovered only by conventional culture methods. The time to detection for isolates recovered from both sets was faster for BACTEC. It was found that BACTEC, with or without the addition of fastidious organisms supplement, exhibited improved sensitivity for the recovery of microorganisms.

Funfstuck R. et al. *[Prevention of reinfection by L-methionine in patients with recurrent urinary tract infection].* Med Klin. 1997; 92(10) : 574-81.p Abstract: PROBLEM: A great variety of different antimicrobial chemotherapeutics is available for the treatment of urinary tract infections. Influencing the course of chronic diseases is a problem because recurrent diseases may result in disturbances of renal and bladder functions as well as in irreversible damages of the renal parenchyma. The present investigations are expected to clarify whether an effective prevention of reinfection in patients with chronically recurrent urinary tract infection is possible by a regular administration of L-methionine (Acimethin). PATIENTS AND METHODS: 33 female patients were included in the examinations. Following acute disease, 23 females (aged: 47.4 +/- 13.3 years) were treated with 3 x 1 tablet of Acimethin (L-methionine) daily over a period of 26 months. Ten female patients (aged: 47.4 +/- 12.2 years) taking 1 tablet of Nevigramon (nalidixic acid) three times daily over 21.6 months served as a control group. Before starting treatment and in the middle of the therapy period control examinations were performed and following the last drug administration so as to assess the therapeutic result. RESULTS: No acute infection occurred during L-methionine treatment. All parameters of inflammation (leucocyte count, C-reactive protein, blood sedimentation rate, alpha 2-globulin concentration) were in the normal range; no impairment of renal function was observed. Although L-methionine, i.e. nalidixic acid, did not yield any significant changes in the range of bacteria, the adherence of uropathogenic microorganisms to the cells of the urinary tract was reduced. Before L-methionine treatment, the average load of the uroepithelial cells was 95.9 +/- 73.6 bacteria per cell. When the observation period was completed, 51.2 +/- 56.4 bacteria per cell were registered ($p < 0.03$). During nalidixic acid treatment, the rate of adherence was reduced from 74.0 +/- 88.4 to 34.4 +/- 37.8 bacteria per cell ($p < 0.25$). During L-methionine treatment, no Escherichia coli strains that are able to produce hemolysin or to form aerobactine were found. Among agents adhering to uroepithelial cells, however, an increase in their ability to produce mannose-resistant hemagglutination was conspicuous. CONCLUSION: L-methionine is suitable to prevent reinfection with chronic urinary tract infection. The therapeutic result is essentially due to its influence on bacterial cytoadherence. In contrast to the established recommendations concerning the prevention of reinfection by the use of antibiotics and sulphonamides selecting resistant strains during long-term treatment, nothing is known about the development of resistance to L-methionine.

Fung C.P. et al. *A 5-year study of the seroepidemiology of Klebsiella pneumoniae: high prevalence of capsular serotype K1 in Taiwan and implication for vaccine efficacy.* J Infect Dis. 2000; 181(6) : 2075-9.p Abstract: Seroepidemiology of Klebsiella pneumoniae was determined for 1000 nonrepetitive K. pneumoniae isolates collected by a medical center in Taiwan during 1993-1997. Of these, 630 isolates (63%) were from community-acquired infections; the rest were from hospital-acquired infections. The isolates were serotyped according to capsular antigen by countercurrent immunoelectrophoresis. About 77% were typeable. Serotypes K1 and K2 accounted for 21.7% and 9.3% of the isolates, respectively, followed by K57 (5.1%), K54 (4.2%), K21 (3. 3%), and K16 (3%). The frequency of serotype K1 among bacteremic isolates (30.8%) far exceeded that reported by other investigators worldwide. Molecular typing of random K1 isolates by pulsed-field gel electrophoresis revealed several different pulsotypes, suggesting a nonclonal spread. This study indicates that a Klebsiella vaccine developed in Europe is not optimal for use in Taiwan because it does not contain the most predominant serotypes-K1, K54, and K57.

Fung C.P. et al. *Antimicrobial resistance of Streptococcus pneumoniae isolated in Taiwan: an island-wide surveillance study between 1996 and 1997.* J Antimicrob Chemother. 2000; 45(1) : 49-55.p Abstract: Between August 1996 and July 1997, 550 clinically significant Streptococcus pneumoniae isolates were collected from 14 geographically separate laboratories in Taiwan. These isolates were serotyped and MICs were determined by agar dilution. Among serotypes covered by the 23-valent vaccine, types 19F, 19A, 23F, 23A and 6B dominated, comprising 255 isolates; among non-vaccine serotypes, types 35, 39, 34, 13 and 31 dominated, comprising 118 isolates. Of the 550 isolates, 310 (56.4%) were resistant to penicillin G (MIC 0. 12 mg/L), 238 (43.3%) with intermediate resistance (MIC 0.12-1 mg/L) and 72 (13.1%) with high-level resistance (MIC 2 mg/L). Most non-susceptible pneumococci were of serotypes 19F and 23F; non-susceptible isolates of these serotypes were distributed across all of Taiwan. Fourteen other antibiotics were tested; 83% of the isolates were resistant to tetracycline, 78% to azithromycin, 74% to erythromycin, 54% to clindamycin and 23% to chloramphenicol. Thus, macrolides can no longer be used as first line agents to treat pneumococcal infections in Taiwan. Multi-resistance (isolates resistant to three or more chemically unrelated antibiotics) was found in each serotype or group, but mostly in types 19F and 23F. The emergence of such strains complicates antibiotic selection, but both types are covered by the 23-valent vaccine, as were 82% of the isolates from blood and eight of the nine from cerebrospinal fluid. Good antibiotic control and appropriate use of this vaccine may improve the current problem in Taiwan, especially for the elderly.

Fung C.P. et al. *Antimicrobial susceptibility and beta-lactamase production of Moraxella catarrhalis isolates in Taiwan.* J Formos Med Assoc. 1995; 94(9) : 548-54.p Abstract: Between 1 August 1993 and 31 July 1994, 135 clinical isolates of Moraxella catarrhalis were collected from 12 large medical laboratories in Taiwan. The majority of specimens came from sputum (124 isolates). Other specimens included four isolates from throats, three isolates from wounds or pus, two isolates from eyes, one isolate from blood and one from cerebrospinal fluid. Epidemiologically, M. catarrhalis isolates were found frequently in winter and spring with a peak in February, and only sporadically from April to September. The overall rate of beta-lactamase producing isolates was 98.5% (132/135). All isolates were considered to be ampicillin-resistant, none were found to be resistant to other beta-lactam agents. Among other antimicrobial agents, all isolates were susceptible to chloramphenicol, erythromycin, roxithromycin, ofloxacin and ciprofloxacin, but uniformly resistant to trimethoprim (minimum inhibitory concentration (MIC) > or = 4 micrograms/mL, zone diameter < or = 19 mm). There were 12 isolates (8.8%) resistant to sulfamethoxazole (MIC > or = 32 micrograms/mL, zone diameter < or = 19 mm) and 19 isolates (14.4%) resistant to tetracycline (MIC > or = 16 micrograms/mL, zone diameter < or = 19 mm). The high level of resistance to ampicillin due to beta-lactamase production indicates that this is no longer a reliable agent for the treatment of M. catarrhalis infections. Among the beta-lactam agents tested, amoxicillin + clavulanate and the cephalosporins were active. These agents appear to be reliable first-line therapies when infection with M. catarrhalis is suspected. Misidentification of the species and difficulties in determining susceptibility to ampicillin are still widespread in Taiwanese laboratories. The application of the butyrate hydrolysis test and an appropriate test for beta-lactamase production is necessary for the resolution of these problems.

Furman A.C. et al. *Lung abscess in patients with AIDS.* Clin Infect Dis. 1996; 22(1) : 81-5.p Abstract: We identified 31 patients with human immunodeficiency virus (HIV) infection and lung abscess. All patients had advanced HIV disease, and the mean CD4 cell count was 17/mm3 (range, 2-50/mm3). Twenty-two patients (71%) had previous opportunistic infections, and 24 (77%) had previous pulmonary infections. Symptoms at the time of presentation included fever (90% of patients), cough (87%), dyspnea (35%), pleuritic chest pain (26%), and hemoptysis (10%). The microbiological etiology was established for 28 patients, and the pathogens recovered were bacteria (65%), Pneumocystis carinii (6%), fungi (3%), and mixed microorganisms (16%). The pathogens included Pseudomonas aeruginosa (11), Streptococcus pneumoniae (6), P. carinii (5), Klebsiella pneumoniae (5), Staphylococcus aureus (4), Aspergillus

species (3), viridans streptococcus (2), Haemophilus influenzae (1), Streptococcus milleri (1), Proteus mirabilis (1), and Cryptococcus neoformans (1). Mycobacterium tuberculosis was not isolated; two patients for whom a microbiological etiology was not established responded to antituberculous therapy. Patients were treated for 2-12 weeks; 25% of the patients received > 4 weeks of therapy. The outcome was poor: 36% of the patients had recurrences, and 19% died. In patients with AIDS, lung abscess is associated with advanced HIV infection, is due to a broad spectrum of pathogens, responds poorly to antibiotics, and has a poor prognosis.

Furukawa K.K. et al. *Effectiveness of chlorine dioxide in disinfection on two soft denture liners.* J Prosthet Dent. 1998; 80(6) : 723-9.p Abstract: STATEMENT OF PROBLEM: Soft tissue denture liners frequently require replacement that necessitates complete removal from the denture base. A high speed lathe located in a "clean laboratory" is often used to facilitate removal of these materials, but it is unclear whether routine disinfection procedures reduce bacterial contamination sufficiently to prevent contamination of the laboratory. PURPOSE: The first phase of this study evaluated the effectiveness of 3-minute chlorine dioxide spray and immersion disinfection procedures on 2 denture liners (Coe Soft and Coe Comfort) and stainless steel specimens used as controls. The second phase evaluated the effectiveness of spray disinfection at time intervals of 1, 3, and 10 minutes. MATERIAL AND METHODS: Specimens made of soft denture liners attached to acrylic resin bases (10 per group) were contaminated with Escherichia coli, Staphylococcus aureus, and Candida albicans. Colony-forming units were counted after different disinfection techniques were applied. Kruskal-Wallis 1-way analysis of variance on ranks and an all pairwise multiple comparison procedures (Dunn's method) were used to test for significant differences among test groups at the P <.05 level of significance. RESULTS: Chlorine dioxide was effective against nonporous stainless steel specimens but was inadequate for denture liners at the recommended 3-minute time of disinfection. The immersion technique was more effective than the spray technique, but the difference was not significant. Increasing the time of disinfection did not significantly reduce the numbers of microorganisms. CONCLUSION: Coe Soft and Coe Comfort denture liners should be removed before entering the laboratory. These materials contain sufficient viable bacteria after routine disinfection procedures to cause contamination of the "clean laboratory.".

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Gabriel M.M. et al. *Effects of silver on adherence of bacteria to urinary catheters: in vitro studies.* Curr Microbiol. 1995; 30(1) : 17-22.p Abstract: Strains of Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Enterococcus faecalis, and Klebsiella pneumoniae, mostly from complicated urinary tract infections, showed reduced adherence to silver-treated silicone or latex catheters as compared with latex or silicone catheters. The relative degrees of cell adherence to catheters at 2 h or 18 h, as indicated by radiolabeled cell assays, were in general agreement with growth rate-reduction assays and scanning-electron-microscopy data. For strains of E. coli, the correlation between cell hydrophobicity and degree of adherence to catheters was not significant. Antibiotic resistance (tetracycline, sulfathiazine, neomycin, kanamycin) and silver resistance were not associated. The radiolabel adherence procedure provided a quantitative method for evaluating the relative antimicrobial efficacy of silver-treated catheters.

Gabryelewicz A. *Critical evaluation of the treatment of peptic ulcer diseases associated with Helicobacter pylori infection.* J Physiol Pharmacol. 1996; 47(1) : 51-8.p Abstract: Current view on the role of Helicobacter pylori (Hp) infection in the pathogenesis of peptic ulcer disease is presented. It was shown that Hp is an important risk factor for the development of the disease for which other cofactors are necessary. Different drug regiments for Hp eradication are discussed. The eradication rates of 80 to 90 percent are achievable—most often including 7-10 days triple therapy (drugs increasing intragastric pH, antibiotics and antimicrobial agents). Resistance of Hp to used antibiotics and antimicrobial drugs is underlined.

Gacon G. et al. *[Two stages reimplantation for infection after knee arthroplasty. Apropos of a series of 29 cases].* Rev Chir Orthop Reparatrice Appar Mot. 1997; 83(4) : 313-23.p Abstract: PURPOSE OF THE STUDY: The purpose of this work was to precise diagnosis and treatment of infected total knee arthroplasty with two stage reimplantation. MATERIAL: 29 infected total knee arthroplasties were operated between 1984 and 1994 and included in this study (mean F.U. 3.5 Y). There were 20 females and 9 males, mean age 70 (46-83). The original arthroplasty was done for OA in 28 patients, RA in one. The arthroplasties were: UHK 2, Bicompartmental 2, Tricompartmental 19. 20 TKA were cementless. 14 patients showed one or several risk factors. Infection was diagnosed in 1 of 2 ways: preoperative aspiration or culture of surgical specimen. There were 12 staphylococcus epidermidis, 8 staphylococcus aureus, streptococcus (n = 2) acinetobacter (n = 2), peptococcus (n = 1) pseudomonas (n = 1), gemella morbidellum (n = 1). 6 were non identified. METHOD: The protocol for two stage reimplantation began with components and cement removal. A synovectomy was performed. The knee cavity was filled with antibiotic cement spacer and the wound was closed. The leg was placed in a splint. All patients underwend a continued antibiotic therapy, specific in 20 cases with isolated organisms. A total knee arthroplasty was performed, using a total posterior cruciate substituting prosthesis, 6 to 8 weeks after components removal (2-24). All patients received parenteral antibiotics after reimplantation for not less than 2 months (2-6). RESULTS: Infection was eradicated in 24 cases, 22 in one time, 2 bad second debridement. At last follow-up the average Hungerford score was 75.6/100, the average Knee society knee score was 80 and the average functional score was 70. Mean range of flexion was 95 degrees. 6 patients had recurrent infection and poor result. They underwent arthrodesis. 5 of the 6 patients had solid mature fusion at last follow-up. DISCUSSION: The results of two stage reimplantation for infected total knee replacement showed that this is the method of choice for infection treatment and acceptable function restoration. As other authors, we get a good success rate (82 per cent). Functional result was better with identified microorganisms, but we did not find any correlation with organisms type or infection length. Punction and bone scanning are of great help for diagnosis in difficult chronical cases. Organism identification is fundamental for infection duration. Staphylococcus epidermidis was the most frequent identified organism. New procedures using articulated cement spacer may improve functional results.

Gadhi C.A. et al. *Antibacterial activity of Aristolochia paucinervis Pomel.* J Ethnopharmacol. 1999; 67(1) : 87-92.p Abstract: Several fractions of the methanolic extract of the rhizome or the leaves of Aristolochia paucinervis Pomel were screened for antibacterial activity using the agar dilution method against fourteen reference bacterial strains. Only three fractions (defatted chloroformic rhizome fraction: APRC, rhizome ethyl acetate fraction: APRE and leaf chloroform fraction: APLC) showed an activity against at least one of the microorganisms tested. The minimum inhibitory concentration (MIC) determination showed that APRC was the most active against Clostridium perfringens, Clostridium difficile, Enterococcus faecalis, Micrococcus luteus and Bacillus subtilis. The high bacteriostatic activity of APRC was confirmed by its MIC determination against clinical strains of C. perfringens (n = 32), C. difficile (n = 31), and E. faecalis (n = 22). Results of this study suggest the potential interest of this highly active fraction and support the use of A. paucinervis Pomel in Moroccan traditional medicine to treat skin and soft-tissue infections, especially gas gangrene and intestinal diseases.

Gaetti-Jardim E. Jr et al. *Oral species of Fusobacterium from human and environmental samples.* J Dent. 1996; 24(5) : 345-8.p Abstract: PURPOSE: The aim of this study was the characterization and identification of oral Fusobacterium in patients with and without periodontal disease, and from spittoons and air-water syringes. The antimicrobial susceptibility of this bacterium was evaluated. METHOD: Subgingival samples were taken using sterilized absorbent paper points. Spittoon samples were collected using sterile swabs around the drain area with shut off, and air-water syringe samples by washing the tip with Ringer solution. Samples were transferred in tubes under CO2 flux. Diluted samples were inoculated on to Omata and Disraely agar and blood agar plates, which were incubated in anaerobiosis, at 37 degrees C, for 4 days. Bacterial species were identified biochemically. MIC was determined using an agar dilution method. RESULTS: Periodontal patients, healthy subjects, spittoons and air-water syringes were 80%, 67.6%, 37.8% and 3.3% positive to Fusobacterium, respectively. Clindamycin, imipenem, lincomycin, metronidazole and tetracycline were active against all human and environmental isolates. Eighteen isolates resistant to ampicillin or penicillin G produced beta-lactamases. The presence of human oral bacteria in items of dental equipment supports the hypothesis that such equipment may serve as a vehicle for the transmission of pathogenic organisms. CONCLUSION: Pieces of dental equipment may serve as a vehicle for the transmission of oral pathogenic organisms.

Gaitán Meza J.J. et al. *Etiología de sepsis neonatal y sensibilidad a los antibióticos en el Nuevo Hospital Civil de Guadalajara.* Enferm. Infecc. Microbiol. 1996; 16(2) : 80-5.p Abstract: OBJETIVO: Identificar las bacterias causantes de sepsis neonatal y sus patrones de sensibilidad a diversos antibióticos en el Nuevo Hospital Civil de Guadalajara. MATERIAL Y MÉTODOS: El estudio se realizó en la unidad de cuidados intensivos neonatales de un hospital de segundo nivel de atención en guadalajara, Jalisco, México. Se analizaron 74 neonatos con sospecha clínica y/o paraclínica de sepsis, bajo un diseño prospectivo, transversal, observacional y comparativo. Se consideró como infectados a los neonatos que en dos hemocultivos tomados de sitios diferentes de venopunción, tuvieron el mismo aislamiento. Los antibiogramas se realizaron por el método de kirby-Bauer, con los puntos recomendados por la NCCLS. RESULTADOS: Hubo 41 (55.4 por ciento) pacientes con hemocultivos positivos. De los aislamientos, 30 (73 por ciento) correspondieron a K. pneumoniae y 8 (19 por ciento) a S. epidermidis. Todas las cepas de K. pneumoniae fueron resistentes a ampicilina, pero 93 por ciento fueron sensibles a los aminoglucósidos y las cefalosporinas de tercera generación probados. Todas las cepas de estafilococos fueron sensibles a vancomicina y sólo dos fueron resistentes a dicloxacilina. CONCLUSIONES: El 98 por ciento de las cepas de K. pneumoniae presentó el mismo patrón de sensibilidad a los antibióticos, lo que sugiere una transmisión horizontal intrahospitalaria. La gran mayoría de los aislamientos fueron sensibles a los antimicrobianos de uso común, por lo que sugerimos que el tratamiento empírico inicial debe incluir a aminoglucósidos como gentamicina o amikacina, asociados a dicloxacilina o en casos específicos vancomicina y dejar como alternativa el uso de cefalosporinas de tercera generación. (AU).

Galan J.C. et al. *[Antibiotic resistance in Salmonella enterica: an increasing problem].* Enferm Infecc Microbiol Clin. 1996; 14(9) : 528-32.p Abstract: OBJECTIVE: To determine the evolution of the frequencies of Salmonella enterica serotypes and their resistance to antimicrobial agents. METHOD: A retrospective study of all S. enterica strains isolated from stool samples in the Hospital Clinico Universitario of Zaragoza over the period 1990-1994. RESULTS: Enteritidis was the most frequently isolated serotype (62.9%), although it showed a progressive decrease (from 76.2% in 1990 to 39.8% in 1994). Typhimurium was the serotype showing the highest resistance levels, 37.1% of its isolates being resistant to ampicillin, streptomycin, chloramphenicol and tetracyclin. There was a distinct increase in the frequency of multiresistant strains, from 9.7% in 1990 to 22.9% in 1994. Of 88 such strains, 78.4% corresponded to serogroup B, whereas only 4.5% to serogroup D. Of the antimicrobial agents traditionally considered elective, only cotrimoxazole maintained acceptable resistance levels (4.4%). Resistance to fluoroquinolones or 3rd-generation cephalosporines was not detected. CONCLUSIONS: The increasing frequency of Typhimurium, a highly resistant serotype, restrains the elective antimicrobial agents to cotrimoxazole in children and fluoroquinolones in adults. 3rd-generation cefalosporines may be a good alternative in case of therapeutic failure.

Gales A.C. et al. *Occurrence of single-point gyrA mutations among ciprofloxacin-susceptible Escherichia coli isolates causing urinary tract infections in Latin America.* Diagn Microbiol Infect Dis. 2000; 36(1) : 61-4.p Abstract: To detect if isolates susceptible to quinolones already carry mutations in the gyrA and parC genes, we selected 12 ciprofloxacin-susceptible Escherichia coli strains collected from patients with urinary tract infections in Latin America in 1998, as part of ongoing SENTRY Antimicrobial Surveillance Program. The isolates studied exhibited minimal inhibitory concentrations (MICs) for ciprofloxacin between < or = 0.015 microg/mL and 0.5 microg/mL. The molecular characterization of quinolone resistance was determinated by amplification of the gyrA and parC by PCR followed by sequencing of the respective amplicons. We observed that E. coli isolates exhibiting MIC, < or = 0.06 microg/mL for ciprofloxacin did not show mutations in either topoisomerase. On the other hand, all isolates with MIC between 0.12 microg/mL and 0.5 microg/mL demonstrated single mutation in the gyrA gene. The most frequent mutation occurred at position 83, where the amino acid serine was replaced by leucine. No mutations in the parC gene were observed. To preserve the potency and prevent the development of resistance, we suggest that quinolone usage should be rational, especially in the treatment of urinary tract infections, and in the prophylaxis of immunosupressed patient populations.

Gales A.C. et al. *Antimicrobial activity and spectrum of the new glycylcycline, GAR-936 tested against 1,203 recent clinical bacterial isolates.* Diagn Microbiol Infect Dis. 2000; 36(1) : 19-36.p Abstract: The in vitro activity of GAR-936, a new semisynthetic glycylcycline, was evaluated in comparison with two tetracyclines and several other antimicrobial agents. A total of 1,203 recent clinical isolates were tested by reference broth or agar dilution methods. Among the members of the family Enterobacteriaceae, GAR-936 was generally two- to four-fold more active than minocycline, and two- to 16-fold more active than tetracycline. All enteric bacilli MIC90 results were < or = 4 microg/mL; the exception being Proteus mirabilis and indole-positive Proteae (> or = 8 microg/mL). GAR-936 demonstrated excellent activity against all gram-positive cocci with 90% of the penicillin-resistant Streptococcus pneumoniae isolates inhibited at 0.03 microg/ml, while the same isolates had a MIC90 of 8 and > 8 microg/mL for minocycline and tetracycline, respectively. All Enterococcus spp., including vancomycin-resistant isolates, were inhibited at 0.25 microg/mL of GAR-936 (MIC90, 0.12 or 0.25 microg/mL). Although GAR-936 (MIC50, 0.25 microg/mL) was two-fold less active than minocycline (MIC50, 0.12 microg/mL) against oxacillin-resistant Staphylococcus aureus, all isolates were inhibited at < or = 0.25 microg/mL. GAR-936 demonstrated good activity against nonfermentative bacteria such as Acinetobacter spp. (MIC90, 2 microg/ml) and Stenotrophomonas maltophilia (MIC90, 4 microg/mL), but the compound exhibited only modest activity against Pseudomonas aeruginosa (MIC50, 8 microg/mL). Haemophilus influenzae (MIC90, 1-2 microg/mL), Moraxella catarrhalis (MIC90, 0.12 microg/mL), and various Neisseria spp. (MIC90, 0.12-0.5 microg/mL) were susceptible to GAR-936. These results indicate that GAR-936 has potent in vitro activity against a wide range of clinically important pathogenic bacteria, and that several gram-positive and -negative isolates resistant to older tetracyclines and other drug classes remain susceptible to GAR-936, the

newest glycylcycline candidate for clinical use.

Gales A.C. et al. *Activity and spectrum of 22 antimicrobial agents tested against urinary tract infection pathogens in hospitalized patients in Latin America: report from the second year of the SENTRY antimicrobial surveillance program (1998).* J Antimicrob Chemother. 2000; 45(3) : 295-303.p Abstract: The potency and spectrum of various antimicrobial agents tested against 434 bacterial isolates causing urinary tract infection (UTI) in hospitalized patients in Latin America were evaluated. The genotypes of the extended-spectrum beta-lactamase-producing and selected multi-resistant isolates were also evaluated by molecular typing techniques. Escherichia coli (60.4%) was the most common aetiological agent causing UTI, followed by Klebsiella spp. (11.2%) and Pseudomonas aeruginosa (8.3%). In contrast, Enterococcus spp. isolates caused only 2.3% of UTIs. Fewer than 50% of E. coli isolates were susceptible to broad-spectrum penicillins. The resistance rates to ciprofloxacin and the new quinolones were also high among these isolates. The molecular characterization of ciprofloxacin-resistant E. coli showed that most of them have a double mutation in the gyrA gene associated with a single mutation in the parC gene. The Klebsiella pneumoniae isolates studied demonstrated high resistance rates to beta-lactam drugs, including broad-spectrum cephalosporins. The carbapenems were the compounds with the highest susceptibility rate among these isolates (100.0% susceptible) followed by cefepime (91.7% susceptible). Meropenem, imipenem and cefepime were also the most active drugs against Enterobacter spp. Among P. aeruginosa isolates, meropenem (MIC(50), 2 mg/L) was the most active compound, followed by imipenem (MIC(50), 4 mg/L), cefepime (MIC(50), 8 mg/L) and ceftazidime (MIC(50), 16 mg/L). The results presented in this report confirm that bacterial resistance continues to be a great problem in Latin American medical institutions.

Gales A.C. et al. *Two-year assessment of the pathogen frequency and antimicrobial resistance patterns among organisms isolated from skin and soft tissue infections in Latin American hospitals: results from the SENTRY antimicrobial surveillance program, 1997-98. SENTRY Study Group.* Int J Infect Dis. 2000; 4(2) : 75-84.p Abstract: OBJECTIVES: This study was conducted to evaluate the frequency of occurrence and antimicrobial susceptibility of bacterial isolates collected from patients with skin and soft tissue infections (SSTI) in Latin American hospitals, as part of the SENTRY Antimicrobial Surveillance Program. The dissemination of multidrug-resistant methicillin-resistant Staphylococcus aureus (MDR-MRSA) among the Latin American countries also was studied. MATERIAL AND METHODS: A total of 885 bacterial isolates were analyzed. At the monitoring laboratory, antimicrobial susceptibility testing utilizing the reference broth microdilution method and confirmation of species identification were performed. Enterobacteriaceae possibly producing extended-spectrum beta-lactamases (ESBL) and MDR-MRSA isolates were genotyped by ribotyping using the RiboPrinter and by pulsed-field gel electrophoresis. RESULTS: Staphylococcus aureus (31%) was the most common etiologic agent causing SSTI, followed by Escherichia coli (13.4%) and Pseudomonas aeruginosa (11%). Thirty-one percent of S. aureus isolates were resistant to oxacillin (methicillin). The presence of ESBL phenotypes was markedly higher among the Klebsiella pneumoniae (35.5%) than E. coli isolates (10. 2%). Meropenem was the compound with the highest susceptibility rate among the Enterobacteriaceae (100%) and P. aeruginosa (95%) isolates. A great genetic similarity was observed among the MDR-MRSA in Latin America. CONCLUSION: High resistance rates to antimicrobial drugs among the most frequent bacterial pathogens were observed in 10 medical centers in Latin America. This study also demonstrated a clonal dissemination of a MDR-MRSA strain in several nations.

Gales A.C. et al. *In vitro activity of ampicillin-sulbactam against clinical multiresistant Acinetobacter baumannii isolates.* J Chemother. 1996; 8(6) : 416-9.p Abstract : We evaluated the in vitro activity of ampicillin-sulbactam in comparison with that of broad-spectrum antimicrobial agents against Acinetobacter baumannii isolates. Two hundred and twelve clinical isolates collected between January 1993 and March 1995 from two tertiary hospitals located in Sao Paulo, Brazil were tested for susceptibility by the disk diffusion method against several broad-spectrum antimicrobial agents, including imipenem, ciprofloxacin, ceftazidime, aztreonam, amikacin, and polymyxin B. All strains were susceptible to polymyxin B. The second most active compound was the combination ampicillin-sulbactam (88% susceptibility). Only 79% of the isolates were susceptible to imipenem. Ciprofloxacin was active against 60 (28%) and amikacin against 34 (16%) isolates. Ceftazidime was the most active cephalosporin; however, only 9% of the isolates were susceptible to this compound. Both aztreonam and ampicillin alone showed very poor activity against this species (1% susceptibility). The prevalence of severe infections due to A. baumannii is increasing very rapidly in the tertiary hospitals of Sao Paulo and there are very few options for the treatment of these infections. Polymyxin B is invariably in vitro active against this species; however, this compound can cause severe side effects and is not commercially available for intravenous use in Brazil and in several other countries. Our results indicated that the combination ampicillin-sulbactam may be an alternative drug for the treatment of infections due to multiresistant A. baumannii; however, further studies are necessary to evaluate the clinical role of this compound for the treatment of severe infections.

Gales A.C. et al. *A comparação das atividades antimicrobianas da cefepima e da ceftazidima em 1015 amostras bacterianas isoladas no Hospital São Paulo.* J. bras. patol. 1995; 31(2) : 55-60.p Abstract: O presente estudo tem como objetivo comparar a atividade in vitro de uma nova cefalospirina (4ª geração), a cefepima, com a da ceftadizima. Foram testadas, através da técnica de microdiluição em placa, 1015 amostras bacterianas clínicas isoladas no Hospital São Paulo/Escola de Medicina no período de junho a julho de 1992. Para as espécies de endobactérias de maneira geral, a concentração de antimicrobianos que inibiu 50 por cento das amostras (MIC 50) variou de <0,12 a u2 g/ml tanto para a cefepima quanto para a ceftazidima. Porém, a porcentagem de amostras de Enterobacter spp. sucetíveis foi superior para a cefepima (74//versus 61 por cento). Contra as amostras de Pseudomonas aeroginosa, a ceftazidima apresentou potˆncia pouco superior àquela demonstrada pela cefepima (MIC50s de ug/ml e 8 ug/ml respectivamente), com porcentagem de sensibilidade também superior (73 por cento versus 59 por cento). Das 569 amostras de bacilos gram-negativos avaliadas, 85 por cento foram suscetíveis à ceftdazidima e 80 por cento à cefepima. Entre os cocos garm-positivos, como os Staphylococcus aureus sensíveis à oxacilina, a cefepima (MIC90 4ug/ml) foi duas a quatro vezes mais ativa que a ceftazidima (MIC90 16ug/ml). Porém, como já era esperado, as amostras de estafilococos resistentes à oxacilina e as amostras de Enterococcus faecalis foram resistentes às duas drogas testadas, com MIC50>16ug/ml. Nesse estudo, a cefepima mostrou atividade e espectro contra gram-negativos semelhantes àquele das cefasporinas de 3ª geração com atividade antipseudomonas (ceftazidima). Além disso, sua atividade contra gram-positivos foi semelhante àquela demosnstrada pelas celafosporinas de 1ª geração. Apesar do avanço conquistado com as cefalosporinas de 4ª geração, o uso extensivo e/ou inapropriado dessas drogas facilitará o aparecimento de cepas resistentes e a pesquisa por substƒncias mais ativas deve continuar (AU).

Gales A.C. et al. *Comparative in vitro activity of meropenem versus other extendedàspectrum antimicrobial agents against 2.085 clinical isolates tested in 13 Brazilian Centers.* Braz. j. infect. dis. 1997; 1(6) : 294-305.p Abstract: Meropenem is a parenteral carbapenem antibacterial agent with a very broad spectrum of antibacterial activity. It is the second agent of its class to become available in Brazil. The in vitro antibacterial activity of meropenem was compared with imipenem and four other antimicrobial agents in a multicenter study. This study involved 13 clinical microbiology laboratories, 10 of which came

from 8 Brazilian states. A total of 2,085 clinical isolates consecutively collected between December 1995 and March 1996 were susceptibility tested using the Etest and following the NCCLS procedures. Meropenem inhibited more than 90 percent of isolates of Enterobacteriaceae at 0.5æg/mL, except for Citrobacter sp. (1æg/ml). Generally, meropenem was slightly more active than imipenem against Gramànegative organisms and its spectrum of antimicrobial activity was broader than those of all other drugs tested. Against Pseudomonas aeruginosa, meropenem (MIC50, 0.38æg/ml) was approximately 8àfold more active than imipenem (MIN 50,3æg/mL). Imipenem was twoàto eightàfold more active than meropenem against some Gramàpositive specees oxacillin, including Enterococcus faecalis (MIC 50 of 0.75æg/mL and 2æg/mL respectively), oxacillinàsusceptible Staphylococcus aureus (MIC 50 of 0.47æg/mL and 0.094æg/mL), oxacillinàsusceptible Staphylococcus epidermidis (MIC 50 of 0.064æg/mL and 0.5mg/mL). Against Streptococcus sp. meropenem was slightly more active than imipenem (MIC 50, 0.016æg/mL). The results of this study may be used to guide empiric therapy in Brazil and indicates that meropenem may have an important role in the treatment of infections caused by multiresistant strains of bacteria. (AU);.

Gallardo F. et al. *Campylobacter jejuni as a cause of traveler's diarrhea: clinical features and antimicrobial susceptibility.* J Travel Med. 1998; 5(1) : 23-6.p Abstract: Traveler's diarrhea is the most common health problem of international travelers. Although enterotoxigenic Escherichia coli seems to be the most frequent cause of traveler's diarrhea, many other microorganisms, such as Campylobacter jejuni, may cause this infectious disease. Campylobacter jejuni is recognized as a leading cause of enteritis in humans both in developing and in developed countries. However, a few reports on the incidence and antimicrobial resistance of Campylobacter spp. as a cause of traveler's diarrhea have been published. The limited data on the treatment of C. jejuni infections suggest that ciprofloxacin may shorten the duration of symptoms. However, treatment failure associated with the emergence of quinolone-resistant strains of C. jejuni has been documented. The purpose of this study was to determine the prevalence of C. jejuni associated with traveler's diarrhea and to analyze the geographic distribution as well as the clinical features and susceptibility to antibiotics.

Gallardo F. et al. *Increase in incidence of resistance to ampicillin, chloramphenicol and trimethoprim in clinical isolates of Salmonella serotype Typhimurium with investigation of molecular epidemiology and mechanisms of resistance.* J Med Microbiol. 1999; 48(4) : 367-74.p Abstract: Antimicrobial resistance patterns of Salmonella serotype Typhimurium isolates obtained during the period 1987-1994 were examined and the molecular epidemiology and the mechanisms of resistance to ampicillin, chloramphenicol and trimethoprim were investigated in 24 strains isolated during 1994. Resistance to ampicillin increased from 18% to 78%, to chloramphenicol from 15% to 78%, to tetracycline from 53% to 89% and to co-trimoxazole from 3% to 37%, whereas resistance to norfloxacin remained at 0%. Of Salmonella serotype Typhimurium strains isolated during 1994, all ampicillin-resistant strains had an MIC > 256 mg/L, except one strain in which the MIC was 64 mg/L. Twelve strains (52%) had a TEM-type beta-lactamase, nine (39%) a CARB-type beta-lactamase and two strains (8%) had an OXA-type beta-lactamase. Chloramphenicol acetyltransferase activity was detected in only nine (47%) of 19 chloramphenicol resistant strains, whereas all eight trimethoprim-resistant strains produced a dihydrofolate reductase type Ia enzyme. Three different epidemiological groups were defined by either low-frequency restriction analysis of chromosomal DNA and pulsed-field gel electrophoresis or repetitive extragenic palindromic-PCR. The latter technique provided an alternative, rapid and powerful genotyping method for S. Typhimurium. Although quinolones provide a good therapeutic alternative, the multiresistance of S. Typhimurium is of public health concern and it is important to continue surveillance of resistance levels and their mechanisms.

Gamarro F. et al. *Trypanosoma brucei dihydrofolate reductase-thymidylate synthase: gene isolation and expression and characterization of the enzyme.* Mol Biochem Parasitol. 1995; 72(1-2) : 11-22.p Abstract: The gene encoding the bifunctional dihydrofolate reductase (DHFR) and thymidylate synthase (TS) of Trypanosoma brucei brucei has been isolated and expressed in Escherichia coli, and the enzyme has been purified and characterized. The coding sequence of the DHFR-TS is 1581 nt, encoding a 527-amino-acid protein of 58,505 Da. The gene was expressed under control of the trc promoter in pKK233-2. The resulting expression plasmid conferred trimethoprim resistance to E. coli DH5 alpha and complemented the TS deficiency in chi 2913recA cells indicating the presence of active DHFR and TS. DHFR-TS was purified by methotrexate-Sepharose chromatography. In addition to the full-length enzyme, the purified enzyme contained 31 and 31.5-kDa forms of the enzyme that cross-reacted with anti-L. major DHFR-TS antibodies; one was truncated at the N- and C termini, and the other at only the C terminus. Despite the presence of sufficient TS for complementation, TS activity was not detectable in the crude extract or in the final purified enzyme preparation. Although the majority of the enzyme appears to be full length, it is possible that the TS domain has been degraded by one of more residues, which would inactivate the ability to synthesize thymidylate. Kinetic analysis of DHFR yielded kcat and Km values similar to those of related enzymes. The T. brucei DHFR has Ki values for antimicrobial antifolates pyrimethamine and trimethoprim which are significantly lower than the closely related T. cruzi or L. major DHFRs or than human DHFR.

Gan H. et al. *Human macrophages acquire a hyporesponsive state of tumor necrosis factor alpha production in response to successive Mycobacterium avium serovar 4 stimulation.* Infect Immun. 1995; 63(5) : 1921-6.p Abstract: Human macrophages (M phi) from most donors respond to inoculation with Mycobacterium avium serovar 4 (M. avium) by tumor necrosis factor alpha (TNF-alpha) production, which is of critical importance for proper defense against microorganisms. An initial infection of M phi with M. avium results in an incapacity to accumulate TNF-alpha mRNA after reinfection with M. avium, indicating adaptation to a hyporesponsive state by preexposure of the cells to M. avium. Adaptation to stimulation with M. avium is abrogated by the cyclooxygenase inhibitor indomethacin. In the presence of prostaglandin E2, indomethacin-exposed, M. avium-treated M phi remain unresponsive to a subsequent M. avium stimulus to increase steady-state TNF-alpha mRNA, suggesting that prostaglandin E2 is instrumental for the adaptation to an M. avium challenge. TNF-alpha mRNA accumulation induced by a second M. avium stimulus in the presence of indomethacin is blocked by the protein tyrosine kinase inhibitor herbimycin. In contrast, the initial M phi response to M. avium is inhibited by staurosporin, an inhibitor of phospholipid Ca(2+)-dependent protein kinases, indicating that the initial and the successive TNF-alpha responses to M. avium are dependent on different mechanisms.

Gandjbakhch I. et al. *[Surgery of infectious endocarditis].* Rev Prat. 1998; 48(5) : 523-7.p Abstract: Thirty to fifty percent of patients with infective endocarditis are operated on during the active phase of the disease; this percentage is higher in case of some valvular localizations (aortic), in case of early prosthetic valve endocarditis, in case of some microorganisms (Staphylococcus aureus, gram-negative, fungus, intracellular microorganism). Operative death (at 30 days) is below 10% in native valve endocarditis, close to 50% in early prosthetic valve endocarditis, and below 20% in late prosthetic valve endocarditis. When active infective disease has been healed by medical treatment alone, half the patients need surgery in the first 2 years of follow-up; the indications for surgery are the functional status, the degree of valvular leaks and other lesions, the degree of ventricular dilatation.

Gant V. et al. *Community-acquired pneumonia.* Curr Opin Pulm Med. 2000; 6(3) : 226-33.p Abstract: Community-acquired pneumonia

(CAP) remains a leading cause of morbidity and mortality worldwide and has significant financial implications for health-care systems. The epidemiology and fundamental biology of the disease has evolved, reflecting the human immunodeficiency virus pandemic, increasing world travel, and, as always, poverty. The promise held out by molecular diagnostic technology has yet to deliver in this arena, and antibiotic resistance continues to drive the quest for new antimicrobial agents. The emergence of multidrug-resistant Streptococcus pneumoniae, the microorganism most often implicated as a cause of CAP, continues to threaten treatment options. The evolution of this organism, the persistently high mortality rate associated with CAP, and increasing health-care costs have prompted the publication of guidelines by various authorities that can be used to assist in the initial assessment of the patient and then guide empirical antimicrobial therapy. It is unclear whether these guidelines will have significant impact on cost and mortality, although the trend toward a rational and evidence-based approach to antimicrobial therapy must be a goal to aspire to.

Ganzle M.G. et al. *Effect of ecological factors on the inhibitory spectrum and activity of bacteriocins.* Int J Food Microbiol. 1999; 46(3) : 207-17.p Abstract: The effect of food components and ecological factors on the activities of nisin, sakacin P and curvacin A was evaluated. Lactobacillus curvatus, Listeria innocua, Salmonella and Escherichia coli including E. coli O157:H7 were used as target organisms. Lecithin, casein, and divalent cations were antagonists of the bacteriocins at 0.1%, 0.1% and 10 mmol l(-1), respectively. A decrease in pH as well as the presence of EDTA, propyl-parabene or NaCl at concentrations of 0-1 mmol y(-1), 0-0.16 g l(-1), and 0-6% (w/w), respectively, increased the activity of all bacteriocins. These compounds as well as a pH < 5.5 rendered the Gram-negative target organisms sensitive against bacteriocins. Of practical importance is the respective effect of NaCl at concentrations > 5% which are achieved in fermentation and ripening processes, e.g. in production of fermented sausages. A characteristic response was observed for each of the bacteriocins. It is suggested that bacteriocins of lactic acid bacteria are effective against a wide range of microorganisms including E. coli O157:H7 if applied in combination with other preservative principles prevailing in foods.

Gao X.M. et al. *Homocysteine modification of HLA antigens and its immunological consequences.* Eur J Immunol. 1996; 26(7) : 1443-50.p Abstract: Homocysteine-treated cells can be specifically lysed by cytotoxic T lymphocytes (CTL) identifiable in patients with ankylosing spondylitis and reactive arthritis. Sensitization of target cells involves disulfide bonding and the interaction between homocysteine and HLA antigens occurs in a pre-Golgi compartment in the cells. Salmonella-infected B cells are also lysed by homocysteine-specific CTL, suggesting that intracellular invading microorganisms may provide homocysteine which would gain access to the newly synthesized intracellular HLA molecules and modify them inside the cells. Two different mechanisms for homocysteine modification of HLA antigens are proposed: homocysteine could bind directly to the unpaired cysteine residues in HLA antigens, or it could bind indirectly to HLA antigens through cysteine-containing peptides bound to them. Thus, HLA antigens containing unpaired cysteine residues (e.g. HLA B27) could be modified by homocysteine directly or indirectly, while HLA antigens without unpaired cysteine residues (e.g. HLA A68) could only be modified indirectly. The results are discussed in relation to the potential involvement of homocysteine-specific CTL in ankylosing spondylitis and reactive arthritis, both of which are related to bacterial infections, associated with HLA B27, and considered to be autoimmune diseases.

Garau J. *Clinical strategies for serious infection: a European perspective.* Diagn Microbiol Infect Dis. 1998; 31(2) : 397-404.p Abstract: Antimicrobial resistance in nosocomial isolates is of increasing concern to the clinician, particularly in intensive care units. With more expensive drugs and prolonged periods of hospitalization required, resistance can result in increased healthcare costs. For the patient, infection with multiply resistant strains of bacteria is associated with high mortality rates. This review focuses on the prevalence of nosocomial infections throughout Europe, with particular emphasis on the prevalence of resistance to common antimicrobial agents. The beta-lactams are the most frequently prescribed antimicrobials, and the growing importance of extended spectrum beta-lactamases and the hyperproduction of chromosomal beta-lactamase by stably derepressed mutants in the development of microbial resistance are discussed. Given that the most common reason for modification of an initial empiric antibiotic treatment is the isolation of microorganisms not susceptible to the initial choice of treatment, the results from two European multicenter trials comparing the efficacy of the carbapenems, meropenem, and imipenem/cilastatin, for the treatment of serious nosocomial infections, are appraised. In light of these results, it can be concluded that the carbapenems are effective as initial empiric monotherapy for nosocomial infections because of their broad spectrum of efficacy and stability to beta-lactamases.

Garau J. et al. *Emergence and dissemination of quinolone-resistant Escherichia coli in the community.* Antimicrob Agents Chemother. 1999; 43(11) : 2736-41.p Abstract: We studied the evolution of resistance to quinolones in Escherichia coli from 1992 to 1997 in Barcelona, Spain. An increasing proportion of quinolone-resistant E. coli (QREC) infections was observed. QREC strains were more common in patients with nosocomial infections but also increased in patients with community-acquired infections (9% in 1992 to 17% in 1996). Seventy (12%) of 572 episodes of E. coli bacteremia were due to QREC. Factors significantly associated with QREC bacteremia were the presence of underlying disease, recent exposure to antibiotics, and bacteremia of unknown origin. In the multivariate analysis, only prior exposure to antimicrobial agents ($P < 0.001$; odds ratio [OR] = 2), specifically, to quinolones ($P < 0.001$; OR = 14), and the presence of a urinary catheter ($P < 0.001$; OR = 2) were significantly associated with QREC bacteremia. Among 16 QREC isolates from cultures of blood of community origin selected at random, 13 different pulsed-field gel electrophoresis patterns were recognized, showing the genetic diversity of these isolates and in turn indicating the independent emergence of QREC in the community. The prevalence of QREC in the feces of healthy people was unexpectedly high (24% in adults and 26% in children). A survey of the prevalence of QREC of avian and porcine origin revealed a very high proportion of QREC in animal feces (up to 90% of chickens harbored QREC). The high prevalence of QREC in the stools of healthy humans in our area could be linked to the high prevalence of resistant isolates in poultry and pork.

Garbutt J.M. et al. *Enteric carriage of vancomycin-resistant Enterococcus faecium in patients tested for Clostridium difficile.* Infect Control Hosp Epidemiol. 1999; 20(10) : 664-70.p Abstract: OBJECTIVE: To identify independent risk factors for enteric carriage of vancomycin-resistant Enterococcus faecium (VREF) in hospitalized patients tested for Clostridium difficile toxin. DESIGN: Retrospective case-cohort study. SETTING: Tertiary-care teaching hospital. PATIENTS: Convenience sample of 215 adult inpatients who had stool tested for C difficile between January 29 and February 25, 1996. RESULTS: 41 (19%) of 215 patients had enteric carriage of VREE Five independent risk factors for enteric VREF were identified: history of prior C difficile (odds ratio [OR], 15.21; 95% confidence interval [CI95], 3.30-70.10; P <.001), parenteral treatment with vancomycin for > or = 5 days (OR, 4.06; CI95, 1.54-10.73; P =.005), treatment with antimicrobials effective against gram-negative organisms (OR, 3.44; CI95, 1.20-9.87; P =.021), admission from another institution (OR, 2.95; CI95, 1.21-7.18; P =.017), and age > 60 years (OR 2.57; CI95, 1.13-5.82; P =.024). These risk factors for enteric VREF were independent of the patient's current C difficile status. CONCLUSIONS: Antimicrobial exposures are the most important modifiable independent risk factors for enteric carriage of VREF in hospitalized patients tested for C difficile.

Garcia-Arata M.I. et al. *Emergence of resistant isolates of Acinetobacter calcoaceticus- A. baumannii complex in a Spanish hospital over a five-year period*. Eur J Clin Microbiol Infect Dis. 1996; 15(6) : 512-5.p Abstract: Acinetobacter calcoaceticus-A. baumannii complex species have emerged as a relevant cause of nosocomial infection and colonization over the past 20 years, mainly in intensive care units. The aim of this study was to investigate the in vitro activity of 14 antimicrobial agents against 177 clinical isolates from patients admitted to a Spanish teaching hospital over a five-year period. Susceptibility rates or 99%, 99%, and 74% were obtained for imipenem, meropenem, ampicillin plus sulbactam, and amikacin, respectively. Increases in resistance were detected mainly for ticarcillin, piperacillin plus tazobactam, ceftazidime, amikacin, and ofloxacin. These results indicate that treatment of nosocomial infections due to Acinetobacter calcoaceticus-A. baumannii complex strains may be difficult.

Garcia-de-Lomas J. et al. *Antimicrobial susceptibility of Streptococcus pneumoniae isolated from pediatric carriers in Spain*. Eur J Clin Microbiol Infect Dis. 1997; 16(1) : 11-3.p Abstract: The in vitro activity of several beta-lactam agents, macrolides, and cotrimoxazole was investigated against 53 Streptococcus pneumoniae isolates recovered from healthy children. The rates of resistance to penicillin or amoxicillin, cefaclor, and cefuroxime were 30%, 51%, and 37%, respectively. No cefotaxime-resistant isolates were found. Rates of resistance to erythromycin, clarithromycin, and cotrimoxazole were 22.6%, 13.2%, and 83%, respectively. Pneumococci with divergent antimicrobial susceptibility profiles (susceptible or moderately resistant vs. resistant isolates) coexisted in 32% samples, with divergencies more often involving beta-lactam agents and/or macrolides. In five of these samples, isolates belonged to different serotypes.

Garcia-de-Lomas J. et al. *New directions in diagnostics.* Pediatr Infect Dis J. 1997; 16(3 Suppl) : S43-8.p Abstract: BACKGROUND: Infectious diseases are still a significant clinical problem in children, and accurate identification of the causal pathogen plays an important role in clinical management. The availability of an etiologic diagnosis enables the clinician to make appropriate therapeutic decisions and to avoid the indiscriminate use of antibiotics. The availability of a microbiologic diagnosis and the susceptibility profile of the pathogen allows the prompt initiation of suitable antibiotic treatment. However, the usefulness of current culture and identification methods is limited by the time needed and by their sensitivity and specificity. Also some microorganisms are difficult or impossible to grow in the laboratory. OBJECTIVES: To review the newer and more rapid diagnostic techniques that are becoming available and consider their application in the diagnosis of specific infections. DISCUSSION: Immunoassays have many advantages and it is hoped that new optical immunoassays will overcome the problems of poor sensitivity. Nucleic acid amplification techniques have enormous potential in the diagnosis of infectious diseases because of their high specificity and sensitivity and the speed with which the results can be obtained. However, there are still a number of difficulties that must be overcome before these methods can be widely adopted for routine testing. These techniques may be particularly relevant for the rapid diagnosis of streptococcal pharyngitis, where throat culture is slow and beset by a number of factors which reduce its accuracy. Polymerase chain reaction methods have been developed for many respiratory pathogens, including Mycoplasma pneumoniae, Chlamydia pneumoniae and Mycobacterium tuberculosis, and are likely to play an increasingly important part in diagnosis. In bacterial meningitis culture is still the gold standard and molecular techniques have not yet been developed to the point where they can be used in routine diagnosis. Nucleic acid techniques are likely to be very valuable in the diagnosis of streptococcal pharyngitis and viral central nervous system infections in the near future.

Garcia de Viedma D. et al. *Heterogeneous antimicrobial resistance patterns in polyclonal populations of coagulase-negative staphylococci isolated from catheters.* J Clin Microbiol. 2000; 38(4) : 1359-63.p Abstract: Most cases of nosocomial bacteremia are catheter related, and coagulase-negative staphylococci (CoNS) are the microorganisms most frequently associated with these infections. Subtle morphological differences are frequently found among CoNS colonies cultured from infected catheters. The aim of this study was to analyze the significance of the morphological heterogeneity observed in these CoNS populations. With this purpose in mind, the clonal composition of the CoNS populations obtained from a selection of nine catheters was analyzed by two different molecular techniques, arbitrarily primed-PCR and DNA macrorestriction analysis by pulsed-field gel electrophoresis. Twenty CoNS morphotypes were included for analysis, and four single colonies representative of each morphotype were selected. Morphological differences between colonies were found to correlate in all cases with differences at the molecular level. Unique fingerprints were also obtained for some isolates which were indistinguishable from other representatives of the same morphotypes. Differences in the molecular patterns among the isolates were associated in most of the cases with differences in the antimicrobial susceptibility patterns. The frequent isolation of polyclonal CoNS populations from catheters, with heterogeneous antimicrobial susceptibility patterns, has relevant epidemiologic and therapeutic implications in the context of catheter-related infections.

Garcia J. *[Epidemiology of acute bronchopulmonary infections in children].* Rev Prat. 1996; 46(17) : 2056-61.p Abstract: In infants and young children acute lower respiratory infection is the most common cause of morbidity and death especially in developing countries. Factors that contribute to the increased susceptibility to respiratory pathogens include young age, season, sex, indoor pollution, large family size, malnutrition, low immunocompetence, socioeconomic disadvantage. The epidemiology of acute respiratory infections in childhood seems similar worldwide. In all countries, respiratory syncytial virus, parainfluenzae virus 1 and 3 influenzae A and B viruses and adenovirus are reported to be the main causes of acute respiratory infections. Six microorganisms are responsible of 90% of documented acute bacterial pulmonary infections, Streptococcus pneumoniae, Mycoplasma pneumoniae, Chlamydia pneumoniae, Chlamydia trachomatis, Haemophilus influenzae, Staphylococcus. Mixed viral and bacterial infections occur frequently (30%). The role of respiratory viruses in predisposing to colonization and invasion of bacterial organisms has often been suggested. In recent years acquired resistance against antibiotic for H. influenzae and S. pneumoniae has emerged.

Garcia-Prats J.A. et al. *Rapid detection of microorganisms in blood cultures of newborn infants utilizing an automated blood culture system*. Pediatrics. 2000; 105(3 Pt 1) : 523-7.p Abstract: BACKGROUND: Neonatal sepsis is a low incidence, high-risk disease with many sepsis workups performed to detect a single case. Seventy-two hours of antibiotic therapy have been traditionally recommended pending negative culture results. Improved culture media and new technology integrated into blood culture systems could shorten incubation time required to detect positive culture results. This would then change the length of antibiotic therapy in the management of the newborn infant with suspected sepsis. In addition, previous data supporting the 72-hour recommendation were retrospectively acquired, utilized nonautomated systems, and reported in an era with a different population of microorganisms cultured in special care nurseries. OBJECTIVE: Evaluate the time of incubation to detect positive blood cultures from newborn infants with suspected sepsis using a computer-assisted, automated blood culture system, ESP (Trek Diagnostic Systems, Inc, Westlake, OH). DESIGN: Prospective, observational study. PATIENTS AND SETTING: All positive blood culture results that were obtained from term and preterm newborn infants born from November 1993 through June 1997 at a publicly funded hospital with over 6000 live births per year. METHODS: As positive blood culture results were identified, data were prospectively obtained from the patient's medical record. The computer algorithm in the automated blood culture system determined the time

to positivity. Time to positivity was determined for blood cultures obtained before the initiation antimicrobial therapy and compared with those cultures obtained after beginning therapy. Time to positivity was also evaluated for clinically important Gram-positive and Gram-negative bacteria and yeast. RESULTS: Four hundred fifty-five positive blood culture results were obtained from 222 patients. Gram-positive organisms accounted for 80% (366/455) of the positive culture results, Gram-negative organisms accounted for 11% (48/455), and yeast for 9% (41/455). Virtually all cultures growing clinically significant Gram-positive and Gram-negative organisms were positive by 24 to 36 hours of incubation. Cultures growing Staphylococcus epidermidis were virtually all positive after 36 to 48 hours of incubation. Of cultures growing yeast, 88% (36/41) were positive by 48 hours of incubation. There was no difference in time to positivity in pretherapy or posttherapy obtained positive blood cultures. Prenatally administered antibiotics did not affect time to positivity in positive cultures drawn on the first day of life. In a selected group of microorganisms that are the frequent cause of bacteremia in term infants, 97% and 99% of cultures were positive by 24 to 36 hours of incubation when only pretherapy cultures are evaluated. CONCLUSIONS: The ESP blood culture system identified 77%, 89% and 94% of all microorganisms at 24, 36, and 48 hours of incubation in aerobic cultures obtained from both term and preterm infants. Introduction of antimicrobial therapy did not affect time to positivity. Reducing duration of antibiotic therapy to 24 to 36 hours should be considered in term, asymptomatic newborn infants undergoing evaluation for suspected sepsis for maternal indications. Confirmation of similar rapidity of detection using other blood culture systems should be undertaken.

García Ramos E. et al. *Caracterización y resistencia de las cepas de H. influenzae y H. parainfluenzae aisladas de la nasofaringe de portadores.* Rev. Inst. Nac. Enfermedades Respir. 1998; 11(1) : 17-24.p Abstract: Introducción: H. influenzae (Hi) y H. parainfluenzae (Hp) forma parte de la flora normal de las vías respiratorias del hombre, el porcentaje de portadores de Hi es muy variable (10-60 por ciento) y depende de la metodología empleada, del grupo etario y del tamaño del universo estudiado. Los niños menores de cinco años están colonizados por esta especie, entre el 10 y 50 por ciento. El serotipo b se asocia a diferentes síndromes y en nuestro país causa del 20 al 45 por ciento de las meningeoencefalitis bacterianas y en las infecciones respiratorias producen morbimortalidad infantil elevada. H. parinfluenzae se ha encontrado asociada a meningitis, artritis, epiglotitis y neumonía, esta bacteria se puede confundir con Hi, la exactitud de estos padecimientos se desconoce. Objetivo. Carat H. influenzae y H. parainfluenzae, aisladas de niños menores de cinco años, mediante pruebas bioquímicas, serológicas, susceptibilidad a los antimicrobianos y producción de beta lactamasa. Material y métodos. Se tomaron 770 exudados nasofaríngeos de niños menores de cinco años y se sembraron en gelosa chocolate bacitracina. La diferenciación de biotipos se realizó por pruebas bioquímicas. Para la tipificación serológica se usó el método de coaglutinación en placa (Phadebact). La beta lactamasa se hizo por tres métodos y la susceptibilidad a los antibióticos por el método de difunsión en disco (Kirby-Bauer modificado). Resultado y discusión. La frecuencia de portadores de H. influenzae fue de 23.7 por ciento y de H. influenzae 16.5 por ciento. En las 159 cepas aisladas, 93 H.influenzae y 66 H parainfluenzae, los biotipos más frecuentes en Hi fueron el V (22.26 por ciento) y el II (20.4 por ciento); los serotipos; Hi tipo b: 30.1 por ciento, del tipo a: 8.6 por ciento, los tipos c-f: 18.2 por ciento y no tipificables: 43.0 por ciento; la beta lactamasa la produjeron Hi en el 27.0 por ciento y Hp en el 18.0 por ciento. Guiscafré y col, reportaron 14.0 por ciento de resistencia a la penicilina en cepas aislada de niños, en el presente encontramos 16.0 por ciento; al clorafenicol sólo el 5.0 por ciento de Hi fue resistente, sin embargo Campos y col. informaron de un 52.0 por ciento en España. Sensibles a la ticarcilina/ac. clavulánico, el 100.0 por ciento; a las cefalosporinas de segunda y tercera generación el 97.0 por ciento y 95.0 por ciento respectivamente.

Garcia-Rodriguez J.A. et al. *In vitro activity of fosfomycin trometamol against pathogens from urinary tract infections: a Spanish multicenter study.* J Chemother. 1997; 9(6) : 394-402.p Abstract: The in-vitro susceptibilities of a total of 1371 urinary tract pathogens to fosfomycin trometamol were determined. According to the NCCLS breakpoints, Enterobacteriaceae and gram-positive microorganisms were, in general, very sensitive to this antimicrobial. More than 90.0% of the Escherichia coli and Citrobacter spp. and more than 70.0% of the Klebsiella pneumoniae, K. oxytoca, Enterobacter spp., Proteus mirabilis, Staphylococcus aureus, coagulase-negative staphylococci and Enterococcus spp. strains tested were susceptible to fosfomycin trometamol. However, Pseudomonas aeruginosa and Acinetobacter spp. strains were more resistant. In general, recent clinical isolates from urinary tract infections (UTIs) in both community and hospital were also very sensitive (> 80.0%) to fosfomycin, its activity being higher than that of the rest of the antimicrobials commonly used for therapy of uncomplicated UTIs. More than 75.0% of the most frequently isolated pathogens from UTIs, except for P. aeruginosa (31.8%) and Acinetobacter spp. (11.1%), were susceptible to fosfomycin trometamol. The results obtained in this study, together with the infrequency of side effects and its pharmacokinetic properties, indicate that fosfomycin trometamol may be a useful alternative for single-dose therapy of uncomplicated UTIs.

Garcia Sanchez J.E. et al. *Aztreonam/clavulanic acid in the treatment of serious infections caused by Stenotrophomonas maltophilia in neutropenic patients: case reports.* J Chemother. 1997; 9(3) : 238-40.p Abstract: Two seriously neutropenic patients (a 23-year-old man with a promyelocytic acute myeloid leukemia [AML-M3] and a 77-year old male with an immature acute myeloid leukemia [AML-M1] diagnosis) with severe infections caused by Stenotrophomonas maltophilia were treated with aztreonam/clavulanic acid (2:1) combination. In the first patient the infection was caused by a multiresistant strain and in the second, by a strain with poor response to trimethoprim-sulfamethoxazole and other antimicrobial agents. After treatment with aztreonam/clavulanic acid both patients evolved favorably.

Garg P. et al. *Expanding multiple antibiotic resistance among clinical strains of Vibrio cholerae isolated from 1992-7 in Calcutta, India.* Epidemiol Infect. 2000; 124(3) : 393-9.p Abstract: Antimicrobial susceptibilities of Vibrio cholerae strains isolated from cholera patients admitted to the Infectious Diseases Hospital, Calcutta, India for 6 years were analysed to determine the changing trends; 840 V. cholerae strains isolated in 1992-1997 were included in this study. Among V. cholerae serogoup O1 and O139, ampicillin resistance increased from 1992 (35 and 70%, respectively) to 1997 (both serogroups 100%). Resistance to furazolidone and streptomycin was constantly high among V. cholerae O1 strains with gradual increase in resistance to other drugs such as ciprofloxacin, co-trimoxazole, neomycin and nalidixic acid. V. cholerae O139 strains exhibited susceptibilities to furazolidone and streptomycin comparable with those of O1 strains. However, after initial increase in resistance to chloramphenicol and co-trimoxazole, all the V. cholerae O139 strains became susceptible to these two drugs from 1995 onwards. Both V. cholerae O1 and O139 remained largely susceptible to gentamicin and tetracycline. V. cholerae non-O1, non-O139 strains, in contrast, exhibited high levels of resistance to virtually every class of antimicrobial agents tested in this study especially from 1995. Kruskal-Wallis one-way analysis showed that V. cholerae O1 Ogawa serogroup exhibited significant yearly increase in resistance to nine antibiotics followed by non-O1 non-O139 and O139 strains to six antibiotics and two antibiotics respectively. Interesting observation encountered in this study was the dissipation of some of the resistant patterns commonly found among V. cholerae non-O1 non-O139 or O1 serogroups to the O139 serogroup and vice versa during the succeeding years.

Garg P. et al. *Treatment outcome of Moraxella keratitis: our experience with 18 cases—a retrospective review.* Cornea. 1999; 18(2) : 176-81.p

Abstract: PURPOSE: To analyze the clinical presentation, predisposing risk factors, in vitro antimicrobial susceptibility, and especially the outcome of therapy of Moraxella keratitis. METHODS: Retrospective review of 18 culture-proven cases of Morarella keratitis. RESULTS: Morarella keratitis was associated with Hansen's disease, uncontrolled diabetes mellitus, herpes zoster ophthalmicus, and chickenpox of the recent past and severe protein energy malnutrition. Other associated ocular conditions included lagophthalmos, blepharitis, steroid therapy, corneal degeneration, and scleritis. In four patients, no systemic or ocular predisposing factors could be identified. Three patients presented with an indolent peripheral, anterior stromal infiltrate while the remaining patients showed a central or paracentral ulceration with or without hypopyon. Moraxella species was the only pathogen isolated in 11 cases, whereas mixed infection was seen in seven cases. All isolates were sensitive to ciprofloxacin. Eight of 18 strains of Moraxella were resistant to cefazolin. All 14 eyes for which the follow-up data were available responded to medical treatment alone. CONCLUSIONS: Although considered to be associated with poor outcome, our experience suggests that a favorable outcome can be expected in Moraxella keratitis. Cefazolin resistance (as seen in our series) may pose a problem and, hence, monitoring of antimicrobial susceptibility would be beneficial. In view of cefazolin resistance, ciprofloxacin monotherapy appears to be an effective method in the medical management of these cases.

Garg P. et al. *Ciprofloxacin-resistant Pseudomonas keratitis.* Ophthalmology. 1999; 106(7) : 1319-23.p Abstract: OBJECTIVE: To determine ciprofloxacin resistance of corneal isolates of Pseudomonas and to review the clinical response to topical therapy in cases of ciprofloxacin-resistant Pseudomonas keratitis, where medical therapy was begun with 0.3% ciprofloxacin. DESIGN: Retrospective noncomparative case series. PARTICIPANTS: Medical and microbiology records of 141 culture-proven cases of Pseudomonas keratitis, examined between January 1991 and June 1998, were reviewed retrospectively. METHODS: All isolates of the Pseudomonas species from corneal scrapings were tested for their susceptibility to routinely used antibiotics by the Kirby-Bauer disc-diffusion method. The minimum inhibitory concentration of ciprofloxacin was determined by the agar-dilution method for most of the isolates found resistant to ciprofloxacin. Clinical response to initial therapy with 0.3% ciprofloxacin was determined in cases of keratitis caused by ciprofloxacin-resistant Pseudomonas. MAIN OUTCOME MEASURES: Resistance of Pseudomonas isolates to ciprofloxacin and clinical response to initial therapy with 0.3% ciprofloxacin. RESULTS: By use of the in vitro antimicrobial susceptibility test, 22 cases of keratitis caused by ciprofloxacin-resistant Pseudomonas were identified. The minimum inhibitory concentration of ciprofloxacin for these isolates was > or =16 microg/ml (mean = 43 microg/ml). Gentamicin resistance occurred in 63.6% of isolates also, but 90.9% ciprofloxacin-resistant isolates were susceptible to amikacin. Fifteen (76.7%) of 19 patients who initially received ciprofloxacin did not show any clinical improvement even after 3 days of intensive medical therapy. The infiltrate resolved in all 8 cases where the antibiotic therapy was modified on the basis of susceptibility test. Four eyes were subjected to penetrating keratoplasty, and three were eviscerated following failure of treatment with ciprofloxacin. CONCLUSION: True resistance to ciprofloxacin is emerging in ophthalmology even among Pseudomonas isolates; therefore, the empiric treatment of infectious keratitis with ciprofloxacin monotherapy must be critically reviewed at this time.

Garrett D.O. et al. *The emergence of decreased susceptibility to vancomycin in Staphylococcus epidermidis.* Infect Control Hosp Epidemiol. 1999; 20(3) : 167-70.p Abstract: BACKGROUND: Coagulase-negative staphylococci (CNS) are the major cause of nosocomial bloodstream infection. Emergence of vancomycin resistance among CNS is a serious public health concern, because CNS usually are multidrug-resistant, and glycopeptide antibiotics, among which only vancomycin is available in the United States, are the only remaining effective therapy. In this report, we describe the first bloodstream infection in the United States associated with a Staphylococcus epidermidis strain with decreased susceptibility to vancomycin. METHODS: We reviewed the hospital's microbiology records for all CNS strains, reviewed the patient's medical and laboratory records, and obtained all available CNS isolates with decreased susceptibility to vancomycin. Blood cultures were processed and CNS isolates identified by using standard methods; antimicrobial susceptibility was determined by using minimum inhibitory concentration (MIC) and disk-diffusion methods. Nares cultures were obtained from exposed healthcare workers (HCWs) to identify possible colonization by CNS with decreased susceptibility to vancomycin. RESULTS: The bloodstream infection by an S. epidermidis strain with decreased susceptibility to vancomycin occurred in a 49-year-old woman with carcinoma. She had two blood cultures positive for CNS; both isolates were S. epidermidis. Although susceptible to vancomycin by the disk-diffusion method (16-17 mm), the isolates were intermediate by MIC (8-6 microg/mL). The patient had received an extended course of vancomycin therapy; she died of her underlying disease. No HCW was colonized by CNS with decreased susceptibility to vancomycin. CONCLUSIONS: This is the first report in the United States of bloodstream infection due to S. epidermidis with decreased susceptibility to vancomycin. Contact precautions likely played a role in preventing nosocomial transmission of this strain, and disk-diffusion methods may be inadequate to detect CNS with decreased susceptibility to vancomycin.

Garrison M.W. et al. *Stenotrophomonas maltophilia: emergence of multidrug-resistant strains during therapy and in an in vitro pharmacodynamic chamber model.* Antimicrob Agents Chemother. 1996; 40(12) : 2859-64.p Abstract: Emergence of Stenotrophomonas maltophilia as a nosocomial pathogen is becoming increasingly apparent. Pleiotropic resistance characterizes S. maltophilia. Furthermore, a slow growth rate and an increased mutation rate generate discordance between in vitro susceptibility testing and clinical outcome. Despite original susceptibility, drug-resistant strains of S. maltophilia are often recovered from patients receiving beta-lactams, quinolones, or aminoglycosides. Given the disparity among various in vitro susceptibility methods, this study incorporated a unique pharmacodynamic model to more accurately characterize the bacterial time-kill curves and mutation rates of four clinical isolates of S. maltophilia following exposure to simulated multidose regimens of ceftazidime, ciprofloxacin, gentamicin, and ticarcillin-clavulanate. Time-kill data demonstrated regrowth of S. maltophilia with all four agents. With the exception of ticarcillin-clavulanate, viable bacterial counts at the end of 24 h exceeded the starting inoculum. Ciprofloxacin only reduced bacterial counts by less than 1.0 log prior to rapid bacterial regrowth. Resistant mutant strains, identical to their parent strain by pulsed-field gel electrophoresis, were observed following exposure to each class of antibiotic. Mutant strains also had distinct susceptibility patterns. These data are consistent with previous reports which suggest that S. maltophilia, despite susceptibility data that imply that the organism is sensitive, develops multiple forms of resistance quickly and against several classes of antimicrobial agents. Standard in vitro susceptibility methods are not completely reliable for detecting resistant S. maltophilia strains; and therefore, interpretation of these results should be done with caution. In vivo studies are needed to determine optimal therapy against S. maltophilia infections.

Garrouste-Orgeas M. et al. *Oropharyngeal or gastric colonization and nosocomial pneumonia in adult intensive care unit patients. A prospective study based on genomic DNA analysis.* Am J Respir Crit Care Med. 1997; 156(5) : 1647-55.p Abstract: Colonization of the digestive tract has been supposed to be the source of many hospital-acquired infections, especially nosocomial pneumonia. To assess the relationship between oropharyngeal and gastric colonization and subsequent occurrence of nosocomial pneumonia, we prospectively studied 86 ventilated, intensive care unit (ICU) patients. Oropharyngeal or gas-

tric colonizations were detected and quantified on admission and twice weekly during ICU stay. When nosocomial pneumonia was suspected on clinical grounds (new chest X-ray infiltrate and purulent tracheal secretions), diagnosis was assessed on fiberoptic bronchoscopy with quantitative cultures of a protected specimen brush sampling and/or a plugged telescoping catheter sampling yielding > or = 10(3) cfu/ml of at least one microorganism. Bacterial strains responsible for colonization and infection (Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacteriaceae, and Staphylococcus aureus) were compared using pulsed-field electrophoresis. A total of 31 cases (36%) of pneumonia were diagnosed. Oropharyngeal colonization, detected either on admission or from subsequent samples, was a predominant factor of nosocomial pneumonia as compared with gastric colonization. For instance, oropharyngeal colonization with A. baumannii yielded a 7.45-fold estimated increased risk of pneumonia as compared with patients not yet or not identically colonized (p = 0.0004). DNA genomic analysis demonstrated that an identical strain was isolated from oropharyngeal or gastric samples and bronchial samples in all but three cases of pneumonia, due to S. aureus. These findings provide better knowledge of the pathophysiology of nosocomial pneumonia in mechanically ventilated patients.

Garvin K.L. et al. *Emerging antibiotic-resistant bacteria. Their treatment in total joint arthroplasty.* Clin Orthop. 1999; (369) : 110-23.p Abstract: Successful treatment of an infected total joint arthroplasty can be achieved in approximately 90% of cases. This outcome may be jeopardized by the emergence of antibiotic resistance in bacteria common to these infections. Staphylococci are the most frequently isolated bacteria in total joint infections, and the prevalence of antibiotic resistance in these organisms among all nosocomial and community-acquired infections has been increasing. As many as 46.7% of Staphylococcus aureus strains and 85.7% of coagulase-negative staphylococci strains are methicillin-resistant. Enterococci also are commonly isolated from infected total joint arthroplasties. The prevalence of vancomycin-resistant enterococci among all enterococci strains is estimated at 23%. As the prevalence of these resistant bacteria continues to increase among all infections, it is anticipated that they will be encountered more regularly in total joint infections. Knowledge of the mechanisms of resistance of these bacteria and currently available and newly developed antimicrobials is key to preventing the expansion of antimicrobial resistance and ensuring the future successful treatment of total joint infections.

Garvin K.L. et al. *Emerging multiresistant strains: recommended precautions in the emergency room and surgical setting.* Instr Course Lect. 2000; 49 : 605-14.p Abstract: The current success in treatment of surgical site infections may be jeopardized by the continued emergence of antibiotic resistance in bacteria common to these infections. The effectiveness of vancomycin against methicillin-resistant staphylococci may decrease as more cases of VISA emerge. No currently available antimicrobial is consistently effective against certain strains of VRE and the potential emergence of VRSA. Orthopaedic surgeons soon may be in the undesirable position of having to eradicate organisms resistant to all available antibiotics. Several new antibiotics show promising activity and may be useful against these multidrug-resistant bacteria. However, as the history of bacterial resistance has taught us, it likely only will be a matter of time until these organisms adapt mechanisms of resistance to these new drugs. The key then lies, as it always has, in preventive measures. Surgeons, and all physicians, must adhere to the precautionary guidelines recently set forth by the CDC and HICPAC. Chief among these guidelines is the elimination of inappropriate antibiotic usage, especially inappropriate vancomycin use.

Gastmeier P. et al. *An analysis of two prevalence surveys of nosocomial infection in German intensive care units.* J Hosp Infect. 1997; 35(2) : 97-105.p Abstract: In 1995, the results of two extensive prevalence studies on hospital-acquired infections were published. Both studies included a prevalence component for German intensive care units (ICUs), but provided very different infection rates. A comparison of the methods used revealed that the data from the ICUs included in the German section of EPIC (European Prevalence of Infection in Intensive Care), reflected the situation in the ICUs of large hospitals. The situation in ICUs with fewer than 600 beds was quite different, and led to the lower overall rate of infection as seen in the NIDEP (Nosocomial Infections in Germany-Surveillance and Prevention) study. Additionally, the NIDEP data permitted the calculation of device-associated, device-day, infection rates for urinary tract infections, pneumonia and bacteraemia. The differences between the ICUs in the two hospital groups were mainly due to a lower use of patient devices with regard to urinary catheters, central venous lines and respiratory ventilators.

Gastmeier P. et al. *Repeated prevalence investigations on nosocomial infections for continuous surveillance.* J Hosp Infect. 2000; 45(1) : 47-53.p Abstract: In order to obtain an overview for the planning of further infection control activities, nine repeated prevalence studies were performed at monthly intervals. These occurred in the surgical units of eight medium-sized German hospitals. A total of 4984 surgical patients were investigated, the number of patients observed in each hospital varied from 365 to 913 patients, an average of 69.2 patients per prevalence study per hospital. A total of 212 nosocomial infections were found, the majority being surgical site (43.9%) and urinary tract infection (33.0%). The overall prevalence rate was 4.0%. More than four repeated investigations had only a minor influence on the 95% confidence intervals, and a follow-up of late microbiological reports increased the prevalence rate by only 7.5%. However, it was very useful to record the presence of urinary catheters on the prevalence day and also the preceding days; for instance, a device-associated prevalence of 7.8 urinary tract infections per 100 patients with urinary catheters was found on the day of investigation. In order to evaluate the situation in one's own surgical department by prevalence studies and for reasons of cost-effectiveness, the workload can be limited to four repeated studies in most hospitals. A further follow-up of later microbiological reports is not recommended, and it seems useful to concentrate on patients with indwelling devices.

Gaszewska-Mastalarz A. et al. *[Diagnostic molecular microbiology—identification of Staphylococcus epidermidis].* Postepy Hig Med Dosw. 1998; 52(1) : 19-34.p Abstract: The species Staphylococcus epidermidis is the predominant coagulase-negative staphylococci (CNS) isolated from clinical sources. S. epidermidis is now recognized as an important nosocomial pathogen. Identification of CNS is often performed using diagnostic kits based on biochemical or immunological reactions. However, these kits are often unreliable for the identification of CNS species including S. epidermidis. Currently, ribosomal RNA (rRNA) analyses are the most powerful methods for determining phylogenetic relationships among microorganisms and also for identification of species. Several aspects of construction of ribosomal probes for identification of CNS species are presented and discussed. Additionally, the application of restriction fragment length polymorphisms (RFLP) of rRNA genes for differentiation of clinical isolates of S. epidermidis is shown.

Gatell J.M. et al. *Severe pulmonary infections in AIDS patients.* Semin Respir Infect. 1996; 11(2) : 119-28.p Abstract: Pulmonary infections are a very common complication in acquired immune deficiency syndrome (AIDS) patients. These infections may be severe enough to initiate the admission of these patients to intensive care units (ICU). Pneumocystis carinii pneumonia (PCP) is the most frequent cause of ICU admission because of acute respiratory failure. Mortality of ICU-admitted patients with this infection has changed with time. Initial reports confirmed a high mortality (80% to 90%). After 1985, the mortality rate decreased (50%). Factors such as the use of corticosteroids, better patient care, and a better knowledge of the disease probably explain this change. In recent years (1990 to 1995), mor-

tality has worsened again, perhaps, because ICU facilities were offered more liberally to patients failing aggressive conventional treatment, including adjuvant therapy with corticosteroids. However, for those patients able to be discharged, the prognosis is not worse than expected according to the stage of their human immunodeficiency virus-1 (HIV-1) infection and immunologic status. Consequently, at least a limited period of ICU care and some respiratory support (either continuous positive airway pressure or mechanical ventilation) should be considered and offered to all HIV-1-infected patients with PCP and respiratory failure. Cytomegalovirus may be another cause of severe pulmonary infection in AIDS patients. This infection is difficult to diagnose; hence, it should be suspected when patients with PCP do not progress appropriately, or when no responsible pulmonary pathogen is found. When associated with PCP, mortality is very high. Disseminated tuberculosis is another potential cause of severe respiratory failure and respiratory secretions should be routinely examined for acid-fast bacilli in AIDS patients with pulmonary infiltrates. Finally, bacterial pneumonia (Streptococcus pneumoniae, Neisseria catarrhalis, Haemophilus influenzae, Staphylococcus aureus, and Pseudomonas aeruginosa) may also be the etiological agents of severe acute respiratory failure. Empiric antibacterial treatment to cover these microorganisms should be given when a bacterial agent is suspected.

Gatter N. et al. *In vitro efficacy of a hydrophilic central venous catheter loaded with silver to prevent microbial colonization.* Zentralbl Bakteriol. 1998; 287(1-2) : 157-69.p Abstract: A method was developed to load the surface of a central venous catheter with silver to prevent bacterial colonization. Silver confers a broad antimicrobial activity with a relatively low risk of resistance. Catheters were incubated with a silver nitrate solution in different concentrations. The solvent, incubation temperature and incubation period were varied to examine the influence on the catheter loading. With increasing incubation temperature, time and concentration of silver nitrate, higher rates of silver elution were observed by atomic absorption spectroscopy. Furthermore, by using ethanol-water as a solvent instead of pure water, the amount of silver bound to the catheter surface was enhanced. The release of silver from the catheter surface is mainly controlled by first order kinetics. Antimicrobial efficacy of the modified catheter, in comparison to unloaded catheters, was tested in a stationary and a dynamic model with different microorganisms. Adherence experiments with Candida albicans showed almost complete inhibition of growth during a period of 72 hours, including initial adherence. While initial adherence of bacteria could not be prevented, these experiments showed an excellent reduction of bacterial colonization. In a perfusion model, adhesion of E. coli could be reduced for at least seven days. Further studies are planned to examine prolonged antimicrobial effects.

Gau M. et al. *[Penetrating and perforating eye injuries with foreign bodies during motorized brush-cutting while wearing head protection gear].* Klin Monatsbl Augenheilkd. 1999; 215(5) : 311-4.p Abstract: BACKGROUND: Protective clothing is prescribed concerning gloves, shoes, protective trousers and a helmet for protection of hearing and the face during brush-cutter work. PATIENTS AND METHODS: Seven patients were observed in a time period from 1994 to 1998. Mostly a nylon head protection had been used. The side of the helmet has no protection shield. The 1- to 4-mm large foreign bodies passed the head protection shield from the side or by entering through the holes of the nylon mesh which may be not small enough to stop the foreign body. A pars plana vitrectomy with foreign body removal was performed after primary wound repair. RESULTS: An endophthalmitis was diagnosed in two patients after primary wound treatment. In these cases, a pars plana vitrectomy and antibiotic instillation was performed. In 5 patients visual acuity increased postoperatively. We measured a postoperative visual acuity from 1/50 to 1.6. The development of proliferative vitreoretinopathy with retinal detachment in 4 patients was the main complication observed after pars plana vitrectomy. CONCLUSIONS: A cosmetically satisfactory appearance of the injured eye was reached by pars plana vitrectomy in all patients. Anatomic and functional success was reached in most of the patients. For prophylaxis, a head-protection seems not safe enough. The additional usage of eye protection glasses may be imperative for the prevention of these eye injuries.

Gaudreau C. et al. *Antimicrobial resistance of clinical strains of Campylobacter jejuni subsp. jejuni isolated from 1985 to 1997 in Quebec, Canada.* Antimicrob Agents Chemother. 1998; 42(8) : 2106-8.p Abstract: The antimicrobial resistance of 158 Campylobacter jejuni strains isolated from humans in Quebec, Canada, from 1995 to 1997 was compared to the resistance of 47 and 86 strains of C. jejuni isolated in 1985 and 1986 and in 1992 and 1993, respectively. Of the 291 C. jejuni strains tested, no strain was resistant to erythromycin. Compared to the C. jejuni strains isolated in 1985 and 1986, the C. jejuni strains isolated in 1992 and 1993 were more resistant to tetracycline (40.7 versus 19.1%, respectively; P = 0. 01) but not to nalidixic acid or ciprofloxacin (P > 0.05). Compared to the C. jejuni strains isolated in 1992 and 1993 and in 1985 and 1986, the C. jejuni strains isolated from 1995 to 1997 were more resistant to tetracycline (55.7% versus 40.7 and 19.1%, respectively; P = 0.03 and P < 0.001, respectively) to nalidixic acid (13.9% versus 4.7 and 0%, respectively; P = 0.02 and P = 0.007, respectively), and to ciprofloxacin (12.7% versus 3.5 and 0%, respectively; P = 0.02 and P = 0.009, respectively).

Gaviria-Ruiz M.M. et al. *Evaluation and comparison of different blood culture techniques for bacteriological isolation of Salmonella typhi and Brucella abortus.* J Clin Microbiol. 1995; 33(4) : 868-71.p Abstract: An experimental study was carried out to evaluate and compare various noncommercial methods of blood culture for the isolation of Salmonella typhi and Brucella abortus from fresh human blood samples that had been artificially inoculated with 1 to 50 microorganisms per ml of blood. The methods compared included the Ruiz-Castaneda blood culture, broth blood culture, leukocyte lysis and direct plating on agar (WBL-P), leukocyte lysis and filtration, Ficoll-Hypaque centrifugation and filtration, Ficoll-Hypaque centrifugation, and Ficoll-Hypaque centrifugation and leukocyte lysis methods. Results with the WBL-P technique showed that S. typhi was isolated in 18 h, and its recovery rate was 36.6% (calculated from the number of CFU recovered per milliliter versus the number inoculated). B. abortus was isolated in 48 h by the same technique, and its recovery rate was 48.8%. The isolation times for the other blood culture techniques were between 36 and 44 h for S. typhi and 66 h for B. abortus. The techniques which relied on filtering systems for the recovery of S. typhi and B. abortus performed poorly. The WBL-P technique for the isolation of S. typhi and B. abortus is faster than the other methods tested.

Ge M. et al. *Vancomycin derivatives that inhibit peptidoglycan biosynthesis without binding D-Ala-D-Ala.* Science. 1999; 284(5413) : 507-11.p Abstract: Vancomycin is an important drug for the treatment of Gram-positive bacterial infections. Resistance to vancomycin has begun to appear, posing a serious public health threat. Vancomycin analogs containing modified carbohydrates are very active against resistant microorganisms. Results presented here show that these carbohydrate derivatives operate by a different mechanism than vancomycin; moreover, peptide binding is not required for activity. It is proposed that carbohydrate-modified vancomycin compounds are effective against resistant bacteria because they interact directly with bacterial proteins involved in the transglycosylation step of cell wall biosynthesis. These results suggest new strategies for designing glycopeptide antibiotics that overcome bacterial resistance.

Ge Y. et al. *In vitro susceptibility to pexiganan of bacteria isolated from infected diabetic foot ulcers.* Diagn Microbiol Infect Dis. 1999; 35(1) : 45-53.p Abstract: During two clinical trials involving the treatment of 835 outpatients with infected diabetic foot ulcers, 2515 bacterial isolates,

including 2337 aerobes and 178 anaerobes, were grown from cultures of the ulcers. The in vitro susceptibility of these isolates was determined to pexiganan, a peptide anti-infective evaluated in these clinical trials, and to other classes of antibiotics. Pexiganan demonstrated broad spectrum antimicrobial activity against Gram-positive and Gram-negative aerobes and anaerobes. The MIC90 values for the most common species among 1735 Gram-positive aerobes isolated, such as Staphylococcus aureus, coagulase-negative staphylococci, Group A streptococci, and Group B streptococci, were 16 micrograms/mL or less. Of 602 Gram-negative aerobes tested, the MIC90 values for pexiganan were 16 micrograms/mL or less for Acinetobacter, Pseudomonas, Stenotrophomonas, Citrobacter, Enterobacter, Escherichia, Klebsiella, and Flavobacterium species. Pexiganan had a MIC90 of 4 to 16 micrograms/mL against the anaerobic isolates of Bacteroides, Peptostreptococcus, Clostridium, and Prevotella species. Importantly, pexiganan did not exhibit cross-resistance with other commonly used antibiotics, including beta-lactams, quinolones, macrolides, and lincosamides. The broad spectrum in vitro antimicrobial activity of pexiganan against clinical isolates from infected diabetic foot ulcers supports its potential as a local therapy for infected diabetic foot ulcers.

Ge Y. et al. *In vitro antibacterial properties of pexiganan, an analog of magainin.* Antimicrob Agents Chemother. 1999; 43(4) : 782-8.p Abstract: Pexiganan, a 22-amino-acid antimicrobial peptide, is an analog of the magainin peptides isolated from the skin of the African clawed frog. Pexiganan exhibited in vitro broad-spectrum antibacterial activity when it was tested against 3,109 clinical isolates of gram-positive and gram-negative, anaerobic and aerobic bacteria. The pexiganan MIC at which 90% of isolates are inhibited (MIC90) was 32 micrograms/ml or less for Staphylococcus spp., Streptococcus spp., Enterococcus faecium, Corynebacterium spp., Pseudomonas spp., Acinetobacter spp., Stenotrophomonas spp., certain species of the family Enterobacteriaceae, Bacteroides spp., Peptostreptococcus spp., and Propionibacterium spp. Comparison of the MICs and minimum bactericidal concentrations (MBCs) of pexiganan for 143 isolates representing 32 species demonstrated that for 92% of the isolates tested, MBCs were the same or within 1 twofold difference of the MICs, consistent with a bactericidal mechanism of action. Killing curve analysis showed that pexiganan killed Pseudomonas aeruginosa rapidly, with 10(6) organisms/ml eliminated within 20 min of treatment with 16 micrograms of pexiganan per ml. No evidence of cross-resistance to a number of other antibiotic classes was observed, as determined by the equivalence of the MIC50s and the MIC90s of pexiganan for strains resistant to oxacillin, cefazolin, cefoxitin, imipenem, ofloxacin, ciprofloxacin, gentamicin, and clindamicin versus those for strains susceptible to these antimicrobial agents. Attempts to generate resistance in several bacterial species through repeated passage with subinhibitory concentrations of pexiganan were unsuccessful. In conclusion, pexiganan exhibits properties in vitro which make it an attractive candidate for development as a topical antimicrobial agent.

Gebara E.C.E. et al. *Estudo in vitro da ação antimicrobiana de substâncias naturais sobre S. mutans e S. sobrinus.* Rev. odontol. Univ. São Paulo. 1996; 10(4) : 251-6.p Abstract: Foi analisada a atividade antimicrobiana das tinturas de malva, salva, camomila, tomilho, cacau e própolis contra S. mutans e S. sobrinus. Tomilho, cacau e própolis apresentaram atividade antimicrobiana. As Concentrações Inibitórias Mínimas (CIM) para S. mutans foram de 0,06 mg de tomilho por ml de meio; para o cacau, de 0,10 mg/ml, e para o própolis, de 0,04 mg/ml.

Geffers C. et al. *[Establishment of a national database for ICU-associated infections. First results from the "Krankenhaus-Infections-Surveillance-System" (KISS)].* Anaesthesist. 2000; 49(8) : 732-7.p Abstract: OBJECTIVES: To establish a surveillance system as an element of internal quality management, participating intensive care units (ICUs) report their ICU-associated infection surveillance data for aggregation into a national database. METHODS: In order to provide data on ICU-associated infections, a nosocomial surveillance system in German intensive care units (Krankenhaus-Infections-Surveillance-System (KISS)) started in 1997. The method of data collection is based on the (adult) ICU surveillance component from the National Nosocomial Infections Surveillance (NNIS)-System. Until now 113 German ICUs (most of them medical/surgical ICUs) were included in this system. We continuously collected and calculated the data from site-specific infections (device-associated pneumonias, blood stream infections and urinary tract infections). RESULTS: There are now a total of 393,177 patient-days (100,015 patients) among them 176,415 ventilator-days, 295,221 central line-days and 316,799 urinary catheter-days in the data base. The data analysis showed the following device-associated infection rates: 11.2 pneumonias/1000 ventilator-days, 1.8 primary bloodstream infections/1000 central line-days and 4.0 urinary tract infections/1000 urinary catheter-days. CONCLUSION: The project has reached high interest in Germany and animated more ICUs to take part or to apply the same method in order to use the reference data for comparison.

Genne D. et al. *[Level of stethoscope contamination in the hospital environment].* Schweiz Med Wochenschr. 1996; 126(51-52) : 2237-40.p Abstract: The aim of this study was to determine the extent of the contamination of stethoscopes and their possible role in transmission of microorganisms. The stethoscopes of the medical doctors of the hospital of La Chaux-de-Fonds, Switzerland, were cultured and the date of the last cleaning recorded. 38 of the 62 stethoscopes surveyed were contaminated with microorganisms (61%). The majority of isolated organisms were gram-positive bacteria, primarily Staphylococcus species (89%). The cleaning of the stethoscopes was frequent for 32% of the doctors, rare for 46% and non-existent for 22%. After more than one day without cleaning of the stethoscope, the level of contamination rose from 0% to 69%. Stethoscope use may be an important factor in the spread of infectious agents, so that regular disinfection should be carried out (once a day at the very least).

George R.C. et al. *Serogroups/types and antibiotic resistance of referred isolates of Streptococcus pneumoniae: 1993 to 1995.* Commun Dis Rep CDR Rev. 1997; 7(11) : R159-64.p Abstract: Surveillance of prevalent serogroups/types of Streptococcus pneumoniae and their susceptibility to antimicrobial agents is important for understanding the epidemiology of pneumococcal infections and for guiding empirical treatment. Current vaccines for prevention of pneumococcal infection utilise serotype specific antigens, so knowledge of the prevalence of particular serotypes is relevant to vaccine use and development. Five thousand seven hundred and ninety-six isolates of S. pneumoniae from separate patients were serogrouped or serotyped by the Streptococcus and Diphtheria Reference Unit between 1993 and 1995. Antibiotic susceptibility testing was carried out by the Antibiotic Reference Unit on 3821 (65.9%) of these isolates. A total of 40 distinct serogroups/types, together with a small number of non-typable isolates, were noted over the three year period. The same five serogroups/types (6, 9, 14, 19, and 23) occurred most commonly in each year of the study, not only in the total population of isolates studied, but also in isolates obtained from blood or cerebrospinal fluid, and among isolates with antibiotic resistance. Ninety-six per cent of the isolates belonged to serogroups/types included in the currently available 23-valent capsular polysaccharide pneumococcal vaccine; the conjugate petna-, hepta-, and nonavalent vaccines covered 51%, 75%, and 80% of isolates respectively. The nonavalent vaccine offers the most promise as 74% of all blood and cerebrospinal fluid isolates and 90% of antibiotic resistant isolates belonged to serogroups or types included in this formulation.

Georgilis K. *Conservative management of PID.* Ann N Y Acad Sci. 2000; 900 : 309-15.p Abstract: The goals in the management of pelvic inflammatory disease (PID) are not only treatment of the infection and prevention of immediate complications, but also prevention of

its long-term consequences. There are criteria for hospitalization, but patients who do not meet them can be safely treated as outpatients. A variety of sexually transmitted and other microorganisms can cause this infection, but the most important are Chlamydia trachomatis and Neisseria gonorrhoeae. Regimens with activity against gonococci, chlamydiae, streptococci, gram-negative bacteria, and anaerobes should be administered. Several such antimicrobial regimens have shown very good clinical and microbiologic efficacy. However, their efficacy in preventing long-term complications, such as infertility, has not been established. Close follow-up is an important part of management. Evaluation of male sexual partners is imperative to prevent reinfection. Better diagnostic techniques and treatment modalities for PID must be developed to prevent its long-term consequences.

Georgiou G. et al. *Display of heterologous proteins on the surface of microorganisms: from the screening of combinatorial libraries to live recombinant vaccines.* Nat Biotechnol. 1997; 15(1) : 29-34.p Abstract: In recent years there has been considerable progress towards the development of expression systems for the display of heterologous polypeptides and, to a lesser extent, oligosaccharides on the surface of bacteria or yeast. The availability of protein display vectors has in turn provided the impetus for a range of exciting technologies. Polypeptide libraries can be displayed in bacteria and screened by cell sorting techniques, thus simplifying the isolation of proteins with high affinity for ligands. Expression of antigens on the surface of nonvirulent microorganisms is an attractive approach to the development of high-efficacy recombinant live vaccines. Finally, cells displaying protein receptors or antibodies are of use for analytical applications and bioseparations.

Georgopoulos A. et al. *Austrian national survey of prevalence of antimicrobial resistance among clinical isolates of Streptococcus pneumoniae 1994-96.* Scand J Infect Dis. 1998; 30(4) : 345-9.p Abstract: The antimicrobial susceptibilities of 1385 clinical isolates of Streptococcus pneumoniae obtained from 25 laboratories across Austria between December 1994 and January 1996 were tested. Minimal inhibitory concentration (MIC) values were determined in tests with penicillin, amoxycillin, amoxycillin/clavulanate, ceftriaxone, cefodizime, cefpirome, cefotaxime, cefpodoxime, cefadroxile, azithromycin, clarithromycin, josamycin and roxithromycin by the agar-dilution method. A total of 40 isolates (2.9%) demonstrated intermediate resistance (MIC 0.125-1 microg/ml) and 28 isolates (2.0%) had high-level resistance (MIC > or = 2 microg/ml) to penicillin. Excepting cefadroxil, with an MIC90 of 2 microg/ml, all other tested beta-lactams had MIC90s of 0.03-0.06 microg/ml. Penicillin-resistant strains were much more likely to be also resistant to the other beta-lactams. The macrolides proved to be very active compounds against pneumococci with MIC90s of 0.06 microg/ml (clarithromycin) and 0.25 microg/ml (all other macrolides). Regional differences within Austria with regard to antimicrobial resistance were not observed.

Geraghty M. et al. *Synthesis and antimicrobial activity of copper(II) and manganese(II) alpha,omega-dicarboxylate complexes.* Biometals. 2000; 13(1) : 1-8.p Abstract: Copper(II) alpha,omega-dicarboxylate complexes of general formulae, [Cu(O2C(CH2)nCO2)].xH2O, [Cu(O2C(CH2)nCO2) (phen)2].xH2O and [Cu(O2C(CH2),CO2)(bipy)y].xH2O (n = 1-8; y = 1, 2; phen = 1,10-phenanthroline; bipy = 2,2'-bipyridine) were synthesised. These copper complexes, some related manganese(II) complexes and the metal-free ligands were screened in vitro for their ability to inhibit the growth of Candida albicans. Metal-free 1,10-phenanthroline and all of the copper(II) and manganese(II) phenanthroline complexes were potent growth inhibitors, with only one bipyridine complex, [Cu(O2C(CH2)CO2)(bipy)2].2H2O, having moderate activity. The remaining substances were effectively inactive. Complexes which were active against C. albicans also proved effective against C. glabratta, C. tropicalis and C. kreusi with the manganese complexes retaining superior activity. For the phenanthroline complexes the active drug species is thought to be the dication [M(phen)2(H2O)n]2+ (M = Cu, Mn). Escherichia coli and Staphylococcus aureus were resistant to all of the metal complexes and also to metal-free 1,10-phenanthroline. Only the copper phenanthroline complexes showed intermediate activity against Pseudomonas aeruginosa.

Gerding D.N. *Antimicrobial cycling: lessons learned from the aminoglycoside experience.* Infect Control Hosp Epidemiol. 2000; 21(1 Suppl) : S12-7.p Abstract: Several discrete strategies have been suggested to prevent or reduce microbial resistance to antimicrobials, including optimal use of the agents (also known as good stewardship); control, removal, or restriction of antimicrobials; use of antimicrobials in combination; and rotational or cyclic use of antimicrobials. The latter strategy is attractive because it periodically removes from the institutional environment certain classes or specific agents that could induce or select resistance. Hospitalwide studies of aminoglycoside substitution employed from the late 1970s through the early 1990s, although not originally intended to test cycling or rotation of aminoglycosides, serendipitously provided data that may be useful in designing future studies. In particular, one 10-year study at the Minneapolis Veterans' Affairs Medical Center (MVAMC) rotated amikacin and gentamicin use over cycles of 12 to 51 months' duration. Significantly reduced resistance to gentamicin was found when amikacin was used, but resistance to gentamicin returned with the first gentamicin recycle. This was followed by reintroduction of amikacin a second time with decreased resistance to gentamicin and, finally, a second reintroduction of gentamicin without resistance to it recurring. Thus, some evidence of proof of principal can be garnered, albeit subject to considerable criticism. Critical examination of the design of the aminoglycoside rotation study and the unforeseen pitfalls is provided as a 13-element guidance list for design of future rotational studies. Rotational usage practices are likely to be most appropriate for drugs active against gram-negative bacilli because of the wide choices available for rotation. Future availability of new agents active against resistant gram-positive organisms will present the opportunity to cycle these agents as vancomycin substitutes. Careful monitoring of clinical outcomes and resistance will be required. Multicenter controlled trials that follow carefully designed protocols are most likely to produce statistically significant and clinically meaningful results.

Gerding D.N. *Is there a relationship between vancomycin-resistant enterococcal infection and Clostridium difficile infection?* Clin Infect Dis. 1997; 25 Suppl 2 : S206-10.p Abstract: The relationship between vancomycin or metronidazole treatment of Clostridium difficile-associated diarrhea (CDAD) and the occurrence of vancomycin-resistant enterococcus (VRE) infection was investigated by review of 18 case-control studies. Fifteen (83%) of 18 studies found vancomycin use, days of use, or grams used to be significantly associated with VRE infection or colonization. Intravenous vancomycin use was a significant risk in nine of 10 studies, and oral vancomycin use was a significant risk in three of four studies that stratified risk by route of administration. Although statistically associated, oral vancomycin use was so infrequent (25% in the study with the most use) that it is likely to have only a minor influence as a risk for VRE infection or colonization when compared with the much more widespread use of intravenous vancomycin. Metronidazole exposure was found to be a significant risk in four of five studies that specifically assessed this variable, but the indication for metronidazole use was not specified. Risk factors for both VRE infection and CDAD include antimicrobial exposure, number of antimicrobials, days of antimicrobial use, specific agents (third-generation cephalosporins, clindamycin, and imipenem), patient age, length of hospitalization, severity of underlying illness, use of electronic rectal thermometers, enteral feedings, environmental contamination, and contamination of the hands of health care workers.

Gerding D.N. et al. *Clostridium difficile-associated diarrhea and colitis.* Infect Control Hosp Epidemiol. 1995; 16(8) : 459-77.p Abstract: OBJECTIVES: To review and summarize the status of diagnosis, epidemiology, infection control, and treatment of Clostridium difficile-associated disease (CDAD). DIAGNOSIS: A case definition of CDAD should include the presence of symptoms (usually diarrhea) and at least one of the following positive tests: endoscopy revealing pseudomembranes, stool cytotoxicity test for toxin B, stool enzyme immunoassay for toxin A or B, or stool culture for C difficile (preferably with confirmation of organism toxicity if a direct stool toxin test is negative or not done). Testing of asymptomatic patients, including those who are asymptomatic after treatment, is not recommended other than for epidemiologic purposes. Lower gastrointestinal endoscopy is the only diagnostic test for pseudomembranous colitis, but it is expensive, invasive, and insensitive (51% to 55%) for the diagnosis of CDAD. Stool culture is the most sensitive laboratory test currently in clinical use, but it is not as specific as the cell cytotoxicity assay. EPIDEMIOLOGY: C difficile is the most frequently identified cause of nosocomial diarrhea. The majority of C difficile infections are acquired nosocomially, and most patients remain asymptomatic following acquisition. Antimicrobial exposure is the greatest risk factor for patients, especially clindamycin, cephalosporins, and penicillins, although virtually every antimicrobial has been implicated. Cases of CDAD unassociated with prior antimicrobial or antineoplastic use are very rare. Hands of personnel, as well as a variety of environmental sites within institutions, have been found to be contaminated with C difficile, which can persist as spores for many months. Contaminated commodes, bathing tubs, and electronic thermometers have been implicated as sources of C difficile. Symptomatic and asymptomatic infected patients are the major reservoirs and sources for environmental contamination. Both genotypic and phenotypic typing systems for C difficile are available and have enhanced epidemiologic investigation greatly. INFECTION CONTROL: Successful infection control measures designed to prevent horizontal transmission include the use of gloves in handling body substances and replacement of electronic thermometers with disposable devices. Isolation, cohorting, handwashing, environmental disinfection, and treatment of asymptomatic carriers are recommended practices for which convincing data of efficacy are not available. The most successful control measure directed at reduction in symptomatic disease has been antimicrobial restriction. TREATMENT: Treatment of symptomatic (but not asymptomatic) patients with metronidazole or vancomycin for 10 days is effective; metronidazole may be preferred to reduce risk of vancomycin resistance among other organisms in hospitals. Recurrence of symptoms occurs in 7% to 20% of patients and is due to both relapse and reinfection. Over 90% of first recurrences can be treated successfully in the same manner as initial cases. Combination treatment with vancomycin plus rifampin or the addition orally of the yeast Saccharomyces boulardii to vancomycin or metronidazole treatment has been shown to prevent subsequent diarrhea in patients with recurrent disease.

Gerding D.N. et al. *SHEA conference on antimicrobial resistance. Society for Healthcare Epidemiology of America.* Infect Control Hosp Epidemiol. 2000; 21(5) : 347-51.p Abstract: Antimicrobial resistance is an increasing problem in healthcare institutions and in the community. Public concern about resistance is also increasing. The issue is broad and complex and not readily addressed by government, industry, or professional societies alone. On October 29-30, 1998, 19 representatives of various professional societies and governmental agencies met under the auspices of the Society for Healthcare Epidemiology of America (SHEA) at Brook Lodge Conference Center in Augusta, Michigan. The purpose of the meeting was to discuss the current status of antimicrobial resistance in the United States and Canada, including present society and governmental efforts to address the problem. Representatives exchanged experiences through presentations and discussions on the first day, then on the second day held a brainstorming session to address future needs and priorities in addressing the resistance problem. It was agreed that a national coordinated effort was needed. As part of this national effort, representatives called for the creation of a National Coalition on Antibiotic Resistance (NCAR) to combat antibiotic resistance through education, research, prevention, and advocacy. Priorities for NCAR were focused in four areas: (1) education of the public and professionals; (2) support of basic and applied research; (3) provision of an information resource and clearinghouse; and (4) advocacy initiatives. At the recommendation of the SHEA Board, discussions with the National Foundation for Infectious Diseases for the joint development of NCAR have begun.

Gerkin T.M. et al. *Are traditional prognostic criteria useful in pancreatic abscess?* Pancreas. 1995; 10(4) : 331-7.p Abstract: Pancreatic abscess remains a potentially lethal disease. Efforts to relate outcome to the severity of associated pancreatitis or the type of surgical drainage employed have yielded conflicting results. This study was designed to test the validity of traditional prognostic criteria in the clinical setting of pancreatic abscess and to determine whether the technique of surgical drainage employed correlated with survival. The records of 40 consecutive patients with pancreatic abscess were reviewed. In each case the diagnosis was confirmed by operation. Prognostic factors analyzed included number of Ranson criteria, etiology, type, and number of microorganisms isolated, extent of abscess, time to diagnosis and operation, and technique of surgical drainage. Of the 11 Ranson criteria evaluated, only an elevation in blood urea nitrogen > 5 mg/dl correlated with decreased survival ($p < 0.001$). Polymicrobial abscesses (three or more organisms) resulted in a higher mortality than abscesses where fewer than three organisms were isolated (45.4 vs 13.8%; $p < 0.05$). Intraperitoneal extension of the abscess was associated with an increased mortality rate compared to those confined to the retroperitoneum (57.1 vs 15.2%; $p < 0.01$). In patients requiring unplanned reexploration, mortality was significantly increased (42.9 vs 11.5%; $p < 0.05$). The technique of surgical drainage employed (open versus closed) did not influence overall mortality (23.5 vs 21.7%; p = NS). Extent of disease at operation, polymicrobial abscess, reexploration for persistent or recurrent disease, and deterioration in renal function were all predictive of increased mortality in cases of pancreatic abscess. (ABSTRACT TRUNCATED AT 250 WORDS).

Geyer A. et al. *Genetic organisation of the M protein region in human isolates of group C and G streptococci: two types of multigene regulator-like (mgrC) regions.* Mol Gen Genet. 2000; 262(6) : 965-76.p Abstract: In addition to beta-haemolytic streptococci belonging to Lancefield group A (Streptococcus pyogenes, GAS), human isolates of group C (GCS) and group G (GGS) streptococci (S. dysgalactiae subsp. equisimilis) have been implicated as causative agents in outbreaks of purulent pharyngitis, of wound infections and recently also of streptococcal toxic shock-like syndrome. Very little is known about the organisation of the genomic region in which the emm gene of GCS and GGS is located. We have investigated the genome sequences flanking the emm gene in GCS by sequencing neighbouring fragments obtained by inverse PCR. Our sequence data for GCS strains 25287 and H46A revealed two types of arrangement in the emm region, which differ significantly from the known types of mga regulon in GAS. We named this segment of the genome mgrC (for multigene regulon-like segment in group C streptococci). In strains belonging to the first mgrC type (prototype strain 25287) the emm gene is flanked up-stream by mgc, a gene that is 61% identical to the mga gene of GAS. A phylogenetic analysis of the deduced protein sequences showed that Mgc is related to Mga proteins of various types of GAS but forms a distinct cluster. Downstream of emm, the mgrC sequence region is bordered by rel. This gene encodes a protein that functions in the synthesis and degradation of guanosine 3',5' bipyrophosphate (ppGpp) during the stringent regulatory response to amino acid deprivation. In the second mgrC type (prototype strain H46A), the genes mgc and emm are arranged as in type 1. But an additional ORF (orf) is inserted in opposite orientation

between emm and rel. This orf shows sequence homology to cpdB, which is present in various microorganisms and encodes 2',3' cyclonucleotide 2'-phosphodiesterase. PCR analysis showed that these two mgrC arrangements also exist in GGS. Our sequence and PCR data further showed that both types of mgrC region in GCS and GGS are linked via rel to the streptokinase region characterised recently in strain H46A. A gene encoding C5a peptidase, which is present at the 3' end of the mga regulon in GAS, was not found in the mgrC region identified in the GCS and GGS strains investigated here.

Ghannoum M.A. et al. *Antifungal agents: mode of action, mechanisms of resistance, and correlation of these mechanisms with bacterial resistance.* Clin Microbiol Rev. 1999; 12(4) : 501-17.p Abstract: The increased use of antibacterial and antifungal agents in recent years has resulted in the development of resistance to these drugs. The significant clinical implication of resistance has led to heightened interest in the study of antimicrobial resistance from different angles. Areas addressed include mechanisms underlying this resistance, improved methods to detect resistance when it occurs, alternate options for the treatment of infections caused by resistant organisms, and strategies to prevent and control the emergence and spread of resistance. In this review, the mode of action of antifungals and their mechanisms of resistance are discussed. Additionally, an attempt is made to discuss the correlation between fungal and bacterial resistance. Antifungals can be grouped into three classes based on their site of action: azoles, which inhibit the synthesis of ergosterol (the main fungal sterol); polyenes, which interact with fungal membrane sterols physicochemically; and 5-fluorocytosine, which inhibits macromolecular synthesis. Many different types of mechanisms contribute to the development of resistance to antifungals. These mechanisms include alteration in drug target, alteration in sterol biosynthesis, reduction in the intercellular concentration of target enzyme, and overexpression of the antifungal drug target. Although the comparison between the mechanisms of resistance to antifungals and antibacterials is necessarily limited by several factors defined in the review, a correlation between the two exists. For example, modification of enzymes which serve as targets for antimicrobial action and the involvement of membrane pumps in the extrusion of drugs are well characterized in both the eukaryotic and prokaryotic cells.

Ghassemi M. et al. *Mycobacterium avium complex activates nuclear factor kappaB via induction of inflammatory cytokines.* Cell Immunol. 1999; 191(2) : 117-23.p Abstract: A variety of microorganisms has been reported to directly induce NF-kappaB, a critical step in the regulation of genes involved in the cellular immune response. In this study, we demonstrate that proinflammatory cytokines such as tumor necrosis factor alpha (TNFalpha) produced upon activation by the Mycobacterium avium complex (MAC) preceed NF-kappaB activity in U937, a human monocytoid cell line. MAC induction of TNFalpha mRNA expression was detected within 15 min after MAC infection, whereas enhanced NF-kappaB binding activity was not detected until 90 to 120 min postinfection. Supershift analysis revealed increased p50 in the MAC-induced NF-kappaB binding complexes. Consistent with an autocrine mechanism, anti-TNFalpha antibody and dexamethasone, a known cytokine inhibitor, both completely suppressed the effect of MAC on the induction of NF-kappaB. Taken together, these findings suggest that exposure of monocyte cell membranes to MAC induces endogenous TNFalpha, which in turn enhances NF-kappaB binding activity. The rapid induction of TNFalpha may be important in the initial host response to MAC infection. Copyright 1999 Academic Press.

Ghosh K. et al. *Erosion of an intraperitoneal chemotherapy catheter resulting in an enterovaginal fistula.* Gynecol Oncol. 2000; 77(2) : 327-9.p Abstract: BACKGROUND: With the pharmacokinetic advantages of intraperitoneal chemotherapy delivery and the increased popularity of immunotherapy and gene therapy, intraperitoneal catheters have moved to the forefront as a delivery system in cancer treatment. This delivery system, however, carries with it an intrinsic morbidity warranting attention in the often prolonged chemotherapy regimens demanded by cancer patients. CASE: In reviewing the literature of intraperitoneal catheter complications, there is no other cited case of a peritoneal catheter erosion into intestine presenting as an enterovaginal fistula. Our patient, diagnosed with persistent ovarian carcinoma, had a peritoneal Tenckoff catheter placed for chemotherapy. Many months after termination of the chemotherapy and 15 months after placement, she presented with bowel contents per vagina. A CT scan revealed an abdominopelvic abscess encompassing the detached catheter which embedded in the rectosigmoid colon, allowing direct communication to the upper vagina. The catheter was removed and the abscess was drained. CONCLUSION: Intraperitoneal catheters have a morbidity that persists after nonuse. Therefore, intraperitoneal catheters should be removed if they are not being used. Copyright 2000 Academic Press.

Giacometti A. et al. *In-vitro activity of cationic peptides alone and in combination with clinically used antimicrobial agents against Pseudomonas aeruginosa.* J Antimicrob Chemother. 1999; 44(5) : 641-5.p Abstract: The in-vitro activity of cecropin P1, indolicidin, magainin II, nisin and ranalexin alone and in combination with nine clinically used antimicrobial agents was investigated against a control strain, Pseudomonas aeruginosa ATCC 27853 and 40 clinical isolates of P. aeruginosa. Antimicrobial activities were measured by MIC, MBC and viable count. In the combination study, the clinically used antibiotics were used at concentrations close to their mean serum level in humans in order to establish the clinical relevance of the results. To select peptide-resistant mutants, P. aeruginosa ATCC 27853 was treated with consecutive cycles of exposure to each peptide at 1 x MIC. The peptides had a varied range of inhibitory values: all isolates were more susceptible to cecropin P1, while ranalexin showed the lowest activity. Nevertheless, synergy was observed when the peptides were combined with polymyxin E and clarithromycin. Consecutive exposures to each peptide at 1 x MIC resulted in the selection of stable resistant mutants. Cationic peptides might be valuable as new antimicrobial agents. Our findings show that they are effective against P. aeruginosa, and that their activity is enhanced when they are combined with clinically used antimicrobial agents, particularly with polymyxin E and clarithromycin.

Giamarellos-Bourboulis E.J. et al. *Comparative in vitro killing activity of meropenem versus imipenem against multiresistant nosocomial Pseudomonas aeruginosa.* J Chemother. 1995; 7(3) : 179-83.p Abstract: In order to compare the in vitro killing activity of meropenem and imipenem against multiresistant P.aeruginosa 14 strains were used. All nosocomial isolates were susceptible to meropenem and imipenem minimum inhibitory concentration (MIC < or = 4 micrograms/ml) and resistant to at least two other antimicrobial agents of diverse chemical class with antipseudomonal activity. Forty-two killing curves were performed by exposing a 5 x 10(5) CFU/ml log-phase inoculum to 1x minimum bactericidal concentration (MBC) of each carbapenem. Meropenem was found to possess a slower killing rate than imipenem over the first 5 hours of P.aeruginosa exposure, but to be equally effective as imipenem after 24 hours of incubation. Forty percent and 11.1% of P.aeruginosa strains developed resistance to imipenem and meropenem respectively after a 24-hour exposure to carbapenem. The authors speculate about the underlying mechanisms explaining the higher rate of resistance development to imipenem than to meropenem.

Giamarellos-Bourboulis E.J. et al. *In-vitro activity of FK 037 (Cefoselis), a novel 4(th) generation cephalosporin, compared to cefepime and cefpirome on nosocomial staphylococci and gram-negative isolates.* Diagn Microbiol Infect Dis. 2000; 36(3) : 185-91.p Abstract: The novel 4(th) generation cephalosporin FK037 was in vitro compared to cefepime and cefpirome on 563 multiresistant nosocomial isolates including methicillin-susceptible (MSSA) and methicillin-resistant

Staphylococcus aureus (MRSA). Their time-kill effect was studied on MSSA, Escherichia coli, Klebsiella pneumoniae, and isolates of Enterobacter cross-resistant to cefotaxime, ceftriaxone, and to ceftazidime, their interaction with amikacin being also evaluated on the latter isolates. Results revealed that FK037 possessed a superior antistaphylococcal activity on MSSA isolates to both other compounds being however equal active to cefepime and cefpirome on multiresistant enterobacteriaceae. Synergy was documented between 4(th) generation cephalosporins and amikacin on K. pneumoniae and on Enterobacter spp. cross-resistant to 3(rd) generation cephalosporins. In the latter species 4(th) generation cephalosporins remained inactive. The presented results support the need of clinical studies with FK037 as monotherapy for nosocomial infections based on the local surveillance data of the level of antimicrobial resistance of each hospital.

Giamarellou H. *Fleroxacin in complicated urinary tract infections.* Chemotherapy. 1996; 42 Suppl 1 : 17-27.p Abstract: The clinical evaluation of antimicrobial agents for the treatment of urinary tract infections (UTIs) requires clinically useful categorization of patients plus concurrent laboratory diagnosis. Appropriate diagnostics include (1) proper collection techniques, (2) quantitative urine culture, (3) urinalysis to determine pyuria, and (4) radiological, urological and gynecological evaluation. Categorization of patients suffering from UTIs should take into consideration (1) the site of infection, (2) the clinical presentation, (3) the frequency of infections, and (4) the coexistence of complicating factors. UTIs in men and older women are mostly complicated. The characterization of a UTI as complicated or uncomplicated is important since in the former condition, multiresistant nosocomial microorganisms are frequently encountered. Experience with fleroxacin 200 or 400 mg once daily (o.d.) in > 1,000 patients with complicated UTIs in noncomparative and comparative trials with other quinolones and cephalosporins has been very promising, with overall clinical and bacteriological cure rates of 86-95 and 89-95%, respectively. As with other quinolones, relapses and superinfections were mostly attributed to Enterococcus, Staphylococcus and Pseudomonas spp. The reported results make oral o.d. fleroxacin appropriate as an alternative to parenteral antimicrobials or for intravenous-to-oral switch therapy in complicated UTIs.

Giamarellou H. *Fourth generation cephalosporins in the antimicrobial chemotherapy of surgical infections.* J Chemother. 1999; 11(6) : 486-93.p Abstract: Surgical infections include a variety of entities such as secondary peritonitis, intra-abdominal abscesses, obstetric and gynecological infections as well as bone-joint and soft-tissue infections. By definition the term "surgical infection" implies that surgery itself plays the major role in therapy, while antimicrobial chemotherapy is only supplementary. Broad-spectrum empirical regimens employed include the combination of a 1st or 2nd generation cephalosporin plus clindamycin or metronidazole +/- aminoglycoside (depending on the severity of the condition). Cefepime and cefpirome are new 4th generation parenteral cephalosporins with a spectrum of activity which makes them suitable for the treatment of infections caused by a wide variety of bacteria. They are active against both gram-positive and gram-negative organisms, including Staphylococcus aureus and Pseudomonas aeruginosa with activity comparable to or greater than that of cefotaxime or ceftazidime respectively. Cefepime in particular is also very active against strains of Enterobacter and Pseudomonas spp resistant to these two agents. In comparison with 3rd generation cephalosporins, cefepime appears to be less likely to induce resistance, due to a lower rate of hydrolysis by beta-lactamases, a low affinity for these enzymes and more rapid permeation into the cell. Despite the fact that a 4th generation cephalosporin is well-suited for the treatment of polymicrobial infections, the following should be kept in mind: (I) MRSA strains and Bacteroides fragilis group are not included in their spectrum of activity. (II) Cefpirome is the only cephalosporin with in vitro activity against Enterococci. (III) Severe surgical infections of nosocomial origin, and particularly in settings where Enterobacter spp predominate, represent the major indication for empirical use of a 4th generation cephalosporin in combination with a nitroimidazole.

Giamarellou H. et al. *The effect of monitoring of antibiotic use on decreasing antibiotic resistance in the hospital.* Ciba Found Symp. 1997; 207 : 76-86; discussion 86-92.p Abstract: In Greece, antibiotic over-consumption and high resistance rates run in parallel. In the spring of 1989 surveillance of 12500 Gram-negative strains, derived from 55 hospitals from all over Greece, revealed that resistance rates of Pseudomonas aeruginosa, Enterobacter spp., Klebsiella spp. and Acinetobacter spp. to antimicrobial agents introduced after 1985 exceeded 50%. As a consequence, the application of (1) rules of hospital hygiene, (2) educational small group programs, and (3) an antibiotic policy aiming to restrict antibiotic use, was decided in Laiko General Hospital. Since 1989, imipenem, the newer quinolones, vancomycin, aztreonam and third-generation cephalosporins were only ordered to the hospital pharmacy after completion of a specific request form, which since 1991 has been more detailed and which can be signed only by physicians with interest in infectious diseases. In 1991, in cooperation with the pharmacy, an audit program was added requiring a final inspection of the already approved request forms by an infectious diseases specialist. Any disagreement was discussed with the physicians in charge. Consumption data were analysed monthly and discussed with each department. Newer antibiotic consumption in a selected month (November) of three consecutive years, before (1991) and after the application of the audit program (1992-1995) has been analysed. Results reveal a decrease in consumption of restricted antibiotics, especially in surgical departments and in kidney transplantation units, without simultaneous increase in consumption of the non-restricted compounds. Since 1994, resistance has decreased remarkably. However, the resistance of quinolones is increasing steeply. Consequently, for the last 12 months quinolones have been removed from the hospital formulary. An audit program requires close cooperation of physicians, pharmacists and, particularly, of surgeons, in the application of a correct prophylaxis regimen. It seems to be efficacious in reducing both resistance rates and total antibiotic consumption.

Giglio M.S. et al. *[Surveillance of gram positive cocci susceptibility to betalactams, glycopeptides, and other antimicrobials].* Rev Med Chil. 1999; 127(8) : 919-25.p Abstract: BACKGROUND: During the last decade, there has been a progressive increase in the resistance of gram (+) cocci to betalactamics and other antimicrobials. Therefore, vancomycin and teicoplanin have incorporated as alternative antimicrobial drugs. AIM: To assess the susceptibility of gram (+) cocci to different antimicrobials including vancomycin and teicoplanin. MATERIAL AND METHODS: We studied 447 strains of gram (+) cocci coming from ambulatory and hospitalized patients. These included 308 Enterococcus sp strains, 99 Staphylococcus aureus strains and 40 coagulase negative Staphylococci strains. Enterococci susceptibility was measured using minimal inhibitory concentrations in agar and that of Staphylococci, through diffusion. Susceptibility to vancomycin and teicoplanin was measured using minimal inhibitory concentrations in all strains. RESULTS: Enterococcus faecalis was 100% susceptible to ampicillin, penicillin, vancomycin and teicoplanin, 23% susceptible to tetracyclin and 47% to chloramphenicol. Susceptibility of E faecium was 61% to penicillin, 49% to chloramphenicol, 41% to tetracyclin, 100% to vancomycin and teicoplanin. Of 19 Enterococcus spp strains, 90% were susceptible to ampicillin, 80% to penicillin, 55% to chloramphenicol and 45% to tetracyclin. Only one E casseiflavus strain had a low level resistance to vancomycin and was susceptible to teicoplanin. No Staphylococcus aureus strain was resistant to vancomycin or teicoplanin. CONCLUSIONS: A permanent surveillance of gram (+) cocci antimicrobial susceptibility is required to update therapeutic schemes.

Giglio M.S. et al. *Microbiology of recurrent parotitis.* Pediatr Infect Dis J. 1997; 16(4) : 386-90.p Abstract: BACKGROUND: Infantile chronic recurrent parotitis (ICRP) is characterized by episodes of recurrent swelling of the parotid gland with decreased salivary flow and purulent secretion. The etiology of this little unknown clinical condition has been attributed to multiple causes such as canalicular system malformations, ascending bacterial infection, hyposialia, parotitis sequelae, viral infections and immunologic disorders, among others. METHODS: We studied the types (with counts) of microorganisms involved in ICRP. Saliva samples were obtained from 56 patients and 20 controls, inoculated onto enriched media and incubated under aerobic and anaerobic conditions. Antimicrobial susceptibility and serotyping of the isolated organisms isolated were performed. RESULTS: Of 57 saliva samples from ICRP patients, 52 (91%) were culture-positive. The most frequently isolated microorganisms were Streptococcus pneumoniae and Haemophilus influenzae. Thirteen of twenty (65%) samples were also culture-positive, mostly for viridans streptococci. However, colony counts were lower than in clinical samples ($P < 0.004$). Approximately one-third of S. pneumoniae strains resistant or moderately resistant to penicillin, and all H. influenzae strains were susceptible to all of the antimicrobials tested. CONCLUSIONS: S. pneumoniae or H. influenzae were isolated in high concentrations in IRCP cases but not in controls, suggesting that these microorganisms may have a role in the development of this clinical entity. Quantitative cultures are very important in assessment of the pathogenic role of these microorganisms in patients but not in controls.

Giglio Maira M.S. et al. *Vigilancia de susceptibilidad de cocáceas grampositivas a betalactámicos, glicopéptidos y otros antimicrobianos.* Rev. méd. Chile. 1999; 127(8) : 919-25.p Abstract: Background: During the last decade, there has been a progressive increase in the resistance of gram (+) cocci to betalactamics and other antimicrobials. Therefore, vancomycin and teicoplanin have incorporated as alternative antimicrobial drugs. Aim: To assess the susceptibility of gram (+) cocci to different antimicrobials including vancomycin and teicoplanin. Material and methods: We studied 447 strains of gram (+) cocci coming from ambulatory and hospitalized patients. These included 308 enterococcus sp strains, 99 staphycoccus aureus strains and 40 coagulase negative staphylococci strains. Enterococci susceptibility was measured using minimal inhibitory concentrations in agar and that of staphylococci, through diffusion. Susceptibility to vancomycin and teicoplanin was measured using minimal inhibitory concentrations in all strains. Results: Enterococcus faecalis was 100 percent susceptible to ampicillin, penicillin, vancomycin and teicoplanin, 23 percent susceptible to tetracyclin and 47 percent to chloramphenicol. Susceptibility of E faecium was 61 percent to penicillin, 49 percent to chloramphenicol, 41 percent to tetracyclin, 100 percent to vancomycin and teicoplanin. Of 19 enterococcus spp strains, 90 percent were susceptible to ampicillin, 80 percent to penicillin, 55 percent to chloramphenicol and 45 percent to tetracyclin. Only one E casseiflavus strain had a low level resistance to vancomycin and was susceptible to teicoplanin. No staphylococcus aureus strain was resistant to vancomycin or teicoplanin. Conclusions: A permanent surveillance of gram (+) cocci antimicrobial susceptibility is required to update therapeutic schemes (AU).

Giglio Maira M.S. et al. *Identificación de especies de enterococcus en muestras clínicas y susceptibilidad a agentes antimicrobianos.* Rev. méd. Chile. 1996; 124(1) : 70-6.p Abstract: The genus enterococcus has 12 species of which, E faecalis and E faecium are most important in human infections. A progressive resistance to penicillin and ampicillin has been detected in these species. The aim of this work was to identify Enterococcus species isolated in a hospital and to study their antimicrobial susceptibility. We studied 209 Enterococcus species coming from patients admitted to a public hospital. Their susceptibility to penicillin, ampicillin, imipenem, vancomycin, tetracycline, chloramphenicol, ciprofloxacin, gentamycin and streptomycin was determined with the agar dilution technique. Eighty seven percent of species were E faecalis and 7,1 percent were E fecium, other isolated species were E hirae, E casseliflaws, E avium, E solitarius and E faecalis variant. 38 percent of these species were isolated from the urinary tract, 22 percent from the skin and 14 percent from surgical wounds. All E faecalis species were susceptible to penicillin, ampicillin, imipenem and vancomycin; 27,3 percent were susceptible to tetracycline, 54,7 percent to chloramphenicol and 80 percent to ciprofloxacin. Seventy three percent of E faecium species were susceptible to penicillin, 80 percent to ampicillin and 60 percent to imipenem. 62 percent of E faecalis and 42.4 percent of E faecium were resistant to streptomycin. It is concluded that the correct identification of Enterococcus species has therapeutic implications (AU).

Giglio Maira M.S. et al. *Streptococcus pyogenes: susceptibilidad in vitro a diversos antimicrobianos en dos períodos / Streptococcus pyogenes: in vitro susceptibility to several antimicrobials in 2 periods.* Rev. méd. Chile. 1996; 124(6) : :715-9.p Abstract: The frequency of Streptococcus pyogenes infections with deep tissue and toxic shock syndrome has increased in the last decade throughout the world. Aim: to compare antimicrobial susceptibility of S. pyogenes strains isolated during 1986 and 1994-95. Eighty two S. pyogenes strains isolated in 1986 and 67 strains isolated in 1994-1995, were studied. MIC 50 and 90 were determined by an agar dilution method for penicillin, ampicillin, cefazolin, cefuroxime, erythromicin. roxithromycin and miocamycin. Eighty eight strains came from skin of soft tissues, 19 from surgical wounds, 18 from invasive infections, 15 from pharyngeal swabs and 9 from other locations. All strains were susceptible to penicillin, ampicillin, cefazolin, cefuroxime, roxithromycin and miocamycin. Ninety nine percent of strains were susceptibel to erythromycin. Strains isolated in 1994-95 had a higher MIC 50 and 90 for erythromycin than those isolated in 1986. The changes in susceptibility to erythromycin of recently isolated strains could be due to the widespread use of macrolides in Chile (AU).

Gikas A. et al. *Repeated multi-centre prevalence surveys of hospital-acquired infection in Greek hospitals. CICNet. Cretan Infection Control Network.* J Hosp Infect. 1999; 41(1) : 11-8.p Abstract: Three prevalence studies for the estimation of hospital-acquired infections (HAIs) were carried out in eight Greek hospitals on an annual basis during the years 1994-1996. The overall prevalence of HAI was 6.8, 5.5 and 5.9% for the three years, respectively. Among these, urinary tract infections ranged from 22.4 to 38.2%, lower respiratory tract infections ranged from 21.1 to 32.6%, surgical site infections ranged from 14.6 to 22.7% and bloodstream infections ranged from 9.0 to 13.2%. The prevalence of antibiotic usage among the hospitalized patients was found to be 49.3% in 1994, 47.3% in 1995 and 52.7% in 1996. Unjustified prescription of prophylactic usage was found to be the major component of these high percentages. Appropriate use of antibiotics for prophylaxis is one of the priorities of the current infection control programmes. The development of a nationwide network for the surveillance of HAIs in Greece is planned using the experience gained.

Gikas A. et al. *Gram-negative bacteremia in non-neutropenic patients: a 3-year review.* Infection. 1998; 26(3) : 155-9.p Abstract: The causative organisms, clinical manifestations, factors influencing prognosis, and other epidemiological characteristics of 81 episodes of bacteremia due to gram-negative organisms, in non-neutropenic patients, were studied retrospectively during a 3-year period (1992-1994) at the Department of Internal Medicine of the University Hospital of Heraklion, Crete, Greece. The gram-negative bacteremia incidence was 2% and the overall mortality 12%. All 81 patients had fever; Escherichia coli was the most frequent organism isolated (from 47 patients—58%) and was associated with shock (9/47), disseminated intravascular coagulation (DIC) (8/47), anuria (5/47), adult respiratory distress syndrome (ARDS) (3/47), and pneumonia (1/47). Other less frequent gram-negative microorganisms were Klebsiella spp. (ten patients; 12%), Pseudomonas spp. (7; 7%), Salmonella spp. (5;

6%), Enterobacter spp. (5; 6%), Proteus spp. (3; 3.4%), Stenotrophomonas spp. (3; 3.4%), and Acinetobacter spp. (1; 1.2%). ARDS. shock, DIC, anuria, presence of central venous catheter, urinary catheter, unknown origin of infection and inappropriate treatment were significantly associated with a higher death rate. Early initiation of appropriate therapy was the most important intervention that favorably affected the outcome of gram-negative bacteremias in this patient population.

Gilad J. et al. *Hospital-acquired brevundimonas vesicularis septicaemia following open-heart surgery: case report and literature review.* Scand J Infect Dis. 2000; 32(1) : 90-1.p Abstract: Brevundimonas vesicularis (B. vesicularis) is a pseudomonad rarely encountered in human infection. A case of nosocomial septicaemia with this organism following open-heart surgery is presented, with a review of the literature. The isolate demonstrated resistance to ciprofloxacin and aztreonam, which has not yet been reported. Treatment with piperacillin/tazobactam resulted in full recovery. A review of the literature reveals that B. vesicularis is a virulent organism involved in serious infections such as central nervous system infection or bacteraemia, some of which are nosocomial. Meanwhile, empiric therapy for B. vesicularis infection should include a broad-spectrum antimicrobial agent until susceptibility results are known.

Gilbert G.L. et al. *Culture shock. Molecular methods for diagnosis of infectious diseases.* Med J Aust. 1999; 171(10) : 536-9.p Abstract: Nucleic acid detection methods, such as polymerase chain reaction (PCR), can often detect specific microbial pathogens, virulence markers and antimicrobial resistance genes more rapidly and with greater sensitivity and specificity than culture and conventional identification and susceptibility testing. Multiplex PCR can detect multiple genes in a single assay; this capability will be greatly extended by new techniques such as the DNA chip. However, limitations and pitfalls of nucleic detection methods remain.

Gilbert W.M. et al. *The safety and utility of pulmonary artery catheterization in severe preeclampsia and eclampsia.* Am J Obstet Gynecol. 2000; 182(6) : 1397-403.p Abstract: OBJECTIVE: The objective of this research was to study the safety and utility of pulmonary artery catheterization in the management of severe preeclampsia and eclampsia. Study Design: In a retrospective chart review from January 1, 1995, through December 31, 1997, a total of 115 patients admitted to the obstetric intensive care unit at Groote Schuur Hospital were found to have required placement of a pulmonary artery catheter. From this population 100 maternal charts were examined for medical and pregnancy history, including indication for pulmonary artery catheter placement, hemodynamic readings, complications, and subsequent management. RESULTS: The initial indications for pulmonary artery catheter placement in cases of severe preeclampsia or eclampsia were renal failure in 53 cases (53%), pulmonary edema in 30 (30%), and eclampsia in 17 (17%). Subjective evaluation demonstrated that the pulmonary artery catheter was helpful in determining management in 93 cases (93%). There was a 4.0% complication rate, which included three venous thromboses and one case of cellulitis. Eleven patients required dialysis, and 3 women died. The mean (+/-SE) duration of catheter placement was 2.1 +/- 0.1 days and the mean (+/-SE) intensive care unit and hospital stays were 3.4 +/- 0.2 days and 11.4 +/- 0.8 days, respectively. The pulmonary artery catheter measurements of pulmonary artery wedge pressure and central venous pressure were increased in the cases of pulmonary edema (21.0 +/- 2.0 mm Hg and 9. 6 +/- 1.2 mm Hg, respectively) but were normal in the cases of renal failure and eclampsia. CONCLUSION: Despite significant maternal morbidity and mortality, pulmonary artery catheter use in cases of severe preeclampsia or eclampsia was subjectively beneficial in 93 of 100 cases (93%), with an acceptable complication rate (4.0%).

Gillespie P. et al. *Cannula related suppurative thrombophlebitis in the burned patient.* Burns. 2000; 26(2) : 200-4.p Abstract: Suppurative thrombophlebitis is a well recognised and potentially fatal complication of intravenous cannulation in burns patients. We report a case of an Afro-Caribbean patient with noninsulin-dependent diabetes who developed signs of systemic sepsis two weeks after a 14% total body surface area flame burn. Despite an initial paucity of clinical signs at the cannulation site, exploratory venotomy revealed frank suppuration within the long saphenous vein from the ankle to the groin. This was treated successfully by total excision of the vein and its tributaries and delayed wound closure. Following this, a retrospective analysis of the measured clinical parameters and blood tests revealed no obvious, missed pointers to the impending sepsis other than a dramatic increase in the overall daily insulin requirement. This had doubled over a 48-h period, preceding the clinical diagnosis by three days. The relevant literature and guidelines for management are reviewed.

Gimeno C. et al. *In vitro interaction between ofloxacin and cefotaxime against gram-positive and gram-negative bacteria involved in serious infections.* Chemotherapy. 1998; 44(2) : 94-8.p Abstract: The checkerboard method was used to determine the antimicrobial activity of the combination cefotaxime/ofloxacin against 217 bacterial isolates involved in serious infections. Synergy or partial synergy was observed against 19 of 34 (55.8%) Staphylococcus aureus methicillin-susceptible isolates, 4 of 47 (8.4%) Streptococcus pneumoniae isolates, 28 of 34 (82.2%) Escherichia coli isolates and 70 of 102 (68.5%) Pseudomonas aeruginosa isolates. Antagonism was not observed with any of the isolates examined.

Ginesu F. et al. *Etiology and risk factors of adult pneumonia.* J Chemother. 1995; 7(4) : 277-85.p Abstract: The authors point out the remarkable importance that pneumonia has today among infectious diseases, and survey the main risk factors and etiological agents both of the forms acquired in the community and in the hospital, also considering the data from the international literature. The authors stress the high incidence of gram-positive microorganisms, among which Streptococcus pneumoniae is the most widespread in the forms acquired in the community, and the absolute prevalence of the gram-negatives in the nosocomial forms and, among the gram-positives, the pre-eminence of Staphylococcus aureus; these are "difficult" bacterial species, whose prevalence has been determined mainly by induced selective pressure through the inadequate use of antibiotics. The authors also point out the principal factors that favor the onset of pneumonia; they are connected to the host and to the environment; their combination with the infectious agent causes the infective event.

Giono C. S. et al. *Vibrio cholerae 01 fenotipos y genotipos México.* Gac. méd. Méx. 1995; 131(1) : 28-35.p Abstract: Se caracterizaron 26922 cepas de Vibrio cholerae aisladas en México de 1991 a 1993, el patrón fenotípico demostró que 100 por ciento pertenece al biovar El Tor y fueron sensibles a los antibióticos, excepto a la furazolidona, la estreptomicina y el sulfixosasol probados en 1993. Se empleó como marcadores epidemiológicos al 97 por ciento de las cepas que fueorn resistentes. Se observó un cambio drástico en la frecuencia de los serotipo Inaba; en 1991 el 99.5 por ciento de las cepas fueron Inaba mientras que para 1992, el 95.0 por ciento fueron del serotipo Ogawa, fueron toxigénicas, y las no 01 dieron negativa la prueba de ELISA, PCR y los cultivos celulares para investigar toxina colérica. Los ribotipos correspondieron en su mayoría al patrón 5, un lote peque o a la 6a y dos al ribotipo 12. En este estudio se buscó el ribotipo 2, que se ha relacionado con las cepas aisladas del Golfo de México entre las cepas hemolíticas, pero hasta ahora no se ha identificado ninguna cepa con dicho patrón. Para estudios fenotípicos y genotípicos en apoyo al análisis epidemilógico de la enfermedad, es conveniente continuar haciendo el cultivo en una fracción de las muestras para recuperar cepas puras, aunque se utilicen pruebas rápidas para el diagnóstico de cólera (AU).

Gismondo M.R. et al. *[Antimicrobial and sporicidal efficacy of various disinfectant solutions].* Minerva Med. 1995; 86(1-2) : 21-32.p Abstract:

The often indiscriminate use of antimicrobial agents has led to increased bacterial resistance over the past years. This phenomenon is above all evident in nosocomial environments but also at a community level. It is therefore important that, in addition to the rational use of antibiotics, an accurate prophylaxis is performed which includes the correct use of disinfectants. This study examines the antimicrobial activity of various commercially available disinfectant solutions consisting of one or more active ingredients. An analysis of the results reveals that products consisting of an association of individual components (quaternary ammonium chloride with o-phenylphenol and/or isopropyl alcohol; chlorhexidine with benzalkonium chloride or with diazolidinylurea and isopropanol) demonstrate a greater efficacy in terms of microbicidal concentration and contact times.

Gjeruldsen S. et al. *[Yellow staphylococci with borderline resistance to methicillin].* Tidsskr Nor Laegeforen. 1998; 118(26) : 4065-7.p Abstract: Over the last four years there has been an increase in the incidence of borderlineresistant Staphylococcus aureus isolated from bacteriological samples at the Ulleval University Hospital, Department of Medical Microbiology. Several severe infections caused by these bacteria have been noticed in the Department of Infectious Diseases at Ulleval University Hospital. From December 1994 to April 1997, 24 patients suffering from this type of S. aureus infection were examined with regard to clinical and microbiological outcome. 15 of the patients had hospital-acquired infections, and all except one had acquired the infection in Norway. 13 of the patients had at least one predisposing factor, 50% had received antibiotics (mainly cefalosporins) beforehand. Three of the 24 patients died from the infection. We discuss etiology, identification of groups at risk and management of the infection.

Gladziwa U. et al. *[Success and failure with the Demers catheter in dialysis (published erratum appears in Zentralbl Chir 2000;125(3):258)].* Zentralbl Chir. 2000; 125(1) : 48-50.p Abstract: Between January 1995 and January 1999 54 Demers atrial catheters were implanted in 48 uraemic patients. Indications for implantation were: urgent need for haemodialysis with missing vascular access (39), fistula occlusion (7), low shunt flow (3) and problems with a previously implanted catheter (5). We observed 7 catheter infections, 5 catheter occlusions, 1 intraoperative air embolism, 3 haematomas and 1 dacron socket dislocation. The average period of use of an atrial catheter was 170 days, the longest period almost 2 years. The majority of catheters were explanted without any dysfunction. The long time of availability makes Demers atrial catheters an alternative to fistula for multimorbid patients on dialysis with poor long-term survival.

Glupczynski Y. *Antimicrobial resistance in Helicobacter pylori: a global overview.* Acta Gastroenterol Belg. 1998; 61(3) : 357-66.p Abstract: Helicobacter pylori resistance to antimicrobial agents is of particular concern because it is a major determinant in the failure of eradication regimens. Antimicrobial drug resistance has been reported to occur for nitroimidazoles, macrolides, fluoroquinolones, rifampin and tetracyclines. Resistance to nitroimidazoles is the most common, in the range of 30-40% on the average in Europe while the overall prevalence rate of resistance to macrolides is lower, probably ranging between 2-10% in most countries. Development of secondary (acquired) resistance to nitroimidazoles and to the macrolides usually occurs as a rule (> 70-100%) in case of failed eradication therapy. Data available from several centres seems however to indicate that a significant shift towards increasing resistance to metronidazole and to the macrolides might have possibly occurred in many countries over the last years. Resistances to both metronidazole and to clarithromycin are the most significant ones because they influence the success of the treatments although this seems to be less marked and more dependent on the treatment regimens considered in the case of metronidazole resistance than in the setting of clarithromycin resistance. These differences may in part relate to methodological variations and to the inherent difficulties in assessing the susceptibility of H. pylori to metronidazole. It is possible that different resistance cut-off might also have to be considered for metronidazole depending on the treatment regimens administered. The mechanisms of resistance have been well defined for the macrolides and are beginning to be unraveled for the nitroimidazoles. In all cases, resistance of H. pylori to antimicrobial agent seems to be due to the development of single mutational events in chromosomal genes rather than to the acquisition of exogenous resistance genes. Owing to the restricted ability of microbiology laboratories with expertise in H. pylori culture and the lack of standardised methodology for susceptibility testing, H. pylori culture is not often performed routinely. It should however be considered after documented treatment failure or in patients from a geographic area or of an ethnic origin with higher likelihood of antimicrobial drug resistance. Likewise it is deemed very important to institute national and regional surveillance programs to follow the evolution of H. pylori resistance and to better adapt treatment regimens to changes in resistance patterns.

Glupczynski Y. et al. *A multicentre survey of antimicrobial resistance in gram-negative isolates from Belgian intensive care units in 1994-1995. Belgian Multicenter ICU Study Group.* Acta Clin Belg. 1998; 53(1) : 28-38.p Abstract: The aim of this prospective study was to evaluate the distribution and antibiotic susceptibility of aerobic Gram-negative bacilli isolated from patients in intensive care units in 18 Belgian hospitals during 1994 and 1995. A standardised method (i.e. the E-test) was used in each center to determine the minimum inhibitory concentrations of 12 major antibiotics against 1435 consecutive, non duplicate, Gram-negative isolates (close to 100 strains per hospital) during a period of 6 months. The isolates were mainly isolated from the lower respiratory tract (57.4%), urinary tract (17.7%), pus (7.9%) or blood specimens (7.8%) and were mainly P.aeruginosa (20.3%), E.coli (19.9%) and Enterobacter spp. (12.6%). Overall inducible Enterobacteriaceae (IE) accounted for 29.8% of all isolates, and E.aerogenes was the most frequently isolated species in this group (27.6%). The overall susceptibility rate (all species confounded) was about 70% to piperacillin, ticarcillin-clavulanic acid and ceftriaxone, 78% to piperacillin-tazobactam; 87% both to ceftazidime and to ciprofloxacin; and 90% to imipenem. Widespread resistance was observed in several IE species to third generation cephalosporins, broad-spectrum penicillins and to ciprofloxacin. By contrast, imipenem and the aminoglycosides still retained excellent activity against most multiresistant species. Although there were wide differences between hospitals in the frequencies of resistance to most antibiotics, these were not related to the types (general vs. university) of hospitals or to the number of beds. Some variations were however observed in the distribution of bacterial species: the prevalence of inducible Enterobacteriaceae was significantly higher in university than in general hospitals and in hospitals located in Brussels and in Wallonia than in the Flanders. Overall few trends in resistance rates were observed in comparison to a similar survey performed in 1991.

Glynn M.K. et al. *Emergence of multidrug-resistant Salmonella enterica serotype typhimurium DT104 infections in the United States.* N Engl J Med. 1998; 338(19) : 1333-8.p Abstract: BACKGROUND: Strains of salmonella that are resistant to antimicrobial agents have become a worldwide health problem. A distinct strain of Salmonella enterica serotype typhimurium, known as definitive type 104 (DT104), is resistant to ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline and has become a major cause of illness in humans and animals in Europe, especially the United Kingdom. METHODS: To characterize typhimurium DT104 infections in the United States, we analyzed data collected by local and state health departments and public health laboratories between 1979 and 1996 in national surveys of the antimicrobial-drug resistance of salmonella. Selected typhimurium isolates with the five-drug pattern of resistance were phage typed. RESULTS: The prevalence of typhimurium isolates with the five-drug pattern of resistance

increased from 0.6 percent in 1979-1980 to 34 percent in 1996. In 1994-1995, such isolates were identified in samples from 36 of the 46 surveillance sites (78 percent). Thirty-nine of 43 typhimurium isolates with the five-drug pattern of resistance identified in 1994-1995 and 1996 were phage type DT104 or a closely related phage type. CONCLUSIONS: Multidrug-resistant typhimurium DT104 has become a widespread pathogen in the United States. More prudent use of antimicrobial agents in farm animals and more effective disease prevention on farms are necessary to reduce the dissemination of multidrug-resistant typhimurium DT104 and to slow the emergence of resistance to additional agents in this and other strains of salmonella.

Gniadkowski M. et al. *[Susceptibility of Pseudomonas aeruginosa isolated from hospital infections to antibiotics].* Pol Merkuriusz Lek. 1998; 5(30) : 346-50.p Abstract: A total of 674 clinical isolates of Pseudomonas aeruginosa were collected from 30 different hospitals located in 26 cities of Poland. These were 12 big regional hospitals, 7 large teaching hospitals, 4 specialised hospitals curing patients from the whole country, 6 small local hospitals and one regional paediatric hospital. The majority of strains were collected from patients hospitalised at ICUs (25.7%), surgical (21.7%), and internal medicine wards (9.9%). The isolates were recovered from different types of infections, mostly from respiratory tract infections (33.7%), wound infections (22.3%), and urinary tract infections (22.0%). All the isolates were subjected to antimicrobial susceptibility testing by MIC values evaluation. MICs of 13 different antibiotics (beta-lactams, aminoglycosides, chinolones) were determined by the agar dilution method. The general level of resistance of P.aeruginosa observed in the study was high, especially when compared to results of surveys obtained in other countries. Out of the antimicrobials used the highest activity in vitro was observed with meropenem, imipenem, piperacillin—tazobactam and ceftazidime. The high in vitro activity of ceftazidime was striking considering the long time of the use of this antibiotic in Polish hospitals. The highest levels of resistance were observed to some of the aminoglycosides. Populations of strains isolated in different wards or hospitals of different size were characterised by different susceptibility patterns.

Godfrey H. et al. *Management of long-term urethral catheters: minimizing complications.* Br J Nurs. 2000; 9(2) : 74-6, 78-81.p Abstract: Urinary tract infections, tissue damage and encrustation of the catheter, which may cause blockage, are all complications that can arise during long-term catheterization. It is important for nurses to provide effective catheter care in order to minimize the incidence of these complications. There is still controversy in the nursing literature about certain aspects of catheter management. This article explores a number of aspects of catheter care and suggests a rationale for effective and safe management, including the choice of catheter, choice of drainage system, care of the individual and the care of catheter and drainage system.

Goetz A.M. et al. *Complications related to intravenous midline catheter usage. A 2-year study.* J Intraven Nurs. 1998; 21(2) : 76-80.p Abstract: The introduction of the Landmark midline catheter (Menlo, Co., CA) brought an alternative to central line catheter placement for prolonged intravenous access. The study was initiated in 1993 to observe for complications, including hypersensitivity-like reactions. The authors hypothesized this i.v. modality would decrease the need for central i.v. lines and accompanying complications. At the time of catheter insertion, the i.v. team nurses completed a survey form that included demographics, underlying disease, and risk factors for infection. The catheter tip was cultured at the time of removal. In the second phase of the study, the authors focused specifically on hypersensitivity-like reactions. During a 2-year period, 248 patients had 334 midline catheters. Patient ages ranged from 23 to 98 years (mean age, 65 years). The bacteremia rate was 0.3%; the colonization rate was 0.9%. Factors associated with infection/ colonization included: length of time in place, chemotherapy, and lack of antibiotic administration. In the second phase of the study, during which an additional 170 catheters were placed in 131 patients, no hypersensitivity-like reactions were noted. The midline catheter appears to be a safe method of i.v. fluid administration for patients with limited peripheral vein access who need extended i.v. therapy.

Goetz A.M. et al. *Nosocomial legionnaires' disease discovered in community hospitals following cultures of the water system: seek and ye shall find.* Am J Infect Control. 1998; 26(1) : 8-11.p Abstract: BACKGROUND: The reservoir for hospital-acquired legionnaires' disease is the water distribution system. The Allegheny County (Pa.) Health Department recommended environmental cultures for all health care facilities for the prevention of hospital-acquired Legionella infection including facilities with no known cases of legionnaires' disease. METHODS: Environmental cultures of hot water tanks, faucets, and showerheads were performed in six health care facilities according to health department guidelines. If hot water tanks, faucets, or showerheads yielded Legionella, monitoring with Legionella culture and urinary antigen was performed for all cases of nosocomial pneumonia. RESULTS: Legionella was isolated from the water distribution system in 83% (five of six) of facilities. Three facilities dropped out of the study; two decided to disinfect the water and one had no Legionella in the water system. The other three facilities all discovered cases of legionnaires' disease during the 1-year study period after introduction of Legionella testing. L. pneumophilia, serogroups 1, 3, and 5, caused 12 cases of hospital-acquired legionnaires' disease. Positive diagnostic tests included: 10 of 12 (83%) urinary antigen, 6 of 8 (75%) respiratory cultures, and 2 of 5 (40%) serology. Molecular typing confirmed that the source of infection was the water supply in two hospitals. CONCLUSION: Routine environmental cultures for Legionella in the water distribution system are recommended even if the hospital had not previously recognized cases of hospital acquired legionnaires' disease. The Allegheny County Health Department guidelines were inexpensive to implement and resulted in the discovery of cases that would have otherwise been undiagnosed.

Goh S.H. et al. *HSP60 gene sequences as universal targets for microbial species identification: studies with coagulase-negative staphylococci.* J Clin Microbiol. 1996; 34(4) : 818-23.p Abstract: A set of universal degenerate primers which amplified, by PCR, a 600-bp oligomer encoding a portion of the 60-kDa heat shock protein (HSP60) of both Staphylococcus aureus and Staphylococcus epidermidis were developed. However, when used as a DNA probe, the 600-bp PCR product generated from S. epidermidis failed to cross-hybridize under high-stringency conditions with the genomic DNA of S. aureus and vice versa. To investigate whether species-specific sequences might exist within the highly conserved HSP60 genes among different staphylococci, digoxigenin-labelled HSP60 probes generated by the degenerate HSP60 primers were prepared from the six most commonly isolated Staphylococcus species (S. aureus 8325-4, S. epidermidis 9759, S. haemolyticus ATCC 29970, S. schleiferi ATCC 43808, S. saprophyticus KL122, and S. lugdunensis CRSN 850412). These probes were used for dot blot hybridization with genomic DNA of 58 reference and clinical isolates of Staphylococcus and non-Staphylococcus species. These six Staphylococcus species HSP60 probes correctly identified the entire set of staphylococcal isolates. The species specificity of these HSP60 probes was further demonstrated by dot blot hybridization with PCR-amplified DNA from mixed cultures of different Staphylococcus species and by the partial DNA sequences of these probes. In addition, sequence homology searches of the NCBI BLAST databases with these partial HSP60 DNA sequences yielded the highest matching scores for both S. epidermidis and S. aureus with the corresponding species-specified probes. Finally, the HSP60 degenerate primers were shown to amplify an anticipated 600-bp PCR product from all 29 Staphylococcus species and from all but 2 of 30 other microbial species, including various gram-positive and gram-negative bacteria, mycobacteria, and fungi. These preliminary

data suggest the presence of species-specific sequence variation within the highly conserved HSP60 genes of staphylococci. Further work is required to determine whether these degenerate HSP60 primers may be exploited for species-specific microbic identification and phylogenetic investigation of staphylococci and perhaps other microorganisms in general.

Golanska E. et al. *Characterisation of a new host-vector system for fast-growing mycobacteria*. Acta Microbiol Pol. 1998; 47(4) : 335-43.p Abstract: In this paper we describe the development of a host-vector system for genetic studies of fast-growing mycobacteria able to biotransform sterols. A wild strain Mycobacterium smegmatis SN38 and a biotechnological mutant Mycobacterium vaccae B3805 were transformed by electroporation with the pSMT3 E. coli-Mycobacterium shuttle plasmid harbouring the hygromycin resistance gene. Both, the pSMT3 plasmid and its derivative pSMT3-ksdD carrying the 3-ketosteroid-delta 1-dehydrogenase gene (ksdD) from Arthrobacter simplex were stably maintained in M. vaccae B3805. The presence of the pSMT3 vector did not affect biotransformation activities of the host strain. We consider the M. vaccae B3805 strain and the pSMT3 plasmid to be a good host-vector system for cloning in mycobacteria genes coding enzymes involved in steroid degradation pathway.

Goldfarb J. *New antimicrobial agents.* Pediatr Clin North Am. 1995; 42(3) : 717-35.p Abstract: In any discussion of new antimicrobial agents in the 1990s, a warning and a plea are necessary. The spreading emergence of resistance among bacteria raises concerns for the effectiveness of antimicrobial therapy. Penicillin-resistant pneumococci are probably of most significance in pediatrics and are increasing in frequency, in part related to the use of antimicrobial therapy in young children to treat such infections as otitis media. New practice guidelines have suggested the more limited use of antimicrobial agents in treating serious otitis media. When pediatricians do treat, they should select effective agents. Limiting therapy to brief courses with effective and narrow-spectrum agents may be helpful also. Treating long enough to ensure eradication in serious infections is equally important. Methicillin-resistant S aureus are also increasing and are increasingly a concern in community-acquired infections and nosocomial infections. Using topical agents, such as mupirocin, to treat impetigo and other superficial skin infections can limit exposure to systemic agents and may delay the spread of resistance. Vancomycin-resistant enterococcal infections, an infrequent pediatric problem, are most frightening because no alternative therapies are available. Their occurrence is directly related to use of vancomycin in the communities that are affected. Containing the spread of drug-resistant bacteria will likely require a concerted effort by both physicians and the public. The indiscriminate use of antimicrobial agents to treat non-bacterial infections should be contained. The public must be educated to understand that antimicrobial agents are ineffective against viral infections. In the setting of managed care, educating administrators who make practice decisions that cheaper is not always better will be crucial. The issues of day-care infections and spread of potential pathogens must take on increasing attention and methods to decrease infection sought. Curbing inappropriate use of antimicrobial agents will be as important as learning the nuances between new agents.

Goldman L.J. et al. *Successful airway control with the laryngeal mask in an infant with Beckwith-Wiedemann syndrome and hepatoblastoma for central line catheterization*. Paediatr Anaesth. 2000; 10(4) : 445-8.p Abstract: We present a case of an infant with severe macroglossia, hypoglycaemia and inguinal hernia associated with hepatoblastoma (Beckwith-Wiedemann syndrome) in which a laryngeal mask airway (LMA) was useful to secure the airway during central line insertion. Carbon dioxide monitoring through LMA proved effective to assess airway patency during positioning for central vein puncture. In this syndrome, where a potentially difficult airway may be encountered, LMA allowed adequate ventilation, avoiding the risk and inconvenience of tracheal intubation.

Goldman M.P. *Antibiotic prophylaxis in the critical care setting.* Crit Care Nurs Clin North Am. 1995; 7(4) : 667-74.p Abstract: The prevention of infection in critically ill patients is a difficult and often frustrating task. Selective digestive decontamination may be a useful means of preventing infections in specific patient populations; however, not all critical care patients will benefit. In this article, mechanisms of antimicrobial resistance are discussed along with the consideration of specific measures to deal with this growing dilemma. Concerns about specific microorganisms, such as vancomycin-resistant enterococcus and multidrug-resistant Enterobacter species, are addressed. It is clear that the use of antimicrobial agents is not the only solution to the problem of infection in critically ill patients.

Goldman R.C. et al. *Inhibition of transglycosylation involved in bacterial peptidoglycan synthesis.* Curr Med Chem. 2000; 7(8) : 801-20.p Abstract: The continuing spectre of resistance to antimicrobial agents has driven a sustained search for new agents that possess activity on drug resistant bacteria. Although several paths are available to reach this goal, the most generalized would be the discovery and clinical development of an agent that acts on a new target which has not yet experienced selective pressure in the clinical setting. Such a target should be essential to the growth and survival of bacteria, and sufficiently different from, or better still non-existent in, the human host. The transglycosylation reaction that polymerizes biochemical intermediates into peptidoglycan qualifies as such a target. This biochemical system accepts the basic unit N-acetylglucosamine-beta-1, 4-N-acetyl-muramyl-pentapeptide-pyrophosphoryl-undecaprenol (lipid II), and leads to polymerization of the N-acetylglucosamine - beta-1, 4-N-acetyl-muramyl-pentapeptide segment into peptidoglycan. Approaches to targeting this reaction include modification of known glycolipid and glycopeptide natural product antibiotics. The synthesis and antibacterial activity of synthetic analogs of moenomycin having novel antibacterial activities not present in the parent structure will be presented, together with the combinatorial chemistry and assay systems leading to their discovery. Likewise, we will discuss chemical modifications to specific glycopeptide antibiotics that have extended their spectrum to include vancomycin resistant enterococci that substitute D-alanyl-D-lactate for D-alanyl-D-alanine in their peptidoglycan. Two differing theories, one positing the generation of high affinity, specific binding to D-alanyl-D-lactate via glycopeptide dimerization and/or membrane anchoring, and the other supporting direct targeting of the modified glycopeptide to the transglycosylation complex, seek to explain the mechanism of action on vancomycin resistant enterococci. Biochemical evidence in support of these two theories will be discussed.

Goldmann D.A. et al. *Control of nosocomial antimicrobial-resistant bacteria: a strategic priority for hospitals worldwide.* Clin Infect Dis. 1997; 24 Suppl 1 : S139-45.p Abstract: The rapid emergence and dissemination of antimicrobial-resistant microorganisms in hospitals worldwide is a problem of crisis dimensions. The root causes of this problem are multifactorial, but the core issues are clear. The emergence of antimicrobial resistance is highly correlated with selective pressure that results from inappropriate use of antimicrobial agents. Dissemination of resistant organisms is facilitated by person-to-person transmission due to inconsistent application of basic infection control practices by hospital personnel. While control strategies exist, the interventions are not likely to be successful unless hospital leaders assume the responsibility for control of antimicrobial resistance. Strategic goals for the control of resistant organisms should be formulated on the basis of multidisciplinary input from hospital personnel. Processes and outcomes relevant to these strategic goals should be measured, and the resultant data should be used to design, implement, and evaluate systematic measures to increase the appropriate use of antimicrobial agents and basic infection control practices. This approach is as relevant to hospitals in countries with limited resources as it is to in fully industrialized countries.

Goldstein E. et al. *Are serum levels of vancomycin useful in the first week of therapy?* Mo Med. 1995; 92(9) : 596-9.p Abstract: Controversy exists regarding the need to monitor serum concentrations of vancomycin with some investigators recommending measurement of peak and trough concentrations in the first week of therapy and regularly thereafter, whereas others contend that empiric dosing produces safe and effective drug concentrations so that testing is unnecessary. Since vancomycin concentrations are measured, routinely in our hospital in the first week of therapy, we conducted a 12 month study to assess their clinical value in patients who were treated when gram positive cocci were detected in blood culture smears. One-hundred-five patients had gram positive cocci on blood culture smears. These bacteria were pathogens in 15 patients with Staphylococcus aureus and in 18 with coagulase negative staphylococci based on microbiologic criteria and a chart review confirming their clinical significance. Ten patients with S. aureus and 8 patients with coagulase negative staphylococci that were pathogens and 10 patients with coagulase negative staphylococci that were contaminants were treated with vancomycin. Serum peak and trough concentrations of vancomycin obtained within the first 5 days of therapy in these 28 patients were 14 to 40 micrograms/ml and 4.8 to 20 micrograms/ml. These concentrations were much above the MIC's of the microorganisms (< 4 micrograms/ml). Five patients had increases of serum creatinine of more than 0.6 mg% and in each patient the increases were attributable to other causes-shock, heart failure, and preexisting renal failure. Fifty five peak and trough concentrations 19 of which were drawn in patients with contaminated cultures were measured at a cost of $2,475.(ABSTRACT TRUNCATED AT 250 WORDS).

Goldstein F.W. et al. *Antimicrobial resistance among lower respiratory tract isolates of Streptococcus pneumoniae: results of a 1992-93 western Europe and USA collaborative surveillance study. The Alexander Project Collaborative Group.* J Antimicrob Chemother. 1996; 38 Suppl A : 71-84.p Abstract: One thousand, eight hundred and fifty-six Streptococcus pneumoniae strains, collected in 1992 and 1993 from 15 centres in Western Europe and USA were tested for susceptibility to 16 antibiotics. The overall resistance to penicillin was 23% (range 6-54%), with the highest prevalences in Madrid, Barcelona, Toulouse and Cleveland. Seven centres reported low-level penicillin resistance only. Amoxycillin was more active than ceftriaxone against strains with intermediate resistance to penicillin, and at least four-fold more active than cefuroxime; cefaclor and cefixime had poor activity. Against penicillin-resistant strains, ceftriaxone was slightly more active than amoxycillin, cefuroxime exhibited borderline activity and cefixime and cefaclor were inactive. Ten strains fully susceptible to penicillin had MICs of ceftriaxone > or = 0.1 mg/L; this may represent a first step towards the development of cephalosporin resistance. With the exception of fluoroquinolones, resistance to non-beta-lactam antibiotics (chloramphenicol, doxycycline, co-trimoxazole, erythromycin, clarithromycin and azithromycin) was considerably higher in penicillin-resistant strains compared with penicillin-susceptible isolates. Erythromycin-resistant isolates were also resistant to the other macrolides tested.

Gollapudi S. et al. *Difloxacin reverses multidrug resistance in HL-60/AR cells that overexpress the multidrug resistance-related protein (MRP) gene.* Oncol Res. 1995; 7(5) : 213-25.p Abstract: In this study, we have examined the in vitro chemosensitizing activity of difloxacin, a quinolone antimicrobial agent, in the multidrug-resistant human myeloid leukemia HL-60/AR cell line. HL-60/AR cells were found to overexpress multidrug resistance-associated protein (MRP) mRNA as compared to HL-60 cells. Difloxacin, in a concentration-dependent manner, increased the sensitivity of HL-60/AR cells to daunorubicin, adriamycin, and vincristine, and partially corrected the altered drug transport. In addition, difloxacin corrected subcellular distribution of adriamycin by inducing redistribution of the drug from the perinuclear region to the nucleus in HL-60/AR cells. The chemosensitizing effect of difloxacin was observed at clinically achievable concentrations. We conclude that difloxacin is an effective chemosensitizer of MRP-associated multidrug-resistant tumor cells and is a potential candidate for clinical use to reverse multidrug resistance.

Gomez-Garces J.L. et al. *Susceptibilities of fluoroquinolone-resistant strains of Campylobacter jejuni to 11 oral antimicrobial agents.* Antimicrob Agents Chemother. 1995; 39(2) : 542-44.p Abstract: The resistance of Campylobacter jejuni strains to the fluoroquinolones is increasingly frequent, and in our area it reaches nearly 50%. We studied the susceptibilities of 60 of these strains to 11 oral antibiotics. All strains except one were susceptible to the macrolides tested, with azithromycin being the most active agent tested. Of the rest of the antibiotics studied, amoxicillin-clavulanic acid, clindamycin, and fosfomycin displayed good in vitro activities. Knowledge of the susceptibilities of these microorganisms to a varied group of oral agents is necessary in view of the appearance of multiresistant strains, such as those included in our series.

Gomez-Garces J.L. et al. *[Factors of pathogenicity, biotype, serotype and antimicrobial sensitivity of 150 clinical isolates of Yersinia enterocolitica (1992-1994)].* Enferm Infecc Microbiol Clin. 1996; 14(10) : 596-9.p Abstract: BACKGROUND: Yersinia enterocolitica is an important pathogen in temperate climates. The heterogeneity of the microorganisms covered by this denomination has a made grouping and identification schemes necessary. METHODS: A series of 150 different, consecutive isolates from patients with diarrheic syndrome living in an urban area with a population of approximately 500,000 inhabitants, were studied in order to evaluate their biochemical, antigenic and sensitivity characteristics. RESULTS: There was a high degree of uniformity among the strains isolated, 144 (96%) of which were identified as Yersinia enterocolitica sensu stricto, biotype 4, serotype 0:3. These strains presented, almost invariably, the same susceptibility pattern, being sensitive to amoxicillin/clavulanic acid, piperacillin, cefamandole, cefoxitin, gentamicin, amikacin, tetracycline and cotrimoxazole, and highly resistant to ampicillin, ticarcillin and cephazotin. In addition, 5 strains of Yersinia frederiksenii were isolated. The biochemical, epidemiological and sensitivity characteristics of these strains differed from those invariably found in the rest of the isolates. CONCLUSIONS: The data obtained in this study, shown a high degree of uniformity in the strains of Yersinia enterocolitica isolated in our area in recent years, with regard to both their biochemical characteristics and their sensitivity patterns. The isolations of the other biogroups may be regarded as extremely infrequent in the stool culture of patients with diarrhea treated in our hospitals.

Gomez-Lus R. et al. *Emerging and reemerging pathogens.* Int J Antimicrob Agents. 2000; 16(3) : 335-9.p Abstract: From 1973 to 1995, 29 new and reemerging pathogenic microbes were recognized. However, in discussions about emerging infectious diseases, the focus is often on the clinical effects of the host-parasite relationship, rather than the examination of the biology of the pathogen. Many of what we refer to as emerging diseases are characterized better as 'diseases of human progress'. Thus, the aerosolization of water has played an important role in the emergence of Legionella pneumophila infections. New diseases are superimposed on endemic diseases such as diarrhoeal diseases, malaria and tuberculosis. In addition, many pathogens are becoming increasingly resistant to standard antimicrobial drugs, making treatment difficult and in some cases impossible. We summarize our experience on emerging parasitic diseases (primary amoebic meningoencephalitis, respiratory cryptosporidiosis, and diplogonoporiasis), and selected problems of bacterial resistance (MDR tuberculosis caused by Mycobacterium bovis and macrolide-resistance mechanisms of Streptococcus pneumoniae and S. pyogenes).

Gómez Marín J.E. et al. *Análisis de polimorfismos de los fragmentos de restricción (RFLP) y epidemiología de la tuberculosis.* Bol. Oficina Sanit.

Panam. 1995; 119(1) : 1-10.p Abstract: Con objeto de estudiar los polimorfismos del elemento de inserción 6110 (IS6110) en cepas de Mycobacterium tuberculosis aisladas de pacientes colombianos y la resistencia a medicamentos antituberculosos en el departamento del Quindío, Colombia, se efectuó un estudio prospectivo con una muestra consecutiva de 59 pacientes con tuberculosis pulmonar sistomática, confirmada por baciloscopia, con y sin historia de tratamiento. Los pacientes, que participaron en el programa de Control de la Tuberculosis del Instituto Seccional de Salud del Quindío en Armenia, Colombia, fueron todos aquellos que consultaron a centros de salud y hospitales locales en zonas urbanas y rurales del Quindío de marzo a julio de 1993. Se hicieron exámenes de esputo con cultivos y pruebas de sensibilidad a medicamentos. Posteriormente se analizaron los polimorfismos del tamaño de los fragmentos de restricción (RFLP) del IS6110, según los protocolos de van Soolingen, et al. (1992). Para clasificar los casos se usó la historia de tratamiento, aplicando los criterios de la OMS (1991). Se encontraron 44 cultivos a M. tuberculosis y uno positivo a M. africanum. Se observó resistencia inicial a los medicamentos en 4 de 42 cultivos, o 9,5 por ciento (IC95 por ciento: 0,6 a 18): 4,8 por ciento mostraron resitencia a la isoniacida (INH) y 4,8 por ciento a isoniacida y estreptomicina (INH-SM). Se observo resistencia adquirida en dos de tres cultivos, o 66 por ciento (a isoniacida, rifampicina y estreptomicina [INH-RM-SM] y a isoniacida, etambutol, rifampicina y estreptomicina [INH-EMB-RM-SM]. En 27 cepas sometidas a análisis de RFLP, el número de copias del IS6110 varió de 6 a 17. Los coeficientes de similitud revelaron cinco grupos distintos. En resumen, el análisis de los RFLP del IS6110 sirve para identificar distintas cepas de micobacterias y tiene amplia utilidad en estudios epidemiológicos y en la toma de decisiones sobre los programas de control de la tuberculosis.

Gomez Rodriguez N. et al. *[Septic arthritis caused by Salmonella enteritidis in systemic lupus erythematosus].* An Med Interna. 1996; 13(1) : 27-30.p Abstract: Systemic Lupus Erythematosus (SLE) is among the chronic diseases thought to predispose patients to severe Salmonella infections. However, arthritis and osteomyelitis due to this microorganisms are more frequently seen in patients with sickle-cell disease than SLE. We report two cases of SLE and osteoarticular infections by Salmonella enteritidis: A 36-years old woman with bilateral knee arthritis associated with femoral osteomyelitis and a 22-years-old woman who presented with left knee arthritis.

Gonçalves A.J.R. *Mudanças dos padrões epidemiológicos e clínicos das doenças infecciosas nos últimos 35 anos.* J. bras. med. 1995; 68(1/2).p Abstract: Nas últimas três décadas, as doenças infecciosas sofreram notáveis transformações na maior parte de seus aspectos. São aqui mostrados apenas os mais importantes concernentes … epidemiologia e os verificados no âmbito clínico. Além de serem identificadas doenças novas e descritos vários agentes causadores dessas moléstias antes desconhecidos, muitas manifestações clínicas foram melhor compreendidas com os avanços nas áreas de patogenia, patologia e imunologia. Nas características de hospedeiros, vetores e agentes produtores de doenças, ocorreram extraordinárias mudanças. Foram detectados novos nichos ecológicos para patógenos tradicionais e apontadas novas formas de transmissão de doenças infecciosas. Fenômenos clínicos inexplicados passaram a ser melhor caracterizados e obtiveram entendimento. Em função da introdução de medicamentos como os novos antimicrobianos, particularmente, foram registradas alterações clínicas em muitas patologias infecciosas. Se em 10 anos de programa (1967-1977) erradicou-se da face da terra a varíola, vimos surgir a síndrome da imunodeficiência adquirida (sida/Aids), já precedida pelos graves problemas referentes …s infecções nosocomiais e …s patologias dos hospedeiros imunossuprimidos, em decorrência dos aperfeiçamentos médicos. Além dos progressos na Medicina e das medidas preventivas, ponderam na responsabilidade por tais metamorfoses fatos de ordem comportamental, social e ambiental. Incluem-se entre eles as mutações nos padrões de inter-relacionamento humano, movimentos migratórios, rupturas de ecossistemas e a intensificação de viagens intercontinentais. Até mesmo as atividades recreativas ou a internacionalização de peculiaridades culinárias são reconhecidas como geradoras de diversificações nos padrões epidemiológicos e clínicos das doenças infecciosas. Em estreita interligação e numa espécie de sinergismo constante, a carência de recursos, empobrecimento, ignorância, miséria, fome, desnutrição, revoluções e guerras, aliados … ausência de uma justa priorização dos valores humanos, representam, especialmente nos países do Terceiro Mundo, ingredientes fortíssimos para a manutenção de endemias e epidemias ou para a enraização de doenças infecciosas de toda sorte. (AU).

Gonzalez-Barca E. et al. *Prognostic factors influencing mortality in cancer patients with neutropenia and bacteremia.* Eur J Clin Microbiol Infect Dis. 1999; 18(8) : 539-44.p Abstract: The purpose of this study was to identify risk factors for mortality in neutropenic patients with cancer and bacteremia. A consecutive sample of 438 neutropenic patients (granulocyte count <0.5 x 10(9)/l) with cancer and bacteremia was studied to identify the clinical characteristics associated with mortality at the onset of bacteremia. The mean age of the subjects was 48 years (range, 15-87 years). Most cases of bacteremia (77%) were hospital-acquired and occurred in patients with acute leukemia (48%). Gram-positive organisms caused 233 (53%) episodes of bacteremia, gram-negative organisms caused 151 (34%) episodes, and 48 (11%) episodes were polymicrobial. The overall mortality within 30 days of the onset of bacteremia was 24.4%. The variables found to be independently associated with increased mortality using logistic regression techniques were as follows: shock at the onset of bacteremia (OR, 10; 95% CI, 4.2-23.8), pneumonia (OR,4.4; 95% CI, 1.9-10), uncontrolled cancer (OR,4.3; 95% CI, 1.5-12.7), and absence of prophylaxis with norfloxacin (OR,2.4; 95% CI, 1.3-4.5). The prognostic factors ascertained in this study may help to identify those patients at higher risk of death. Medical intervention addressing some of these factors may improve the outcome of bacteremia in neutropenic patients with cancer.

Gonzalez C.J. et al. *Bacterial microflora of wild brown trout (Salmo trutta), wild pike (Esox lucius), and aquacultured rainbow trout (Oncorhynchus mykiss).* J Food Prot. 1999; 62(11) : 1270-7.p Abstract: Initial numbers of bacteria associated with wild (brown trout and pike) and cultured (rainbow trout) freshwater fish as well as with the water in which they were caught were determined. Subsequently, a total of 979 randomly selected isolates were characterized and identified to the genus level. For all counts performed (aerobes, psychrotrophs, anaerobes, Enterobacteriaceae, and enterococci), no significant differences were observed in water samples, the highest level corresponding to psychrotrophs in pike environments (4.23 X 10(3) CFU/ml). Overall, the skin and intestinal content of brown trout were the most contaminated, while rainbow trout specimens (gills and gut) yielded the lowest numbers. For all bacterial groups, pike gills had the highest numbers. Counts for all of the sampling sites compare well with findings in other temperate geographical environments. Biological characteristics (feeding and skin properties) and the use of antimicrobials in aquaculture might have influenced these results. Motile and nonmotile aerobic gram-negative bacteria together with Enterobacteriaceae accounted for 50 to 70% of the psychrotrophs isolated from water. Micrococcaceae, lactic acid bacteria, Bacillus, and coryneforms were also found. The groups represented in psychrotrophic isolates from the outer surfaces do not reflected those detected in water, so it was common that those organisms recovered in significant numbers from fish were not detected in surrounding habitat of the fish. Motile aeromonads and Carnobacterium were the dominant psychrotrophs in the guts of pike and brown trout, respectively. The intestinal content of reared fish gave a high incidence of Bacillus and coryneforms, while Enterobacteriaceae was absent. Again, rearing practices could have influenced this finding. Listeria monocytogenes was not detected in any of the examined samples. Two strains of Salmonella, which belonged to the same serovar and lysotype, were recovered from

pond-water samples taken from one facility on different sampling days. From the gut of a pike specimen and from the pike's environment, two Plesiomonas shigelloides strains of different serovars were recovered. These latter four strains were resistant to a considerable number of antimicrobial compounds (multiple antibiotic resistance indices > 0.2).

Goodwin C.S. *Antimicrobial treatment of Helicobacter pylori infection.* Clin Infect Dis. 1997; 25(5) : 1023-6.p Abstract: Helicobacter pylori is susceptible to many antimicrobials, but clinically only a few are effective. Two antimicrobials with bismuth or ranitidine or a proton pump inhibitor such as omeprazole are required to achieve a cure rate of >90% and to avoid resistance, which occurs when clarithromycin or metronidazole is the single antimicrobial used. Bismuth plus metronidazole and tetracycline is effective but causes more side effects than does treatment with omeprazole, amoxicillin, and clarithromycin; metronidazole can replace clarithromycin. To ensure a high cure rate, treatment is required for 10 days, but 7-day regimens have sometimes been as successful. A course of ranitidine bismuth citrate for 28 days, given with clarithromycin for the first 14 days, cures 80%-85% of patients, but given with amoxicillin it cures only 74%. In developing countries resistance to metronidazole can reach 95%. An inexpensive regimen is bismuth subsalicylate (two tablets) plus furazolidone (100 mg), four times daily for 4 weeks; however, as this yields a cure rate of only 72%, this regimen is not truly cost-effective.

Gorduysus O. *An evaluation of antimicrobial efficiency of Endo-Fill root canal sealant and filling material.* J Endod. 1999; 25(10) : 652.p Abstract: The antimicrobial efficiency of Endo-Fill root canal sealant and filling material was microbiologically evaluated. The zones of inhibition around the Endo-Fill by agar diffusion method were measured. Staphylococcus aureus, Streptococcus faecalis, Streptococcus pyogenes, Escherichia coli, Candiada albicans, and Pseudomonas aeruginosa were used as the selected microorganisms. No zone of inhibition was seen around the Endo-Fill in any of the examples.

Gotfried M.H. *Comparison of bacteriologic eradication of Streptococcus pneumoniae by clarithromycin and reports of increased antimicrobial resistance.* Clin Ther. 2000; 22(1) : 2-14.p Abstract: OBJECTIVE: To determine whether reported increases in Streptococcus pneumoniae resistance, as determined by in vitro antimicrobial susceptibility testing, correlate with the clinical efficacy of clarithromycin in treating patients with acute exacerbations of chronic bronchitis (AECB) or community-acquired pneumonia (CAP). BACKGROUND: Surveillance data on antimicrobial resistance suggest that the overall rate of S. pneumoniae resistance in vitro in the United States has increased to approximately 45% during the past decade. S. pneumoniae is showing increased resistance to penicillin, other beta-lactams, and macrolides. Despite this increased resistance, the clinical efficacy of clarithromycin does not appear to be diminished to the degree suggested by reported resistance rates. The author examined several studies of clarithromycin in patients with AECB or CAP that demonstrate S. pneumoniae eradication rates in vivo of approximately 92%. The discordance between reported increases in resistance of S. pneumoniae isolates in vitro and the eradication rate with clarithromycin in vivo is discussed in light of 5 observations. RESULTS: First, surveillance data on S. pneumoniae resistance rates to clarithromycin may be overestimated. Second, efflux mutant strains may not be clinically resistant. Third, host immune defenses play a role in treatment outcomes. Fourth, in vitro resistance may not correlate with in vivo clinical success. Finally, clarithromycin and its active metabolite, 14-OH-clarithromycin, attain high concentrations in patients. CONCLUSION: Reported increases in the prevalence of S. pneumoniae resistance do not appear to have had proportional effects on the clinical efficacy of clarithromycin in the treatment of patients with AECB or CAP caused by S. pneumoniae.

Gottenbos B. et al. *Initial adhesion and surface growth of Staphylococcus epidermidis and Pseudomonas aeruginosa on biomedical polymers.* J Biomed Mater Res. 2000; 50(2) : 208-14.p Abstract: The infection risk of biomaterials implants varies between different materials and is determined by an interplay of adhesion and surface growth of the infecting organisms. In this study, we compared initial adhesion and surface growth of Staphylococcus epidermidis HBH(2) 102 and Pseudomonas aeruginosa AK1 on poly(dimethylsiloxane), Teflon, polyethylene, polypropylene, polyurethane, poly(ethylene terephthalate), poly(methyl methacrylate), and glass. Initial adhesion was measured in situ in a parallel plate flow chamber with microorganisms suspended in phosphate-buffered saline, while subsequent surface growth was followed in full and in 20 times diluted growth medium. Initial adhesion of both bacterial strains was similar to all biomaterials. In full growth medium, generation times of surface growing S. epidermidis ranged from 17 to 38 min with no relation to wettability, while in diluted growth medium generation times increased from 44 to 98 min with increasing surface wettability. For P. aeruginosa no influence of surface wettability on generation times was observed, but generation times increased with decreasing desorption rates, maximal generation times being 47 min and minimal values down to 30 min. Generally, generation times of adhering bacteria were shorter than of planktonic bacteria. In conclusion, surface growth of initially adhering bacteria is influenced by biomaterials surface properties to a greater extent than initial adhesion. Copyright 2000 John Wiley & Sons, Inc.

Gottlieb T. et al. *The independent evolution of resistance to ciprofloxacin, rifampicin, and fusidic acid in methicillin-resistant Staphylococcus aureus in Australian teaching hospitals (1990-1995). Australian Group for Antimicrobial Resistance (AGAR).* J Antimicrob Chemother. 1998; 42(1) : 67-73.p Abstract: Methicillin-resistant Staphylococcus aureus (MRSA) is endemic in teaching hospitals in eastern Australian states, with prevalence rates averaging 25-30% of all S. aureus. Between 1990 and 1995, 1467 non-duplicate MRSA isolates from clinically infected sites were tested in Sydney, Melbourne, and Brisbane as part of a national survey of staphylococcal susceptibility. We reviewed the differing evolution of resistance to ciprofloxacin, rifampicin, and fusidic acid. Despite similarities in community and hospital antibiotic use and MRSA prevalence rates, trends in resistance to the oral antibiotics in these cities have progressed independently of each other. In the 1995 survey in individual hospitals in Melbourne, 16-24% of strains were ciprofloxacin-resistant, compared with 80-100% in Sydney and 30-44% in Brisbane. There was great diversity of phage type patterns for ciprofloxacin-resistant strains, suggesting heterogeneous development of resistance. Rifampicin resistance was more closely associated with distinct dominant epidemic phage types, common to institutions in the same city, but without spread to the other cites. Between 1990 and 1995, these comprised 30-60% of all MRSA in Brisbane, compared with 5-10% in Melbourne and < 25% in Sydney. Fusidic acid resistance was uncommon and sporadic (< 5%), and was distributed equally between methicillin-resistant and methicillin-susceptible strains. Resistance to the oral agents in MRSA is due to a complex mix of antibiotic selection pressures and cross-infection with local and epidemic strains in closely related institutions. Each of these mechanisms can predominate, dependent on local factors and the antibiotics used.

Gourley D.G. et al. *The two types of 3-dehydroquinase have distinct structures but catalyze the same overall reaction.* Nat Struct Biol. 1999; 6(6) : 521-5.p Abstract : The structures of enzymes catalyzing the reactions in central metabolic pathways are generally well conserved as are their catalytic mechanisms. The two types of 3-dehydroquinate dehydratase (DHQase) are therefore most unusual since they are unrelated at the sequence level and they utilize completely different mechanisms to catalyze the same overall reaction. The type I enzymes catalyze a cis-dehydration of 3-dehydroquinate via a covalent imine intermediate, while the type II enzymes catalyze a trans-

dehydration via an enolate intermediate. Here we report the three-dimensional structures of a representative member of each type of biosynthetic DHQase. Both enzymes function as part of the shikimate pathway, which is essential in microorganisms and plants for the biosynthesis of aromatic compounds including folate, ubiquinone and the aromatic amino acids. An explanation for the presence of two different enzymes catalyzing the same reaction is presented. The absence of the shikimate pathway in animals makes it an attractive target for antimicrobial agents. The availability of these two structures opens the way for the design of highly specific enzyme inhibitors with potential importance as selective therapeutic agents.

Graça R. et al. *Infecção pós-operatória: estudo de cirurgias ortopédicas realizadas no Hospital Universitário Pedro Ernesto-UERJ em um ano.* Rev. bras. ortop. 1997; 32(1) : 70-4.p Abstract: Os autores realizaram um estudo prospectivo de cirurgias limpas que evoluíram com infecção pós-operatória no Serviço de Ortopedia e Traumatologia do HUPE-UERJ no período de junho de 1995 a maio de 1996. Foram avaliados aspectos epidemiológicos, etiológicos, profiláticos e terapêuticos em 558 operações. Foi de 5,01 por cento o índice geral de infecção em cirurgias limpas, das quais 0,71 por cento evoluíram com osteomielite. O germe mais encontrado foi o Staphylococcus aureus, com 30,77 por cento dos casos. A cefalotina foi o antibiótico mais usado tanto na profilaxia quanto no tratamento. (AU).

Grados P. et al. *Comparative effectiveness of co-trimoxazole and tetracycline in the treatment of cholera.* Bull. Pan Am. Health Organ. 1996; 30(1) : 36-42.p Abstract: The purpose of the study reported here was to compare the bactericidal effectiveness of tetracycline and co-trimoxazole (a combination of sulfamethoxazole and trimethoprim) in treating cholera. The study, an open-ended random trial using adult patients with cholera cases confirmed by stool culture, was carried out in March 1993 at the Cholera Treatment Unit (CTU) of the Hospital de Apoyo Departamental María Auxiliadora in Lima, Peru. A total of 107 subjects were divided into two groups (A and B). The 50 in Group A received 500 mg of tetracycline orally every 6 hours for 3 days; the 57 in Group B received co-trimoxazole (160 mg of trimethoprim and 800 mg of sulfamethoxazole) orally every 12 hours for 3 days. The two groups were comparable in terms of age, sex, duration of symptoms prior to hospital admission, time at which antibiotic treatment was initiated, and clinical evolution. Control stool cultures of specimens obtained after treatment showed Vibrio cholerae 0-1 present in 2 percent of the Group A and 12.3 percent of the Group B patients, and also showed V. cholerae non-0-1 present in 2 percent of the group A patients and 3.5 percent of the Group B patients. Overall, it was concluded that both therapeutic treatment regimens were effective and that the strains of V. cholerae observed in the southern sector of the city of Lima were still susceptible to both antibiotics (AU).

Grados P. et al. *Eficacia comparada del cotrimoxazol y la tetraciclina en el tratamiento del cólera.* Bol. Oficina Sanit. Panam. 1995; 118(5) : 403-9.p Abstract: El objetivo del presente estudio fue comparar la eficacia bactericida de la tetracilcina y el cotrimoxazol (combinación de sulfametoxazol y trimetoprina) en casos de cólera. El estudio se realizó en marzo de 1993 en la unidad de tratamiento del cólera (UTC) del hospital de Apoyo Departamental María Auxiliadora (HADMA) en Lima, Perú. Se trata de un estudio abierto y aleatorio en pacientes adultos con cólera confirmado por coprocultivo. Los pacientes se distribuyeron en dos grupos: los del grupo A recibieron 500 mg de tetracicliona cada 6 horas por vía oral durante 3 días; los del grupo B fueron tratados con cotrimoxazol a razón de 160 mg de trimetoprima y 800 mg de sulfametoxazol cada 12 horas por vía oral durante 3 días. En total se estudió a 107 pacientes, 50 en el grupo A y 57 en el B. Ambos grupos resultaron comparables en edad, sexo, duración de los síntomas antes del ingreso, momento en que se inició el tratamiento con antibióticos y evolución clínica. El coprocultivo de control después del tratamiento reveló Vibrio cholerae 01 en 2 por ciento de los pacientes del grupo A y en 12, 3 por ciento del los del grupo B, y V. cholerae NO-01 en 2 por ciento de los pacientes del grupo A y en 3,5 por ciento de los del grupo B. Se concluye que ambos esquemas terapéuticos son eficaces y que las cepas de V. cholerae observadas en la parte sur de la ciudad de Lima, Perú siguen sensibles a ambos antibióticos.

Graham D.Y. *Clarithromycin for treatment of Helicobacter pylori infections.* Eur J Gastroenterol Hepatol. 1995; 7 Suppl 1 : S55-8.p Abstract: BACKGROUND: A better appreciation of the causal relationship between Helicobacter pylori infection and peptic ulcer disease and the benefit conferred by curing this infection has led to the recommendation that all patients with duodenal ulcer disease receive anti-H. pylori treatment. Multi-drug regimens, including bismuth, metronidazole and tetracycline or amoxycillin with an antisecretory agent, are successful in > 90% of treated patients but the emergence of metronidazole-resistant H. pylori has begun to limit their effectiveness. DESIGN: The search for the optimal anti-H. pylori treatment has focused on simplifying the regimen (to decrease adverse drug-related events and increase patient compliance), while retaining the excellent clinical results of the traditional multi-drug regimens. This article reviews the data concerning clarithromycin for treatment of H. pylori infections. RESULTS: Numerous evaluations have shown that clarithromycin has desirable attributes for anti-H. pylori treatment: clarithromycin is resistant to gastric acid, penetrates in high concentrations into gastric tissue and mucus, shows excellent antimicrobial activity against H. pylori, results in a high cure rate when used in two- and three-drug combinations, is associated with a low incidence of acquired H. pylori resistance and is well tolerated. Successful clarithromycin therapies include clarithromycin+omeprazole, clarithromycin+ amoxycillin, or clarithromycin+omeprazole+ tinidazole or metronidazole, and clarithromycin triple therapy. CONCLUSION: Clarithromycin may become an integral component of anti-H. pylori therapy.

Graham D.Y. et al. *Twice a day quadruple therapy (bismuth subsalicylate, tetracycline, metronidazole plus lansoprazole) for treatment of Helicobacter pylori infection.* Aliment Pharmacol Ther. 1997; 11(5) : 935-8.p Abstract: BACKGROUND: Quadruple therapy (bismuth, metronidazole and tetracycline (BMT) + proton pump inhibitor) is touted as being > 95% effective, regardless of metronidazole resistance. We tested a 10-day b.d. quadruple therapy for treatment of H. pylori infection. METHODS: Anti-H. pylori therapy consisted of lansoprazole 15 mg b.d. plus tetracycline 500 mg b.d., metronidazole 500 mg b.d., and swallowable Pepto-Bismol caplets (2 b.d.) for 10 days. H. pylori status was evaluated by culture and histology before and 4 or more weeks after therapy. RESULTS: The cure rate for intention-to-treat was 70%. Treatment success was calculated overall and separately in relation to antimicrobial resistance patterns. The cure rate among the metronidazole-sensitive isolates was 89.7% (26 of 29) vs. 41.2% (7 of 17) of the metronidazole-resistant isolates ($P < 0.005$). Moderate ($n = 1$) or severe ($n = 3$) side-effects were experienced in four patients with only one withdrawing because of side-effects. CONCLUSION: Twice a day quadruple therapy is effective for metronidazole-sensitive strains but its usefulness is markedly reduced by the presence of pre-treatment metronidazole resistance. Twice a day quadruple therapy can be recommended in locations where background metronidazole resistance is uncommon. Possibly, 14-day therapy or a higher dosage of metronidazole provide better results with metronidazole-resistant H. pylori.

Graham D.Y. et al. *Furazolidone combination therapies for Helicobacter pylori infection in the United States.* Aliment Pharmacol Ther. 2000; 14(2) : 211-5.p Abstract: BACKGROUND: Antibiotic resistance has begun to impair the ability to cure Helicobacter pylori infection. AIM: To evaluate furazolidone as a component of combination therapies for treatment of H. pylori infection in the United States. METHODS: Patients with active H. pylori infection received furazolidone combination therapy for 14 days (furazolidone 100 mg and tetracycline 500 mg t.d.s.; omeprazole 20 mg o.d. in the morning

and, depending on the pre-treatment antimicrobial susceptibility pattern, 500 mg of metronidazole or clarithromycin t.d.s.). RESULTS: A total of 27 patients received the metronidazole containing combination (cure rate 100%) and seven received the clarithromycin combination (cure rate 86%). Overall the cure rates for intention-to-treat was 97% (95% CI: 85% to 100%). The single failure took the clarithromycin containing combination for only 2 days (per protocol cure rate = 100%). Side-effects were common and led to discontinuation of therapy in 26% of patients. An attempt to eliminate metronidazole and clarithromycin and use furazolidone, tetracycline, and lansoprazole b.d. produced an unsatisfactory cure rate of 72%. CONCLUSION: Furazolidone combination therapy appears to be effective. Additional studies with different antimicrobial combinations and duration of therapy are warranted.

Graham J.E. et al. *Identification of Mycobacterium tuberculosis RNAs synthesized in response to phagocytosis by human macrophages by selective capture of transcribed sequences (SCOTS).* Proc Natl Acad Sci U S A. 1999; 96(20) : 11554-9.p Abstract: A widely applicable, positive cDNA selection method was developed to identify RNAs synthesized by Mycobacterium tuberculosis in response to phagocytosis by cultured human primary macrophages. cDNAs for sigE and sigH (alternative sigma factors), aceA (isocitrate lyase), ponA (class I penicillin-binding protein), pks2 (polyketide synthase), uvrA (UvrABC endonuclease), and ctpV (putative cation transporter) were obtained from macrophage-grown bacteria. cDNAs for ORFs Rv3070, Rv3483c, Rv0903c (encoding a putative bacterial two-component transcriptional activator), and Rv0170 of the mce1 virulence operon also were obtained from phagocytized bacilli. cDNAs for these genomic regions were not obtained from approximately 1, 000-fold more bacteria grown in laboratory broth. Methods described here, which have identified M. tuberculosis genes expressed in response to host interaction, will allow the study of gene expression in a variety of microorganisms, including expression resulting from interaction with human tissues in natural disease states.

Gralewicz S. et al. *[Neurotoxicity of penicillin and other beta-lactam antibiotics—importance in clinical practice].* Przegl Lek. 1997; 54(7-8) : 565-7.p Abstract: Epileptogenic properties of penicillin, applied either directly to the brain or systemically, have been known for many years and may be also of clinical importance. In the present work different aspects of this action, including clinical ones, as well as risk factors for the occurrence of epileptic seizures, and mechanism of penicillin action in the central nervous system have been shortly described. Moreover, results of experimental studies confirming epileptogenic properties of many antibiotics, mainly b-lactams, have been mentioned. Data from experimental studies, revealing the possibility of long-term adverse effects of repeated injections of convulsants, have been emphasized, and the absence of relevant clinical studies has been pointed out. Widespread usage of beta-lactam antibiotics should encourage medical personnel to pay more attention to all these problems in everyday clinical practice.

Granitto K. *Antimicrobial resistance: the threat to health and health care.* Int J Health Care Qual Assur Inc Leadersh Health Serv. 1998; 11(6-7) : viii-xi.p Abstract: This article addresses antimicrobial resistance and the threat it poses to an individual's health and the health care system. Diseases, such as pneumococcus have gained an overabundance of antimicrobial resistance. In addition, previously unknown diseases are surging and sounding alarm bells worldwide. The history and causes of this surge are examined globally. One such cause is the overuse of antibiotics in long-term care facilities. International strategies that have been implemented by organizations, such as the World Health Organization, to control the spread of infectious diseases, are also reviewed. The prevalence, causes and consequences of antibiotic resistant organisms, are found in long-term care facilities and hospitals specifically in Canada, are reviewed. Recommendations are made.

Grasbon T. et al. *[Coagulase-negative staphylococci in normal and chronically inflamed conjunctiva].* Ophthalmologe. 1995; 92(6) : 793-801.p Abstract: This study examines the prevalence of coagulase-negative Staphylococcus species in normal and mildly inflamed conjunctiva, their sensitivity to antibiotics, and their relationship to the remaining flora. PATIENTS AND METHODS: In 99 patients including 9 HIV-positives in an early stage of the infection, 100 conjunctival swabs were taken and microbiologically investigated for bacteria and fungi. Thirty-four were from healthy eyes. 40 were from patients with chronic (n = 28) and unspecific (n = 12) conjunctivitis, 17 were from patients with a variety of outer inflammatory ocular conditions, and 9 were from the HIV group from uninfected (n = 6) and infected (n = 3) conjunctivae. Samples from each patient were collected with three moistened cotton swabs and directly inoculated onto five different agars, followed by immersion into three specific culture broths. Staphylococci were identified species-wise, the other microorganisms genus-wise. Sensitivity to a broad spectrum of antibiotics was determined by agar diffusion tests. OUTCOME: Staphylococci were found in 89%, which was the highest prevalence genus-wise. Of those, coagulase-negative species accounted for 86%, while coagulase-positive Staphylococcus aureus was isolated in 12% of all swabs. In the 86 smears positive for coagulase-negative staphylococci, 151 different strains were isolated. In these strains, resistance to the 13 tested antibiotics varied from 0% for vancomycin to 66% for penicillin. Strains which were isolated from patients with chronic conjunctivitis showed a greater range of resistance than those from normal flora, with significant levels for ciprofloxacin, gentamycin and kanamycin (Mann-Whitney) U-test: $P < 0.05$). All except six strains of staphylococci were identified strains represented ten species, of which Staphylococcus epidermidis was most prevalent (74%), but only made up 70% of all isolated strains of the coagulase-negative staphylococci. Staphylococcus aureus and gram-negative bacteria were found significantly more commonly in patients which chronic conjunctivitis than in healthy eyes, while coagulase-negative species of the Micrococcaceae family were significantly more prevalent in the healthy than in the chronically inflamed conjunctiva (chi-square: $P < 0.05$). CONCLUSION: The conjunctiva can simultaneously host several stems of coagulase-negative staphylococci, which differ in regard to species and resistance to antibiotics. This variety might indicate a microbiological balance of the conjunctiva and be reduced in chronic inflammatory conditions. In patients with chronic conjunctivitis the risk for multiresistant coagulase-negative staphylococci is increased.

Gray J. et al. *Experience of changing between signal and Bactec 9240 blood culture systems in a children's hospital.* J Clin Pathol. 1998; 51(4) : 302-5.p Abstract: AIM: To compare experience of positive blood cultures in successive years before and after changing from Signal (Unipath) to Bactec 9240 (Becton Dickinson) blood culture systems. METHODS: Analysis of data collected prospectively on 7967 Signal and 7062 Bactec blood culture sets. RESULTS: Significant growths occurred in 5.7% of Signal and 8.9% of Bactec cultures; 33.0% more significant isolates and 24.0% more episodes of bacteraemia were detected in the second year, following introduction of the Bactec system. Inpatient hospital activity increased by 8.2% between the first and second years, although the numbers of blood cultures received actually fell by 11.4%. There were striking increases in numbers of isolates of coagulase negative staphylococci (47.7%) and Enterobacteriaceae (56.8%) from Bactec cultures. Two anaerobic bacteraemias were detected in Signal blood cultures, whereas none was detected by the Bactec system, despite 12.1% of sets including an anaerobic bottle. Of significant positive cultures, 90.2% were detected within one day with the Bactec 9240, compared with only 50.0% of Signal cultures; 20.7% of significant positive Signal blood cultures were detected only on terminal subculture. Microorganisms that were not significant were isolated from 5.1% Signal and 3.8% Bactec cultures. CONCLUSIONS: Compared with the Signal system, the Bactec 9240 offers markedly more rapid and sensitive detection of bacteraemia, together with a lower rate of non-signifi-

cant isolates. However, using a single PEDS PLUS/F bottle the few episodes of anaerobic bacteraemia that occur in children are likely to be missed.

Greenberg M. et al. *Antecubital central venous catheter placement complicated by a persistent left superior vena cava.* J Neurosurg Anesthesiol. 2000; 12(2) : 114-7.p Abstract: A 14-year-old female in whom we encountered a persistent left superior vena cava during placement of a central venous catheter is presented. The patient had a history of coarctation of the aorta, but the left superior vena cava was unknown. Since the incidence of persistent left superior vena cava in patients with congenital heart disease is ten times as great as those without, in this patient population it may be useful to obtain radiographic confirmation of catheter position before use.

Greenblatt C.L. et al. *Diversity of Microorganisms Isolated from Amber.* Microb Ecol. 1999; 38(1) : 58-68.p Abstract: > Abstract Claims that organisms can be cultured from amber, if substantiated, would be significant contributions to our understanding of the evolution, tenacity, and potential spread of life. Three reports on the isolation of organisms from amber have been published. Cano and Borucki recently reported the isolation of Bacillus sphaericus and Lambert et al. have described a new species designated Staphylococcus succinus from 25-40 million year old Dominican amber. These characterized organisms were phylogenetically distant from extant relatives and the Staphylococcus sp. sufficiently far removed from other extant staphylococci to be considered a new species. Here we report the culture of bacteria from Dominican and previously untested 120 million year old Israeli (Lebanese lode) amber. Twenty-seven isolates from the amber matrix have been characterized by fatty-acid profiles (FAME) and/or 16S rRNA sequencing. We also performed a terminal restriction fragment pattern (TRF) analysis of the original amber before prolonged culture by consensus primer amplification of the 16S rRNA followed by restriction enzyme digestion of the amplicons. Sample TRFs were consistent with a sparse bacterial assemblage and included at least five of the isolated organisms. Finally, we microscopically mapped the internal topography of an amber slice.http://link.springerny.com/link/service/journals/00248/bibs/38n1p58.html.

Greene J.N. et al. *New directions in antimicrobial therapy.* Chest Surg Clin N Am. 1999; 9(1) : 39-61, vii-viii.p Abstract: The virulent microorganisms that we try to contain with new antimicrobial agents quickly find the gap in our defenses and exploit it. Resistance to all available antibiotics at the same time, however, rarely occurs. The authors report the most current antimicrobials used as monotherapy or in combination to successfully treat the more resistant pathogens. The higher mortality and subsequent cost to treat these infections are reviewed.

Greenstein G. *Clinical significance of bacterial resistance to tetracyclines in the treatment of periodontal diseases.* J Periodontol. 1995; 66(11) : 925-32.p Abstract: Tetracyclines are frequently employed during the treatment of clinical infections in medicine and dentistry, however, emergence of resistant bacterial strains has decreased the utility of these drugs. Accordingly, there is concern that indiscriminant administration of tetracyclines during periodontal therapy will further contribute to the development of additional resistant microorganisms which can complicate infectious disease therapy. This review paper briefly discusses the utility of tetracyclines as an antimicrobial agent in the treatment of periodontal diseases. It then focuses on the clinical significance of bacterial resistance to tetracyclines. Patterns of resistance that may be associated with the following scenarios are addressed: short- and long-term antibiotic therapy, individuals with a history of prior tetracycline therapy, patients with refractory periodontitis, and following controlled local drug delivery. It appears that selection and development of bacterial resistant strains is an inevitable consequence of antibiotic therapy. Nevertheless, prudent administration of tetracyclines may help delay or prevent the emergence of resistant microorganisms.

Gremiakova T.A. et al. *[The interrelationship of the capacity for the expression of different serovariants of the Yersinia pestis capsular antigen with the degree of reduction of the lipopolysaccharide of the bacterial cells].* Zh Mikrobiol Epidemiol Immunobiol. 1995; (1) : 3-6.p Abstract: The immunochemical study of the expression of different serovariants of Y. pestis capsular antigen in Escherichia coli HB 101, Salmonella minnesota R595 and Y. pestis EV recipient strains with different degrees of LPS reduction was made. Plasmids pFS1, pFBK7 and pFBK10 coding initial and serologically atypical variants of the capsular antigen were introduced into microbiol cells. Altered LPS structures were shown to have no influence on the serological specificity of the capsular antigen. Immunochemical activity was determined in the diffuse precipitation test, the passive hemagglutination test and the antibody neutralization test. Changes in the structure of LPS were shown to produce no effect on the serological activity of the capsular antigen coded by intact fra operon (plasmid pFS1). The transfer of hybrid plasmids pFBK7 and pFBK10 to recipient microorganisms led to the synthesis of serovariant Fl1 in recombinant strains with O-LPS, which was immunochemically different from serovariant Fl2 synthesized in strains with R-LPS.

Grenby T.H. et al. *Laboratory studies of sweets re-formulated to improve their dental properties.* Oral Dis. 1996; 2(1) : 32-40.p Abstract: OBJECTIVES: To evaluate the potential dental effects of ten new types of sugar-free sweets formulated with Lycasin or isomalt as bulk sweeteners instead of sugars. METHODS: Examination of the sweets for their acidity, fermentability by oral microorganisms, influence on the demineralisation of dental enamel, and their influence on human interdental plaque pH, compared with conventional sugar-containing sweets. FINDINGS: The importance of reducing the levels of flavouring acids in the sweets was demonstrated. It was not straightforward to evaluate chocolate products in this system, but the potential benefits of re-formulating fruit gums, lollipops, chew-bars, toffee and fudge with Lycasin or isomalt in place of sugars were shown by determining their reduced acidogenicity and fermentability compared with conventional confectionery. CONCLUSIONS: The extent of demineralisation of dental enamel was related to both the acidity and the fermentability of the sweets. Re-formulating sweets with reduced acidity levels and bulk sweeteners not fermentable by dental plaque microorganisms can provide a basis for improving their potential dental effects.

Griffin D.W. et al. *Detection of viral pathogens by reverse transcriptase PCR and of microbial indicators by standard methods in the canals of the Florida Keys.* Appl Environ Microbiol. 1999; 65(9) : 4118-25.p Abstract: In order to assess the microbial water quality in canal waters throughout the Florida Keys, a survey was conducted to determine the concentration of microbial fecal indicators and the presence of human pathogenic microorganisms. A total of 19 sites, including 17 canal sites and 2 nearshore water sites, were assayed for total coliforms, fecal coliforms, Escherichia coli, Clostridium perfringens, enterococci, coliphages, F-specific (F(+)) RNA coliphages, Giardia lamblia, Cryptosporidium parvum, and human enteric viruses (polioviruses, coxsackie A and B viruses, echoviruses, hepatitis A viruses, Norwalk viruses, and small round-structured viruses). Numbers of coliforms ranged from <1 to 1, 410, E. coli organisms from <1 to 130, Clostridium spp. from <1 to 520, and enterococci from <1 to 800 CFU/100 ml of sample. Two sites were positive for coliphages, but no F(+) phages were identified. The sites were ranked according to microbial water quality and compared to various water quality standards and guidelines. Seventy-nine percent of the sites were positive for the presence of enteroviruses by reverse transcriptase PCR (polioviruses, coxsackie A and B viruses, and echoviruses). Sixty-three percent of the sites were positive for the presence of hepatitis A viruses. Ten percent of the sites were positive for the presence of Norwalk viruses. Ninety-five percent of the sites were positive for at least one of the virus groups. These results indicate that the canals and nearshore waters throughout the Florida Keys are being impacted by human fecal material carrying human enteric viruses through

current wastewater treatment strategies such as septic tanks. Exposure to canal waters through recreation and work may be contributing to human health risks.

Grogan T. et al. *An update on "special stain" histochemistry with emphasis on automation*. Adv Anat Pathol. 2000; 7(2) : 110-22.p Abstract: For nearly 100 years, pathologists have utilized "special histochemical stains" to assist in tissue-based diagnosis. As illustrated in Figures 1 and 2, histochemical stains have been used to identify infectious microorganisms (e.g., Mycobacterium tuberculosis with acid-fast bacillus (AFB) stain), to detail inflammatory stromal or structural alterations (e.g., fibrosis in liver cirrhosis with Masson trichrome), to identify microanatomic sites of disease (e.g., basement membrane in glomerulonephritis with Jones methenamine silver), to identify abnormal chemical deposits (e.g., iron in hemochromatosis with Prussian blue stain), or abnormal immune deposits (e.g., amyloid via Congo red stain). The current surgical pathology laboratory may employ a repertoire of 20 to 25 "special stains" to ensure the full diagnostic complement. While the diagnostic repertoire and the biochemical recipes for the stains are now a well-established, codified part of surgical pathology, there is an ever-moving, leading edge of new developments including new reagents, applications, and methods. This review seeks to update the reader on some of the new applications including both new reagents and methods. Particular emphasis will be placed on the recent technologic advance of automating special stains in kinetic-mode (1-4). The authors consider in turn: 1. In brief, the "news" (recent literature review) of new staining applications; 2. In greater detail, two new applications for detection of Microsporidia and Helicobacer pylori; 3. The new technologic advancement of kinetic mode automation of special stains.

Grones J. et al. *Transformation of microorganisms with the plasmid vector with the replicon from pAC1 from Acetobacter pasteurianus.* Biochem Biophys Res Commun. 1995; 206(3) : 942-7.p Abstract: A number of gram-negative and gram-positive bacteria species was screened for the expression of the gram-negative plasmid pACK5 and pACT72 with replicon of pAC1 plasmid from Acetobacter pasteurianus. As was described previously, both plasmids were expressed in Escherichia coli, Acetobacter pasteurianus, Acetobacter aceti, Shigella spp. and Citrobacter spp. Expressions of plasmids were successful in twelve species tested, Comamonas terrigena, Salmonella typhimurium, Serratia marcescens, Bacillus cereus, Bacillus megatericum, Bacillus subtilis, Lactobacillus helveticus, Micrococcus luteus, Sarcina lutea, Staphylococcus aureus, Staphylococcus epidermidis, Streptoccocus feacalis, and the stability of plasmid DNA was tested after cultivation in non-selective conditions.

Groody E.P. *Detection of foodborne pathogens using DNA probes and a dipstick format*. Mol Biotechnol. 1996; 6(3) : 323-7.p Abstract: The detection of foodborne microorganisms has traditionally been done using microbiologically based methods. Such "gold standard" methods are generally reliable but have the disadvantages of being labor intensive, subjective, and time consuming. Over the last several years, the development of DNA probe-based methods has simplified the methods used to detect organisms such as Salmonella, Listeria, and E. coli by targeting the unique DNA or RNA sequences of these organisms using DNA probes and nonradioactive detection.

Gross M.E. et al. *Antimicrobial activities of beta-lactam antibiotics and gentamicin against penicillin-susceptible and penicillin-resistant pneumococci*. Antimicrob Agents Chemother. 1995; 39(5) : 1166-8.p Abstract: The MICs of penicillin and cefotaxime for a range of penicillin-susceptible and penicillin-resistant isolates of Streptococcus pneumoniae were unchanged by the addition of gentamicin. In time-kill studies the rate of killing was greater for 18 of 20 isolates in the presence of gentamicin. However, mean differences in killing after 6 h of incubation were modest, not exceeding 1 log10 unit.

Grosset J. *[Bacteriological diagnosis of tuberculosis]*. Rev Prat. 1996; 46(11) : 1337-43.p Abstract: Ziehl-Neelsen or fluorescence microscopy, culture and drug sensitivity test onto Loewenstein-Jensen medium or with the more rapid radiometric BACTEC system are still the reference diagnostic tests for tuberculosis. However the slow growth of mycobacteria, the severity of the disease caused and the lack of a suitable sub-typing scheme for epidemiological studies have made tuberculosis a popular application for molecular techniques. The four major diagnostic areas molecular techniques have been applied for: rapid identification of cultured mycobacteria; sub-typing of strains by a DNA fingerprinting method in contact tracing; rapid detection of antimicrobial resistance by direct DNA sequencing of target site genes, single strand conformation polymorphism analysis (PCR-SSCP) or line probe assay (LIPA); detection of M. tuberculosis complex in clinical material.

Grossman R.F. *Cost-effective therapy for acute exacerbations of chronic bronchitis.* Semin Respir Infect. 2000; 15(1) : 71-81.p Abstract: Pharmacoeconomic analysis involves the measurement of a ratio determining the extra costs required to achieve an additional unit of clinical benefit. Various techniques including modeling studies, retrospective analysis of databases, "piggy-back" economic analysis of prospective randomized clinical trials, and prospective randomized pharmacoeconomic trials have been developed to aid in economic and health decisions. In acute exacerbations of chronic obstructive pulmonary disease, it is possible to identify a group of patients that are at high risk of treatment failure from routine antimicrobial therapy, hospitalization, respiratory failure, and death. The cost of therapy for this relatively small group of patients is extraordinarily high. Data from a variety of approaches have suggested that aggressive antimicrobial therapy may lead to improved outcomes in these patients. The corollary is that aggressive therapy directed toward patients with either acute bronchitis (mainly a viral infection) or exacerbations of trivial chronic obstructive lung disease leads to emergence of resistance and increased costs.

Grotto I. et al. *Meningococcal disease in the Israel Defense Force: epidemiologic trends and new challenges.* Isr J Med Sci. 1995; 31(1) : 54-8.p Abstract: To determine recent trends in its epidemiology and the need to reconsider prophylactic interventions, meningococcal disease in the Israel Defense Force (IDF) from 1975 through 1993 was studied. All cases of meningitis or meningococcemia were included. A considerable increase in the number of cases has been observed since 1991, with serogroup C becoming predominant (76% of cases) since then. Serogroup Y was the second most frequent serogroup during this period, while serogroup B, predominant in the civilian population of Israel, was rare. Most cases occurred during the first 6 months of military service. Seasonality was important, with most of the cases occurring between December and March, although a small summer peak was also noted. Since 1992, three small clusters of meningococcal disease were encountered in the IDF, for the first time, with all cases caused by group C meningococci. In one cluster, the emergence of rifampicin resistance resulted in failure of chemoprophylaxis. The rise in group C and Y cases since 1991, and the occurrence of rifampicin resistance, necessitate considering meningococcal vaccines and new antimicrobial agents for prophylaxis.

Gruneberg R.N. *Chairman's introduction—the importance of good quality surveillance data today.* J Chemother. 1999; 11 Suppl 1 : 22-5.p Abstract: The Alexander Project is a continuing, international, multicenter, longitudinal study of the antimicrobial susceptibility of pathogens commonly associated with community-acquired lower respiratory tract infections (LRTI). The study began in 1992 to provide high-quality surveillance data, comparable between regions and through time. As antimicrobial resistance becomes more prevalent, reliable surveillance data are required for clinical decision-making. Accurate current susceptibility data are required to predict clinical success through the determination of pharmacodynamic breakpoints. The Alexander Project provides the information required for

clinicians to improve the likelihood of microbiological and clinical cure in the antibiotic treatment of LRTI.

Gruneberg R.N. et al. *The role of glycopeptide antibiotics in the treatment of infective endocarditis.* Int J Antimicrob Agents. 1999; 12(3) : 191-8.p Abstract: There are several sets of guidelines for the treatment of infective endocarditis, reflecting the need for differing treatment in various countries and times. This review considers the need for differing treatment modalities and in particular the utility of the glycopeptide antibiotics vancomycin and teicoplanin. Specific recommendations are offered as to when to consider the use of glycopeptides, appropriate dosage, length of treatment course and whether to use monotherapy or combined therapy. Used judiciously, the glycopeptides give results as good as can be achieved with other antimicrobial agents without exceptional toxicity. The potential of teicoplanin for use in the outpatient treatment of infective endocarditis is considered.

Gruneberg R.N. et al. *Results of the Alexander Project: a continuing, multicenter study of the antimicrobial susceptibility of community-acquired lower respiratory tract bacterial pathogens.* Diagn Microbiol Infect Dis. 1996; 25(4) : 169-81.p Abstract: In 1992, an ongoing, international multicenter study was established to investigate the antimicrobial susceptibility of community-acquired lower respiratory tract bacterial pathogens: the Alexander Project. Isolates cultured from patients living in geographically separated areas, ten in the European Union (EU) and five in the United States (US), were collected and tested using standard methods in a central laboratory. A total of 4,155 isolates of Haemophilus influenzae was collected during the period 1992-1994. beta-lactamase production was the principal mechanism of resistance observed with overall rates in the US (1992 = 26.3%; 1993 = 28.2%; and 1994 = 30.1%) generally twice those seen in the EU (1992 = 12.3%; 1993 = 14.4%; and 1994 = 15.5%). Chloramphenicol resistance was generally low except in Spanish centers where rates ranging from 4.0 to 15.9% were observed during the study period. One thousand one hundred ninety-three isolates of Moraxella catarrhalis were tested. beta-lactamase production was the only mechanism of resistance of any importance detected, with the vast majority of isolates producing the enzyme. Two thousand eight hundred twenty-nine isolates of Streptococcus pneumoniae were tested. French and Spanish centers provided isolates with the highest rates of either low-level (intermediate) or high-level penicillin resistance, which in 1994 ranged from 10.2 to 31.4% and 30.4 to 40.1% for each resistance category, respectively. With the exception of the fluoroquinolones, rates of resistance to other antimicrobials including the macrolides, doxycycline, chloramphenicol, and trimethoprim/sulfamethoxazole were high, generally, in centers with a high prevalence of penicillin resistance. However, in some centers (Toulouse, France and Genoa, Italy) this association was not complete for the macrolides.

Gruson D. et al. *Rotation and restricted use of antibiotics in a medical intensive care unit. Impact on the incidence of ventilator-associated pneumonia caused by antibiotic-resistant gram-negative bacteria.* Am J Respir Crit Care Med. 2000; 162(3 Pt 1) : 837-43.p Abstract: To test the hypothesis that a new program of antibiotic strategy control can minimize the incidence of ventilator-associated pneumonia (VAP) caused by potentially antibiotic-resistant microorganisms, we performed a prospective before-after study in 3, 455 patients admitted to a single intensive care unit over a 4-yr period. Regarding the bacterial ecology and the increasing antimicrobial resistance in our medical intensive care unit (MICU), we decided to vary our choice of empiric and therapeutic antibiotic treatment, with a supervised rotation, and a restricted use of ceftazidime and ciprofloxacin, which were widely prescribed before this scheduled change. For all patients, VAP was diagnosed based on the results of quantitative culture of bronchoalveolar lavage specimens (>/= 10(4) cfu/ml). We studied 1,044 and 1,022 patients requiring more than 48 h of mechanical ventilation (MV), respectively, in the before-period (2 yr: 1995-1996) and the after-period (2 yr: 1997-1998). We observed a decrease from 231 consecutive episodes of VAP in the before-period to 161 episodes of VAP in the after-period ($p < 0.01$), particularly for VAP occurring before 7 d of MV. The total number of potentially antibiotic-resistant gram-negative bacilli responsible for VAP such as Pseudomonas aeruginosa, Burkholderia cepacia, Stenotrophomonas maltophilia, and Acinetobacter baumanii decreased from 140 to 79 isolated bacilli. The susceptibilities of these bacteria to the antibiotics regimen increased significantly, especially for P. aeruginosa and B. cepacia. The percentage of methicillin-sensitive Staphylococcus aureus increased significantly from 40% to 60% of S. aureus responsible for VAP. These results suggest that a new strategy of antibiotics use could be an efficient means to reduce the incidence of VAP caused by antibiotic-resistant bacteria. Nevertheless, further studies are needed to validate these data.

Gruson D. et al. *Impact of colony-stimulating factor therapy on clinical outcome and frequency rate of nosocomial infections in intensive care unit neutropenic patients.* Crit Care Med. 2000; 28(9) : 3155-60.p Abstract: OBJECTIVES: To determine whether the use of recombinant human granulocyte colony-stimulating factor (G-CSF, filgrastim) reduces the mortality rate and the frequency rate of nosocomial infections in neutropenic patients requiring intensive care unit (ICU) admission. DESIGN: Retrospective consecutive case series analysis. SETTING: Medical ICU of a teaching hospital. PATIENTS: We compared two groups of patients, according to whether or not they received G-CSF. In the ICU, 28 leukopenic patients received filgrastim (5 microg of body weight per day intravenously). In all these patients, G-CSF was continued until recovery from leukopenia, defined as a leukocyte count >1,000/mm3. A total of 33 ICU leukopenic patients did not receive G-CSF. End points included leukocyte count, bone marrow recovery, frequency of ICU nosocomial infections (pneumonia, urinary tract, and catheter-related infections), and mortality rate. MEASUREMENTS AND MAIN RESULTS: There were no differences in number of patients who recovered from leukopenia or in whom blood leukocyte count increased. Nosocomial infections occurred in the same percentage in both groups. The percentage of patients who died was identical in both groups. The percentage of patients with and without filgrastim therapy who recovered from leukopenia but died, was 86% and 78%, respectively. CONCLUSION: In the ICU, clinical outcome of neutropenic patients was not changed by G-CSF therapy. It is possible that G-CSF therapy may not be helpful in improving the ICU clinical outcome of neutropenic patients. Additional controlled studies designed to address this question are warranted.

Grzybowski J. et al. *Antimicrobial properties of copper-coated electroconductive polyester fibers.* Polim Med. 1999; 29(1-2) : 27-33.p Abstract: Three synthetic copper-coated EURO-static fibers (PET—polyester, PA—polyamide, and PAC—polyacrylamide) manufactured by EUROPA Corporation S.C., Poland, were tested as potential antimicrobial agents. The inhibitory properties of the fibers were examined using different microorganisms as follows: i. Staphylococcus aureus ATCC 25293, and Pseudomonas aeruginosa ATCC 27853 reference strains, ii. 8 strains of S. aureus (4 MRSA and 4 MSSA) and 5 strains of P. aeruginosa isolated from infected wounds, and iii. fungal pathogen Scopulariopsis sp. isolated from onychomycosis case. The results of experiments have evidenced that polyester (PET) copper-coated EURO-static fibers inhibit the growth of all the strains used.

Guay D.R. *Macrolide antibiotics in paediatric infectious diseases.* Drugs. 1996; 51(4) : 515-36.p Abstract: Erythromycin and other macrolides have enjoyed a renaissance in the 1970s, 1980s and 1990s secondary to the discovery of "new' pathogens such as Chlamydia, Legionella, Campylobacter and Mycoplasma spp. Erythromycin is an important therapeutic agent in the paediatric age group for several reasons: (a) it exhibits proven efficacy for a wide range of infections (upper and lower respiratory tract infections, skin/skin structure infections, prophylaxis of endocarditis/acute rheumatic fever/ophthalmia neonato-

rum and pre-colonic surgery, campylobacteriosis, chlamydial and ureaplasmal infections, diphtheria, whooping cough, streptococcal pharyngitis) and gastrointestinal (GI) dysmotility states; (b) intravenous formulations are widely available; and (c) it is available in a number of formulations as a generic product, which is likely to result in significant cost savings. Nevertheless, erythromycin and similar earlier macrolides are characterised by a number of drawbacks including a narrow spectrum of antimicrobial activity, unfavourable pharmacokinetic properties and poor GI tolerability. Newer macrolides such as clarithromycin and azithromycin are useful in serving the needs of paediatric patients who are erythromycin-intolerant or who have infections caused by organisms that are intrinsically erythromycin-resistant, or for which a high percentage of strains are resistant (e.g. Haemophilus influenzae, Helicobacter pylori, Mycobacterium avium complex). In addition, these newer macrolides may be considered as alternatives to oral amoxicillin-clavulanic acid, second or third generation cephalosporins, or erythromycin plus sulphonamide in this patient population. Selection between specific macrolides and between macrolides and other antibiotics in the paediatric population is likely to depend, at least for the immediate future, on separate comparisons of product availability, cost, effectiveness and tolerability profiles.

Guengerich F.P. *Cytochrome P450 proteins and potential utilization in biodegradation.* Environ Health Perspect. 1995; 103 Suppl 5 : 25-8.p Abstract: The cytochrome P450 enzymes are major catalysts involved in the oxidations of xenobiotic chemicals in microorganisms as well as higher animals and plants. Because of their functional roles, they offer potential in biodegradation technology. A number of microbial P450s have already been characterized and offer advantages in terms of their high catalytic rates and facile expression in microorganisms. One approach to extending the catalytic selectivity to more compounds in the environment is rational design. In three cases, the three-dimensional structures of bacterial cytochrome P450 enzymes are available and can be further understood through studies with molecular dynamics. Many mammalian cytochrome P450 enzymes have been studied extensively and have potential for biodegradation because of their broad catalytic selectivities (e.g., P450 2E1). Several advances have been made in the heterologous expression of these proteins in microorganisms. Improvements under development include electron transfer from flavodoxin and the use of cytochrome P450:NADPH-cytochrome P450 reductase fusion proteins. Random mutagenesis offers the potential of improving the catalytic activities of some of these proteins. Future challenges include the use of cytochrome P450 expression vectors in microorganisms capable of thriving in the environment; recent success in expression of vectors in Salmonella genotoxicity tester strains may be encouraging in this regard.

Guerra B. et al. *Antimicrobial resistance and spread of class 1 integrons among Salmonella serotypes.* Antimicrob Agents Chemother. 2000; 44(8) : 2166-9.p Abstract: The resistance profiles, for 15 antimicrobial agents, of 333 Salmonella strains representing the most frequent nontyphoidal serotypes, isolated between 1989 and 1998 in a Spanish region, and 9 reference strains were analyzed. All strains were susceptible to amikacin, ceftazidime, ciprofloxacin, and imipenem, and 31% were susceptible to all antimicrobials tested. The most frequent types of resistance were to sulfadiazine, tetracycline, streptomycin, spectinomycin, ampicillin, and chloramphenicol (ranging from 46 to 22%); 13% were resistant to these six drugs. This multidrug resistance pattern was found alone or together with other resistance types within serotypes Typhimurium (45%), Panama (23%), and Virchow (4%). Each isolate was also screened for the presence of class 1 integrons and selected resistance genes therein; seven variable regions which carried one (aadA1a, aadA2, or pse-1) or two (dfrA14-aadA1a, dfrA1-aadA1a, oxa1-aadA1a, or sat1-aadA1a) resistance genes were found in integrons.

Guggenbichler J.P. et al. *A new technology of microdispersed silver in polyurethane induces antimicrobial activity in central venous catheters.* Infection. 1999; 27 Suppl 1 : S16-23.p Abstract: Metal ions or metal ions in complexes or compounds have been used for centuries to disinfect fluids, solids and tissues. The biocidal effect of silver, with its broad spectrum of activity including bacterial, fungal and viral agents, is particularly well known and the term "oligodynamic activity" was coined for this phenomenon. Silver ions have an affinity to sulfhydryl groups in enzyme systems of the cell wall, through which they interfere with the transmembranous energy transfer and electron transport of bacterial microorganisms. Silver ions also block the respiratory chain of microorganisms reversibly in low concentrations and irreversibly in higher concentrations. Binding to the DNA of bacteria and fungi increases the stability of the bacterial double helix and thus inhibits proliferation. There is no cross resistance with antibiotics and also no induction of antimicrobial resistance by silver ions. The concentrations required for bactericidal activity are in the range 10(-9) mol/l. These concentrations can be achieved in solution by the interaction of metallic silver with electrolytes only if there is a large enough surface of silver. By a novel technology, metallic silver is distributed in submicron particles in polyurethane and results in a concentration of 0.8% in an active surface of 450 cm2/g polyurethane. Polyurethane is hygroscopic and rapidly attracts water; the interaction of electrolyte solutions with the extremely finely distributed silver throughout the polyurethane releases bactericidal concentrations of silver ions over a period of years to the surface of the material. The electronegatively charged surface of bacteria attracts the positively charged silver ions. The concentrations released from the polyurethane are far below the toxic concentrations for humans.

Guirguitzova B. et al. *[Enterococci as uropathogens. Frequency of isolation and sensitivity to antibacterial agents].* Ann Urol (Paris). 1998; 32(1) : 15-9.p Abstract : 221 clinically significant enterococcal strains (191: E. faecalis, 27: E. faecium, 3 others) were isolated from the urine of patients hospitalised with UTI over an 18-month period (1995-1996). The susceptibility of the isolates to 8 antimicrobial agents was determined by agar dilution method (NCCLS). All enterococci were sensitive to vancomycin and most of them (over 92%) to penicillin and ampicillin. Only 3.14% of E. faecalis and 3.70% of E. faecium were resistant to ciprofloxacin. A relatively high incidence of resistance of enterococci to aminoglycosides was observed: 46.07% and 51.85% to streptomycin, 42.41% and 44.44% to gentamicin, 70.68% and 77.78% to amikacin for E. faecalis and E. faecium, respectively. Among the resistant to penicillin and amino glycosides enterococci of the two species was found a great percent "high level" resistance. There were no beta-lactamase producers among our strains. The established multiresistance accompanied by "high level" resistance requires careful consideration of antimicrobial therapy of enterococcal UTI.

Guneri S. et al. *Chylous ascites due to constrictive pericarditis.* Int J Card Imaging. 2000; 16(1) : 49-54.p Abstract: Chylous ascites due to constrictive pericarditis is an extremely rare clinical entity, possibly caused by the augmented lymph production and high impedance to lymph drainage due to central venous hypertension. The authors describe a patient with chylous ascites caused by constrictive pericarditis in the absence of lymphatic obstruction. Cardiac catheterization is essential for the confirmation of accurate diagnosis of constrictive pericarditis. Magnetic resonance imaging of the heart is also very helpful in the diagnosis. The patient was symptom free and his ascites and edema completely resolved after pericardiectomy.

Gunseren F. et al. *A surveillance study of antimicrobial resistance of gram-negative bacteria isolated from intensive care units in eight hospitals in Turkey.* J Antimicrob Chemother. 1999; 43(3) : 373-8.p Abstract: This study was carried out with the participation of eight hospitals in Turkey to determine the frequency of gram-negative bacteria isolated in intensive care units (ICU) and to compare their resistance rates to selected antibiotics. Aerobic gram-negative bacteria isolated from ICUs during 1996 were studied. Antibiotic susceptibilities to

imipenem, ceftazidime, ceftazidime-clavulanate, ceftriaxone, cefotaxime, cefepime, cefodizime, cefuroxime, piperacillin/tazobactam, amoxycillin-clavulanate, gentamicin, amikacin and ciprofloxacin were determined by Etest. A total of 748 isolates were obtained from 547 patients. The majority of organisms were isolated from the respiratory (38.8%) and urinary tracts (30.9%). Pseudomonas spp. were the most frequently isolated gram-negative species (26.8%), followed by Klebsiella spp. (26.2%). Escherichia coli, Acinetobacter spp. and Enterobacter spp. were the other commonly isolated organisms. High resistance rates were observed for all antibiotics studied. Imipenem appeared to be the most active agent against the majority of isolates. Although resistance rates exceeded 50%, ciprofloxacin, cefepime and amikacin were found to be relatively effective. Extended-spectrum beta-lactamase (ESBL) production appeared to be a major mechanism of resistance to beta-lactam antibiotics. In contrast to ceftazidime-clavulanate, piperacillin/tazobactam showed poor activity against organisms thought to produce ESBL, suggesting the presence of an enzyme resistant to tazobactam action. This study has yielded high rates of resistance in aerobic gram-negative isolates from ICUs in Turkey. High resistance rates to all the other antibacterials studied leave imipenem as the only reliable agent for the empirical treatment of ICU infections in Turkey.

Gupta A. et al. *Outbreak of cholera in arid zone of Bikaner.* Indian J Med Res. 1999; 110 : 126-7.p Abstract: Bikaner being an arid zone was more or less unaffected by cholera until 1994 when an outbreak of clinical cholera occurred. We isolated 64 Vibrio cholerae strains out of 475 stool samples received (isolation rate 13.47%). All the Vibrio strains belonged to biotype El Tor serotype Ogawa. Low isolation rate was probably related to the poor transportation and medical facilities available at remote areas and indiscriminate and irrational use of antibiotics. The antimicrobial susceptibility testing of the isolates has not shown significant resistance against commonly used antimicrobials.

Gupta A. et al. *Molecular basis for resistance to silver cations in Salmonella.* Nat Med. 1999; 5(2) : 183-8.p Abstract: Here we report the genetic and proposed molecular basis for silver resistance in pathogenic microorganisms. The silver resistance determinant from a hospital burn ward Salmonella plasmid contains nine open reading frames, arranged in three measured and divergently transcribed RNAs. The resistance determinant encodes a periplasmic silver-specific binding protein (SilE) plus apparently two parallel efflux pumps: one, a P-type ATPase (SilP); the other, a membrane potential-dependent three-polypeptide cation/proton antiporter (SilCBA). The sil determinant is governed by a two-component membrane sensor and transcriptional responder comprising silS and silR, which are co-transcribed. The availability of the sil silver-resistance determinant will be the basis for mechanistic molecular and biochemical studies as well as molecular epidemiology of silver resistance in clinical settings in which silver is used as a biocide.

Gupta K. et al. *The prevalence of antimicrobial resistance among uropathogens causing acute uncomplicated cystitis in young women.* Int J Antimicrob Agents. 1999; 11(3-4) : 305-8.p Abstract: Four hundred and fifty-two urine isolates from women with acute uncomplicated cystitis and a positive urine culture presenting to a sexually transmitted disease clinic were collected during 1989-1991, and 213 specimens were collected over 1995-1997. The predominant species was Escherichia coli, representing 68% of the isolates; others included Staphylococcus saprophyticus (8%), Group B streptococci (7%), Proteus spp. (6%), Klebsiella spp. (4%) and Enterococcus spp.(3%). More than 10% of the E. coli isolates were resistant to ampicillin, cephalothin, tetracycline and trimethoprim sulfamethoxazole (TMP SMX) during both study periods, with the greatest increase in resistance to ampicillin and TMP/SMX between the two periods. Six hundred and four urinary tract infection isolates, including 83% E. coli, 7% S. saprophyticus, 3%, Klebsiella spp. 2% Proteus spp., 2% enterococci, 1% Enterobacter spp. and 2% other organisms, were collected from women with acute cystitis attending a university student health service during 1995. Among E. coli isolates, 25% were resistant to ampicillin, 24% to tetracycline and 11%, to TMP SMX. Resistance to fluoroquinolones was essentially absent among gram-negative pathogens. Continued evaluation of susceptibility patterns of pathogens causing acute uncomplicated cystitis to traditional as well as new antimicrobials in well defined populations is necessary to ascertain the optimal empiric therapy.

Gupta K. et al. *Increasing prevalence of antimicrobial resistance among uropathogens causing acute uncomplicated cystitis in women.* JAMA. 1999; 281(8) : 736-8.p Abstract: CONTEXT: Guidelines for the management of acute uncomplicated cystitis in women that recommend empirical therapy in properly selected patients rely on the predictability of the agents causing cystitis and knowledge of their antimicrobial susceptibility patterns. OBJECTIVE: To assess the prevalence of and trends in antimicrobial resistance among uropathogens causing well-defined episodes of acute uncomplicated cystitis in a large population of women. DESIGN: Cross-sectional survey of antimicrobial susceptibilities of urine isolates collected during a 5-year period (January, May, and September 1992-1996). SETTING: Health maintenance organization. PATIENTS: Women aged 18 to 50 years with an outpatient diagnosis of acute cystitis. MAIN OUTCOME MEASURES: Proportion of uropathogens demonstrating in vitro resistance to selected antimicrobials; trends in resistance over the 5-year study period. RESULTS: Escherichia coli and Staphylococcus saprophyticus were the most common uropathogens, accounting for 90% of the 4342 urine isolates studied. The prevalence of resistance among E coli and all isolates combined was more than 20% for ampicillin, cephalothin, and sulfamethoxazole in each year studied. The prevalence of resistance to trimethoprim and trimethoprim-sulfamethoxazole rose from more than 9% in 1992 to more than 18% in 1996 among E coli, and from 8% to 16% among all isolates combined. There was a statistically significant increasing linear trend in the prevalence of resistance from 1992 to 1996 among E coli and all isolates combined to ampicillin (P<.002), and to cephalothin, trimethoprim, and trimethoprim-sulfamethoxazole (P<.001). In contrast, the prevalence of resistance to nitrofurantoin, gentamicin, and ciprofloxacin hydrochloride was 0% to 2% among E coli and less than 10% among all isolates combined, and did not change significantly during the 5-year period. CONCLUSIONS: While the prevalence of resistance to trimethoprim-sulfamethoxazole, ampicillin, and cephalothin increased significantly among uropathogens causing acute cystitis, resistance to nitrofurantoin and ciprofloxacin remained infrequent. These in vitro susceptibility patterns should be considered along with other factors, such as efficacy, cost, and cost-effectiveness in selecting empirical therapy for acute uncomplicated cystitis in women.

Guthrie L.L. et al. *Comparison of MicroScan MICroSTREP, PASCO, and Sensititre MIC panels for determining antimicrobial susceptibilities of Streptococcus pneumoniae.* Diagn Microbiol Infect Dis. 1999; 33(4) : 267-73.p Abstract: The MicroScan MICroSTREP MIC panel was compared with PASCO and Sensititre systems against 157 isolates of Streptococcus pneumoniae chosen to include penicillin-susceptible, intermediate, and resistant strains. Arbitration testing was performed by microbroth dilution using National Committee for Clinical Laboratory Standards guidelines. Overall essential agreement of 94-97% and categorical agreement of 91-94% with the reference method was achieved for the three systems. There were 8 very major errors (false susceptibility) for PASCO, 10 for Sensititre, and 9 for MICroSTREP; 4 major errors (false resistance) each for PASCO and MICroSTREP, and 6 for Sensititre. Most of these errors occurred with trimethoprim/sulfamethoxazole. Minor errors (susceptible or resistant versus intermediate) totaled 47 for PASCO, 69 for Sensititre, and 53 for MICroSTREP. Minor interpretive errors were most common with penicillin and ceftriaxone. This study showed that all three MIC panels provided interpretive results comparable to one another and to the reference method.

Gutierrez Rodero F. et al. *Endocarditis caused by Stenotrophomonas maltophilia: case report and review.* Clin Infect Dis. 1996; 23(6) : 1261-5.p Abstract: Stenotrophomonas (Xanthomonas) maltophilia is a rare cause of endocarditis. The extensive resistance of this organism to several antibiotics leaves few options for antimicrobial therapy. In vitro synergism of the combination of trimethoprim-sulfamethoxazole (TMP-SMZ) and ticarcillin/clavulanic acid (TIC/CA) has been demonstrated. To our knowledge, we report the first case of ventriculoatrial cerebrospinal fluid shunt-associated endocarditis due to S. maltophilia. The patient was cured with combination therapy with TMP-SMZ and TIC/CA along with catheter removal. This is also the first report of S. maltophilia endocarditis successfully treated with this antibiotic combination. In a review of the medical literature, only 16 cases of S. maltophilia endocarditis were found. Most patients were intravenous drug users (43.8%) or had either prosthetic heart valves (50%) or an indwelling vascular catheter (18.8%). Although S. maltophilia is usually considered a nosocomial pathogen, about one-half of the cases were community-acquired. Twelve of sixteen patients had left-sided endocarditis. Therapy with a combination of two or more antibiotics was employed in most cases. Seven patients had been given TMP-SMZ therapy, but none had been treated with TIC/CA before. One-half of the patients required cardiac surgery. The overall mortality rate was 33%. Although the optimal antibiotic treatment for S. maltophilia endocarditis remains unknown, the case reported herein reinforces in vitro findings that the combination of TMP-SMZ and TIC/CA may be effective therapy.

Guyot A. et al. *Molecular epidemiology of multi-resistant Escherichia coli.* J Hosp Infect. 1999; 43(1) : 39-48.p Abstract: In this case-control study multi-resistant Escherichia coli isolates were characterized on a molecular level and risk factors for their development were identified. Thirty-two multi-resistant E. coli strains were isolated from the urine of 13 patients attending a renal clinic for chronic urinary tract infection (UTI) and from different sites of 11 terminally ill patients with nosocomial infections hospitalized on five different wards. All 32 isolates were resistant to ciprofloxacin, cotrimoxazole and produced beta-lactamase. All strains contained plasmids of 2-110 MDa of which a 50 MDa and a 100 MDa plasmid were present in 81% of the strains. Pulse-field gel electrophoresis (PFGE) analysis demonstrated 17 genotypes among 32 strains which indicates a polyclonal outbreak with some geographic clustering. Monitoring of patients over the study period showed that either the resident genotype remained the same and that these retained strains underwent changes in their plasmid contents, or that they were replaced by a different genotype after several months of therapy for chronic UTI. Univariate analysis indicated that multi-resistant E. coli develop in the presence of long-term selective ciprofloxacin pressure at a dosing regimen of 250 mg bid for more than 20 days and that treatment with a broad spectrum antimicrobial for more than three days favours the selection of multi-resistant E. coli in the flora of terminally ill patients with multiple disorders. Copyright 1999 The Hospital Infection Society.

Guyot A. et al. *Antimicrobial resistance of Neisseria gonorrhoeae in Liberia.* Trans R Soc Trop Med Hyg. 1998; 92(6) : 670-4.p Abstract: The prevalence and molecular characteristics of penicillinase-producing Neisseria gonorrhoeae (PPNG) and tetracycline-resistant N. gonorrhoeae (TRNG) were determined in 10 clinics in Monrovia, Liberia, to assess the likely effectiveness of the current standard treatment with penicillin or tetracycline. One hundred gonococcal strains were isolated from 146 urethral swabs and 261 cervical swabs and screened for susceptibility to ceftriaxone, penicillin, spectinomycin and tetracycline by the disk diffusion method; 83% were resistant to penicillin and 63% to tetracycline. Twenty-one strains from 18 men and 3 women with uncomplicated gonorrhoea were subjected to more detailed characterization. These 21 strains belonged to 5 auxotype/serovar classes; 86% were PPNG/TRNG. Three PPNG harboured the 4.4 MDa penicillinase plasmid and 16 the 3.2 MDa plasmid. All TRNG harboured the 25.2 MDa plasmid and their MICs for tetracycline were > 32 mg/L. They gave a PCR product which, according to its restriction pattern, corresponded to the American type tetM gene. By the agar dilution method, all strains exhibited intermediate resistance to sulphamethoxazole-trimethoprim (19:1) (co-trimoxazole) with MICs of 8-32 mg/L. All strains were susceptible to spectinomycin and ciprofloxacin. The MICs for gentamicin were 4-8 mg/L. The use of effective and affordable antimicrobial chemotherapy with either 500 mg ciprofloxacin or a single dose of gentamicin is discussed, with consideration of molecular biological, pharmacological and public health aspects.

Guzman-Blanco M. et al. *Bacterial resistance to antimicrobial agents in Latin America. The giant is awakening.* Infect Dis Clin North Am. 2000; 14(1) : 67-81, viii.p Abstract: Resistant bacteria are emerging in Latin America as a real threat to the favorable outcome of infections in community- and hospital-acquired infections. Despite present extensive surveillance, healthcare workers who most need the information may be unaware of this growing problem. Outbreaks of meningococci with diminished susceptibility to penicillin have been reported in the region; a constant increase of resistance to penicillin in pneumococci and poor activity of commonly used oral antibiotics for the treatment of community-acquired urinary tract infections have made the treatment of these infections more difficult. Reports from tertiary hospitals are similar to many other areas of the world, with increasing frequency of Klebsiella pneumoniae-carrying extended-spectrum beta-lactamase, multiresistant strains of Pseudomonas aeruginosa and Acinetobacter baumanni in ICU settings, and reports of methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci. A surveillance network readily accessible to those who prescribe antibiotics in Latin America is highly desirable.

Gwaltney J.M. Jr. *Acute community acquired bacterial sinusitis: To treat or not to treat.* Can Respir J. 1999; 6 Suppl A : 46A-50A.p Abstract: The paranasal sinuses, normally sterile, are prone to bacterial invasion as a complication of viral illnesses such as the common cold. Using computed tomograms, abnormalities of the sinuses can be seen in 90% of healthy adults with upper respiratory tract infections; only 2% of these patients will develop bacterial sinusitis. Possible rationales for antibiotic treatment of sinusitis include the normal sterility of the sinuses, the clinical morbidity associated with sinusitis, the possibility of serious intracranial and periorbital complications in untreated cases, and the possible progression of acute infections to chronic sinus disease. Evidence from the literature supports antibiotic treatment of sinusitis to eradicate infection and to reduce symptoms. There is insufficient literature evidence to prove that antibiotic treatment reduces serious complications or reduces progression to chronic sinus disease. Treatment should include an antimicrobial with a spectrum likely to cover the important pathogens, including those with high levels of resistance.

Gylys K.H. *Pharmacology department. Antimicrobial resistance.* J Cardiovasc Nurs. 1999; 13(2) : 66-9.p Abstract: Patients with cardiovascular disease are often predisposed to multiple infections. The degree of resistance to antibiotics that has developed in the last decade makes a significant contribution to the severity of infections in this patient population. Mechanisms for development and spread of resistance between organisms are described and related to a clinical example.

Gyo K. et al. *Residual bacterial infection in the tympanic cavity following surgery for ears with chronic discharge.* Auris Nasus Larynx. 1996; 23 : 13-9.p Abstract: In surgical treatment of ears with chronic discharge, pathogenic microorganisms may remain in the middle ear even after meticulous tympanomastoidectomy, and cause recurrent infection unless an appropriate antimicrobial agent is administered. The present study was conducted to determine the incidence of residual bacterial infection in the tympanic cavity by examining secretions from

a drainage tube placed there via the mastoid cavity during surgery. Comparison of the bacterial flora before and after surgery demonstrated that some of the microorganisms continued to be present in the tympanic cavity for up to 2 weeks despite medication, and that the incidence of Pseudomonas aeruginosa and Staphylococcus epidermidis remained fairly high.

Gyssens I.C. et al. *[Clinical results and costs due to improved antibiotics policies (see comments)].* Ned Tijdschr Geneeskd. 1999; 143(47) : 2361-4.p Abstract: Major reasons to conduct antibiotic policies are to improve the quality of patient care, to limit the emergence of resistance, and to contain costs. Many studies have addressed overconsumption and misuse of antibiotics. Studies have shown a correlation between antibiotic use in hospitals and the development of microbial resistance. Recommendations for the content and management of future antibiotic policy strategies in hospitals include educational programmes, consultation by infectious diseases physicians, restriction of the formulary, timely narrowing of empirical broad spectrum therapy ('streamlining'), and automatic stop orders. A recent study in a Dutch university hospital revealed overconsumption of antibiotics for prophylaxis in surgery and undertreatment with antibiotics in internal medicine departments. Intervention resulted in better compliance with guidelines, reduction of the consumption of antibiotics in surgical prophylaxis, and cost containment. However optimation of antimicrobial therapy also sometimes resulted in an increase of antimicrobial drug consumption.

Gyurko C. et al. *Candida albicans mutants deficient in respiration are resistant to the small cationic salivary antimicrobial peptide histatin 5.* Antimicrob Agents Chemother. 2000; 44(2) : 348-54.p Abstract: Histatins are a group of small cationic peptides in human saliva which are well known for their antibacterial and antifungal activities. In a previous study we demonstrated that histatin 5 kills both blastoconidia and germ tubes of Candida albicans in a time- and concentration-dependent manner at 37 degrees C, whereas no killing was detected at 4 degrees C. This indicated that killing activity depends on cellular energy. To test histatin 5 killing activity at lower cellular ATP levels at 37 degrees C, respiratory mutants, or so-called petite mutants, of C. albicans were prepared. These mutants are deficient in respiration due to mutations in mitochondrial DNA. Mutants were initially identified by their small colony size and were further characterized with respect to colony morphology, growth characteristics, respiratory activity, and cytochrome spectra. The killing activity of histatin 5 at the highest concentration was only 28 to 30% against respiratory mutants, whereas 98% of the wild-type cells were killed. Furthermore, histatin 5 killing activity was also tested on wild-type cells in the presence of the respiratory inhibitor sodium azide or, alternatively, the uncoupler carbonyl cyanide m-chlorophenylhydrazone. In both cases histatin 5 killing activity was significantly reduced. Additionally, supernatants and pellets of cells incubated with histatin 5 in the presence or absence of inhibitors of mitochondrial ATP synthesis were analyzed by sodium dodecyl sulfate gel electrophoresis. It was observed that wild-type cells accumulated large amounts of histatin 5, while wild-type cells treated with inhibitors or petite mutants did not accumulate significant amounts of the peptide. These data showed first that cellular accumulation of histatin 5 is necessary for killing activity and second that accumulation of histatin 5 depends on the availability of cellular energy. Therefore, mitochondrial ATP synthesis is required for effective killing activity of histatin 5.

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Haarr E. et al. *[First infection with vancomycin resistant type VanA enterococci in a Norwegian hospital].* Tidsskr Nor Laegeforen. 1998; 118(8) : 1188-90.p Abstract: Enterococci are part of the normal human and animal bowel flora. They are considered bacteria of relatively low virulence, but are important nosocomial pathogens. In the context of their intrinsic resistance to a number of antimicrobial agents, the rapid emergence of multiresistant enterococci is alarming. As inhabitants of the gastrointestinal tract, they come into close contact with other bacteria and may pass antibiotic resistance genes to them. We report the first case of infection with a VanA vancomycin-resistant. Enterococcus in Norway. The strain was identified as Enterococcus faccium with high level resistance to aminoglycosides, ampicillin, teicoplanin and vancomycin. The VanA phenotype was confirmed by PCR detection of the vanA gene. Transmission, treatment, prevention, and control of infections with vancomycin-resistant enterococci is discussed.

Haberal M. et al. *Visceral injuries, wound infection and sepsis following electrical injuries.* Burns. 1996; 22(2) : 158-61.p Abstract: Visceral injuries, wound infection and sepsis were investigated in 226 inpatients who sustained electrical burns over a period of 15 years. Four patients who sustained thoracic and abdominal organ injuries were noted in this series. The patients had injuries of the small intestine, stomach, colon and the lung. All the patients received operative treatment. Two of them died of sepsis. Injuries to the internal organs should always be considered following high-voltage injuries, and they should be managed as early as possible. The data concerning wound infection and sepsis following electrical injuries were evaluated in three consecutive 5-year periods. Over this period of 15 years, different antibiotic regimens were used for prophylaxis and treatment. Most patients in the current series had been contaminated or infected by various pathogens prior to admission. Long-lasting administration of prophylactic antibiotics in these patients showed no improvement in controlling the sepsis. After 1987, most of the microorganisms were eliminated following more effective antimicrobial therapy. The progressive decrease in infection frequency of species such as Pseudomonas aeruginosa, Proteus mirabilis and Enterobacter cloacae, appeared to be causally related to the changes in the general therapeutic protocol which included new antibiotics. The infections caused by E. coli and Staphylococcus aureus showed a rather steady state. A marked increase in frequency of negative wound cultures was also noted between the years 1989 and 1993. A gradual decrease in mortality rates was observed from the first to the last 5-year period, whereas mortality rates due to sepsis showed a gradual but slower decline. Sepsis (142 patients comprising 62.8 per cent of the total mortality rate) was the most frequent complication resulting in death.

Hachicha M. et al. *Regulation of chemokine gene expression in human peripheral blood neutrophils phagocytosing microbial pathogens.* J Immunol. 1998; 160(1) : 449-54.p Abstract: Production of chemokines (chemotactic cytokines) by neutrophils is likely to be important in the regulation of inflammation and the control of infection. In this study we show that exposure of human neutrophils to various microbial pathogens leads to the production of both macrophage inflammatory protein 1alpha (MIP-1alpha) and IL-8. The bacterial microbes, Salmonella typhimurium and Pseudomonas aeruginosa, and Staphylococcus aureus all strongly induced both IL-8 and MIP-1alpha secretion, whereas Streptococcus pneumoniae, Staphylococcus epidermidis, and the opportunistic yeast Candida albicans were less potent. Saccharomyces cerevisiae and zymosan both induced IL-8 secretion but failed to stimulate that of MIP-1alpha. Coincubation of neutrophils with the proinflammatory cytokine TNF-alpha and the micro-organisms also led to differential expression of MIP-1alpha and IL-8. Significant enhancement of the induction of both MIP-1alpha and IL-8 by S. typhimurium, P. aeruginosa, and S. pneumoniae as well as by C. albicans was observed. In contrast, while IL-8 production in response to S. cerevisiae and zymosan was enhanced in the presence of TNF-alpha, no MIP-1alpha was produced. These combined results indicate that while neutrophils exposed to some micro-organisms alone or in the presence of inflammatory cytokines such as TNF-alpha will produce both MIP-1alpha and IL-8, resulting in generation of signals for the

recruitment of mononuclear leukocytes and neutrophils, respectively, certain types of microorganisms can skew this response toward synthesis of IL-8.

Hagelskjaer L.H. et al. *[Peritonitis in continuous ambulatory peritoneal dialysis. An evaluation of the empiric initial antibiotic treatment].* Ugeskr Laeger. 1996; 158(18) : 2532-7.p Abstract: Retrospectively, the clinical outcome and the initial empiric antibiotic treatment of peritonitis in 106 patients on continuous ambulatory peritoneal dialysis (CAPD) were evaluated during a two-year period. A mean frequency of 0.89 episodes of peritonitis per year of dialysis was found. There was a tendency towards an increased frequency of peritonitis in older patients. Diabetic patients constituted a younger age group and had a tendency towards having a lower risk of peritonitis. Patients with polycystic renal disease had a significantly increased risk. The risk of episodes with coagulase-negative staphylococci increased significantly with age. Repeated peritonitis episodes with coagulase-negative staphylococci was associated with a significant increase in the appearance of methicillin drug resistance. Carriers of Staphylococcus aureus had a significantly increased risk of Staphylococcus aureus peritonitis. Microorganisms were cultured in 94% of the episodes. The initial antibiotic therapy was only sufficient in 66% due to antimicrobial drug resistance. The initial antibiotic treatment was changed in 58% of the episodes. The treatment could have been changed to antibiotics with a narrower antimicrobial spectrum in 51% of the episodes. Relapse was seen in 11% of culture positive episodes. In 16% of the episodes (29% of patients with peritonitis) it was necessary to remove the dialysis catheter and transfer the patient to haemodialysis to clear the infection. Only 15% of these patients returned to CAPD again. We found that an initial empiric antibiotic regime of vancomycin combined with an aminoglycoside is to be recommended as achieving an antibiotic coverage of 88%, and this is now the standard regime in the department.

Hagiwara T. et al. *[Massive and progressive hepatosplenomegaly caused by disseminated nontuberculous mycobacteriosis in a patient with acquired immunodeficiency syndrome].* Kekkaku. 1995; 70(7) : 423-9.p Abstract: A 28-year-old hemophilia A patient was admitted to our hospital in July, 1991 because of high fever, chronic diarrhea and anemia. The patient had been recognized as a asymptomatic carrier of human immunodeficiency virus (HIV) in 1985 and had developed Pneumocystis carinii pneumonia and had been diagnosed as acquired immunodeficiency syndrome (AIDS) in 1990. Hematologic laboratory examinations on admission revealed pancytopenia and a CD4+ cell count of 3/mm3. X-ray findings of chest and abdomen were normal and bacterial cultures of sputum, urine, blood, stool, cerebrospinal fluid and bone marrow yielded no pathogenic microorganisms. Microscopical examination of the stained specimens showed no acid-fast bacilli. On his fifth hospital day, his liver and spleen enlarged markedly and an abdominal CT scan obtained on the 13th day revealed high-grade hepatosplenomegaly. Administration of several kinds of antibiotics, antifungal agents, antiviral agents, antituberculous agents and gamma-globulin medicines did not relieve the symptoms. On the 28th day the patient had developed a subarachnoid hemorrhage and died five days later. Retrospectively all cultures for acid-fast bacilli of the specimens on his admission yielded nontuberculous mycobacteria. The bacteria were identified as Mycobacterium avium by polymerase chain reaction and his disease was eventually diagnosed as disseminated Mycobacterium avium complex (MAC) infection. The liver and spleen weighed 2,660 g and 1,840 g respectively at autopsy. Although hepatosplenomegaly is commonly recognized in AIDS patients with disseminated MAC infection, such massive and rapid enlargement has been rarely observed. This case study emphasize the importance of diagnosis and rapid treatment at the early stage of MAC infection.

Hagman H.M. et al. *Vancomycin-resistant enterococci. The 'superbug' scourge that's coming your way.* Postgrad Med. 1996; 99(5) : 60-5, 69-71.p Abstract: Strains of vancomycin-resistant enterococci (VRE) have emerged and spread widely throughout the United States during the last few years. Multiply-resistant strains of Enterococcus faecium are especially troublesome because they are often resistant to all commercially available antimicrobial agents. At present, VRE infections occur most often in hospitalized patients with severe underlying disease who have undergone invasive procedures and received prolonged courses of broad-spectrum antimicrobial therapy. Because therapeutic options are limited, prevention of spread from patients with known cases to other vulnerable patients is essential.

Hajjar J. et al. *[Surveillance of nosocomial infections related to anesthesia. A multicenter study (see comments)].* Ann Fr Anesth Reanim. 2000; 19(1) : 47-53.p Abstract: OBJECTIVES: To determine incidence rate, main characteristics and risk factors of nosocomial infections associated with anesthesia (NIAA). STUDY DESIGN: Prospective, descriptive multicentre survey. PATIENTS: All patients aged more than 15 years and undergoing surgery (except cardio-thoracic, ENT or ambulatory surgery) under general or regional anaesthesia. METHODS: Voluntary participation of surgical units from public or private hospitals. Use of pre-established definitions of infections and a 72 hours postanesthetic follow-up. Anaesthesia and operation related risk factors collected. End point based on occurrence, or not, of clinical infection. Record, control, treatment and analysis of the data by Epi Info—5.0 software. Statistics used: Fischer's exact test, Mantel-Haenszel test, Anova method, Kruskall-Wallis test. RESULTS: Among 7,300 patients belonging to 13 hospitals, 25 developed an infection (nine vascular catheter related infections, 12 respiratory tract infections, two infections of the eye and two of the mouth). Only two infections have been bacteriologically documented. The overall incidence of NIAA was 3.4 per 1,000 patients. It was significantly higher after an anaesthetic of more than 2 hours and after transfusion. CONCLUSIONS: This first prospective survey of NIAA confirmed that nosocomial infections are a real problem in the practice of anaesthesia and the necessity to use preventive measures. A survey with a larger sample size would allow to specify the respective part of the various risk factors and to develop a risk index.

Hajmeer M.N. et al. *Computational neural networks for predictive microbiology. II. Application to microbial growth.* Int J Food Microbiol. 1997; 34(1) : 51-66.p Abstract: The growth of a specific microorganism on a certain food is influenced by a number of environmental factors such as temperature, pH, and salt concentration. Methods that delineate the history of the growth of microorganisms are always subject to a considerable debate and scrutiny in the field of predictive microbiology. Regardless of its types, a growth model (e.g., modified Gompertz model) contains several parameters that vary depending on the microorganisms/food combination and the associated prevailing environmental conditions. The growth model parameters for a set of operating conditions are commonly determined from expressions developed via multiple linear regressions. In the present study, a substitute for the nonlinear regression-based equations is developed using computational neural networks. Computational neural networks are applied herein on experimental data pertaining to the anaerobic growth of Shigella flexneri. Results have indicated that predictions by neural networks offer better agreement with experimental data as compared to predictions obtained via corresponding regression equations.

Hakanen A. et al. *Detection of decreased fluoroquinolone susceptibility in Salmonellas and validation of nalidixic acid screening test.* J Clin Microbiol. 1999; 37(11) : 3572-7.p Abstract: We evaluated 1,010 Salmonella isolates classified as fluoroquinolone susceptible according to the National Committee for Clinical Laboratory Standards guidelines for susceptibility to nalidixic acid and three fluoroquinolones. These isolates were divided into two distinct subpopulations, with the great majority (n = 960) being fully ciprofloxacin susceptible and a minority (n = 50) exhibiting reduced ciprofloxacin susceptibility (MICs ranging between 0.125 and 0.5 microg/ml).

The less ciprofloxacin-susceptible isolates were uniformly resistant to nalidixic acid, while only 12 (1.3%) of the fully susceptible isolates were nalidixic acid resistant. A similar association was observed between resistance to nalidixic acid and decreased susceptibility to ofloxacin or norfloxacin. A mutation of the gyrA gene could be demonstrated in all isolates for which the ciprofloxacin MICs were >/= 0.125 microg/ml and in 94% of the nalidixic acid-resistant isolates but in none of the nalidixic acid-susceptible isolates analyzed. Identification of nalidixic acid resistance by the disk diffusion method provided a sensitivity of 100% and a specificity of 87.3% as tools to screen for isolates for which the MICs of ciprofloxacin were >/= 0.125 microg/ml. We regard it as important that microbiology laboratories endeavor to recognize these less susceptible Salmonella strains, in order to reveal their clinical importance and to survey their epidemic spread.

Hakanen A. et al. *Increasing fluoroquinolone resistance in salmonella serotypes in Finland during 1995-1997.* J Antimicrob Chemother. 1999; 43(1) : 145-8.p Abstract: Antimicrobial resistance trends were examined for 811 salmonella isolates from humans collected in Finland during 1995-1997. The material was divided into domestic and foreign isolates according to the origin of infection. A total of 2.3% of the 387 domestic and 7.8% of the 424 foreign isolates were quinolone-resistant (P < 0.001). Among the domestic isolates we detected an emergence of ciprofloxacin resistance (MIC > or = 0.25 mg/L) with the proportion of resistant isolates increasing from 0 to 2.2% (P = 0.2). Among the foreign isolates this increase was even more dramatic, from 2.0% to 8.4% (P = 0.037) during the study period.

Hakansson A. et al. *A folding variant of alpha-lactalbumin with bactericidal activity against Streptococcus pneumoniae.* Mol Microbiol. 2000; 35(3) : 589-600.p Abstract: This study describes an alpha-lactalbumin folding variant from human milk with bactericidal activity against antibiotic-resistant and -susceptible strains of Streptococcus pneumoniae. The active complex precipitated with the casein fraction at pH 4.6 and was purified from casein by a combination of anion exchange and gel chromatography. Unlike other casein components, the active complex was retained on the ion-exchange matrix and eluted only with high salt. The eluted fraction showed N-terminal and mass spectrometric identity with human milk alpha-lactalbumin, but native alpha-lactalbumin had no bactericidal effect. Spectroscopic analysis demonstrated that the active form of the molecule was in a different folding state, with secondary structure identical to alpha-lactalbumin from human milk whey, but fluctuating tertiary structure. Native alpha-lactalbumin could be converted to the active bactericidal form by ion-exchange chromatography in the presence of a cofactor from human milk casein, characterized as a C18:1 fatty acid. Analysis of the antibacterial spectrum showed selectivity for streptococci; Gram-negative and other Gram-positive bacteria were resistant. The folding variant of alpha-lactalbumin is a new example of naturally occurring molecules with antimicrobial activity.

Hakenbeck R. et al. *Resistant penicillin-binding proteins.* Cell Mol Life Sci. 1998; 54(4) : 332-40.p Abstract: Low-affinity penicillin-binding proteins (PBPs), which participate in the beta-lactam resistance of several pathogenic bacteria, have different origins. Natural transformation and recombination events with DNA acquired from neighbouring intrinsically resistant organisms are responsible for the appearance of mosaic genes encoding two or three low-affinity PBPs in highly resistant strains of transformable microorganisms such as Neisseria and Streptococcus pneumoniae. Methicillin-resistant Staphylococcus aureus and coagulase-negative staphylococcal strains possess the mecA determinant gene, which probably evolved within the Staphylococcus genus from a closely related and physiologically functional gene that was modified by point mutations. The expression of mecA is either inducible or constitutive. A stable high-level resistant phenotype requires the synthesis of a normally constituted peptidoglycan. Enterococci have a natural low susceptibility to beta-lactams related to the presence of an intrinsic low-affinity PBP. Highly resistant enterococcal strains overexpress this PBP and/or reduce its affinity.

Hakimelahi G.H. et al. *Synthesis and biological evaluation of an electronically activated isooxacephem.* Bioorg Med Chem. 1996; 4(8) : 1361-4.p Abstract: New isooxacephem (+/-)-3-ethyl 2-hydrogen (6RS,7RS)-8-oxo-7-(phenylacetamido)-4-oxa-1-azabicyclo [4.2.0]oct-2-ene-2, 3-dicarboxylate (8) was synthesized from (+/-)-dibenzyl 2-[cis-2-oxo-3-(phenylacetamido)-4-styryl-1-azetidinyl]-2-[t- butyldimethylsiloxy(methoxycarbonyl)methyl]malonate (1) in six steps. This bicyclic beta-lactam was found to possess notable biological activities against several pathogenic microorganisms in vitro, including Staphylococcus aureus 95, S. aureus FDA 209P, Escherichia coli ATCC 39188, Salmonella typhi O-901, Pseudomonas aeruginosa 18S-H, P. aeruginosa 1101-75, and Klebsiella pneumoniae NCTC 418. The electronic activation of the beta-lactam moiety by an ester group plays a prominent role in the biological activity of this novel isooxacephem.

Hall L.M. et al. *Genetic relatedness within and between serotypes of Streptococcus pneumoniae from the United Kingdom: analysis of multilocus enzyme electrophoresis, pulsed-field gel electrophoresis, and antimicrobial resistance patterns.* J Clin Microbiol. 1996; 34(4) : 853-9.p Abstract: A collection of 54 isolates of invasive Streptococcus pneumoniae of serotypes 3 and 14 and serogroups 6, 9, 19, and 23 was investigated. Multilocus enzyme electrophoresis and pulsed-field gel electrophoresis suggested that two clones were represented in the collection, one of serotype 14 isolates, most of which were resistant to erythromycin, and one of serotype 9V isolates, in which resistance to penicillin (MIC, 1 microgram/ml), cefotaxime, and co-trimoxazole was common. Among other isolates there were only a limited correlation between genetic relatedness measured by multilocus enzyme electrophoresis and expression of the same capsule type. However, isolates with highly related pulsed-field gel electrophoresis patterns always shared the same serotype and highly related allele profiles. Calculation of the index of association suggests a freely recombining population structure with epidemic spread of successful clones.

Hall-Stoodley L. et al. *Biofilm formation by the rapidly growing mycobacterial species Mycobacterium fortuitum.* FEMS Microbiol Lett. 1998; 168(1) : 77-84.p Abstract: Rapidly growing mycobacteria (RGM) are found in soil and diverse aquatic environments. Two species, Mycobacterium fortuitum and Mycobacterium chelonae, are associated with disease and are difficult to eradicate. Biofilm formation may be a contributing factor to their mode of transmission and their resistance to antimicrobial agents. We investigated the ability of the RGM species M. fortuitum to colonise surfaces using a modified Robbins device. M. fortuitum formed dense biofilms within 48 h. The high numbers of sessile organisms recovered and the swiftness of colonisation suggest that M. fortuitum readily forms biofilms. These results suggest a novel mechanism for mycobacteria in evading antimicrobial treatment and also indicate that biofilms should be considered possible sites for mycobacterial contamination.

Hamer D.H. *Treatment of nosocomial pneumonia and tracheobronchitis caused by multidrug-resistant Pseudomonas aeruginosa with aerosolized colistin.* Am J Respir Crit Care Med. 2000; 162(1) : 328-30.p Abstract: Gram-negative bacilli including multidrug-resistant (MDR) Pseudomonas aeruginosa are responsible for a significant proportion of episodes of nosocomial pneumonia. Since the development of new antibiotics with activity against gram-negative organisms has not kept pace with the increase in prevalence of MDR pathogens, there has been renewed interest in antimicrobial agents that had previously been used but had been abandoned because of toxic side effects. This report describes three patients with nosocomial pneumonia or tracheobronchitis due to multiresistant strains of P. aeruginosa for whom aerosolized colistin proved beneficial as supplemental therapy. Aerosolized colistin merits further consideration as a

therapeutic intervention for patients with pulmonary infections due to MDR P. aeruginosa.

Hamilton-Miller J.M. et al. *Public health issues arising from microbiological and labelling quality of foods and supplements containing probiotic microorganisms.* Public Health Nutr. 1999; 2(2) : 223-9.p Abstract: OBJECTIVE: To assess the accuracy and helpfulness of labelling on products containing probiotic bacteria. DESIGN AND SETTING: 52 such products - 44 from the UK (21 supplements, 15 fermented functional foods, eight 'health-care' products) and eight from continental Europe - have been tested for microbiological content, and results compared to the information available on their labels. Products were stored in the dark at 4 degrees C and analysed before their expiry or sell-by date. Careful note was taken of wording on labels, package inserts, packaging, promotional literature and catalogue descriptions, as applicable. Products were cultured on appropriate bacteriological media, and organisms grown were counted and identified. RESULTS: Bioyoghurts gave no indication of numbers, and only five accurately described their bacterial content; results of culture were usually satisfactory. 'Healthcare' products (mostly intended for the bowel) usually indicated the presence of bacteria, but the numerical content was hard to ascertain, and cultural results fell short of label claims. Supplements were sometimes incorrectly labelled in bacteriological terms, and often contained markedly reduced numbers and/or had extraneous strains and/or strains specified on the label were missing. Products from continental Europe (that were sold for specific medical indications) seemed of a higher microbiological standard. The potential pathogen Enterococcus faecium was found in nine products. The most successful of the new functional foods in Britain now contain probiotics, and probiotic preparations are prominent among the expanding range of nutritional supplements presently available to consumers. CONCLUSIONS: Our findings have public health implications, and suggest that improvements are needed in labelling and quality assurance procedures for products containing probiotic organisms. The presence of the potential pathogen Enterococcus faecium (intentionally or as a contaminant) in some products calls for a review of the value of this species as a probiotic.

Hammen P.K. et al. *Investigation of a side-chain-side-chain hydrogen bond by mutagenesis, thermodynamics, and NMR spectroscopy.* Protein Sci. 1995; 4(5) : 936-44.p Abstract: Anomalous NMR behavior of the hydroxyl proton resonance for Ser 31 has been reported for histidine-containing protein (HPr) from two microorganisms: Escherichia coli and Staphylococcus aureus. The unusual slow exchange and chemical shift exhibited by the resonance led to the proposal that the hydroxyl group is involved in a strong hydrogen bond. To test this hypothesis and to characterize the importance of such an interaction, a mutant in which Ser 31 is replaced by an alanine was generated in HPr from Escherichia coli. The activity, stability, and structure of the mutant HPr were assessed using a reconstituted assay system, analysis of solvent denaturation curves, and NMR, respectively. Substitution of Ser 31 yields a fully functional protein that is only slightly less stable (delta delta G(folding) = 0.46 +/- 0.15 kcal mol-1) than the wild type. The NMR results confirm the identity of the hydrogen bond acceptor as Asp 69 and reveal that it exists as the gauche- conformer in wild-type HPr in solution but exhibits conformational averaging in the mutant protein. The side chain of Asp 69 interacts with two main-chain amide proteins in addition to its interaction with the side chain of Ser 31 in the wild-type protein. These results indicate that removal of the serine has led to the loss of all three hydrogen bond interactions involving Asp 69, suggesting a cooperative network of interactions. A complete analysis of the thermodynamics was performed in which differences in side-chain hydrophobicity and conformational entropy between the two proteins are accounted for.(ABSTRACT TRUNCATED AT 250 WORDS).

Hammond J.M. et al. *Long-term effects of selective decontamination on antimicrobial resistance.* Crit Care Med. 1995; 23(4) : 637-45.p Abstract: OBJECTIVE: To determine whether selective decontamination of the digestive tract exerts any long-term effects on antimicrobial resistance patterns. DESIGN: A surveillance and interventional study comparing the antimicrobial sensitivity patterns of clinically important bacterial isolates the year before a 2-yr, double-blind, randomized, controlled study of selective decontamination of the digestive tract, and for the year thereafter when no use of the regimen was made. SETTING: A ten-bed respiratory intensive care unit (ICU) in a 1,200-bed teaching hospital. PATIENTS: All 1,528 patients admitted to the ICU over the 4-yr study period were included. There were 406 patients admitted in the year before the study of decontamination of the digestive tract (65% medical, 23% surgical, and 12% trauma), of whom 76% required mechanical ventilation. There were 719 patients admitted during the 2-yr study of selective decontamination (55% medical, 28% surgical, and 17% trauma), of whom 79.6% required mechanical ventilation. There were 403 patients admitted in the subsequent year (61% medical, 25% surgical, and 14% trauma), of whom 76.9% required mechanical ventilation. INTERVENTIONS: We performed daily clinical monitoring to detect nosocomial infection, with microbiological investigation when clinically indicated, as well as twice-weekly routine microbiological surveillance sampling. Antimicrobial susceptibility testing using standard laboratory methods was also performed. Selective decontamination of the digestive tract included parenteral cefotaxime and oral and enteral polymyxin E, amphotericin B, and tobramycin. MEASUREMENTS AND MAIN RESULTS: The occurrence rate of nosocomial infection was 20.6%, 16.6%, and 25.3%, respectively, in the three study periods. In the year after selective decontamination, there was an increase in the occurrence rate of infection ($p = .005$), with an associated increase in infections caused by the Enterobacteriaceae, while a reduction in the level of resistance to the third-generation cephalosporins were found ($p = .07$). There was a progressive increase in the occurrence rate of infections caused by Acinetobacter species ($p = .05$). Only 11 infections over the 4 yrs were caused by Enterococcus species. Staphylococcal infections were uncommon (5.7% of admissions), and the level of methicillin resistance did not change. No increase in aminoglycoside resistance occurred. CONCLUSION: No long-term effects on antimicrobial resistance or the spectrum of nosocomial pathogens could be attributed to the use of selective decontamination of the digestive tract over a 2-yr period in a respiratory ICU admitting all categories of patients.

Hammond J.M. et al. *The etiology and antimicrobial susceptibility patterns of microorganisms in acute community-acquired lung abscess.* Chest. 1995; 108(4) : 937-41.p Abstract: OBJECTIVE: To determine the spectrum and antibiotic susceptibility patterns of microorganisms causing acute community-acquired lung abscess. DESIGN: A prospective survey. SETTING: Medical emergency department and wards of a tertiary teaching hospital. PATIENTS: Thirty-four adult patients with both clinical and radiologic features compatible with a diagnosis of acute community-acquired lung abscess who had received less than 48 h of antibiotic therapy. INTERVENTIONS: Microbiologic specimens obtained by percutaneous lung aspiration and with a protected specimen brush via fiberoptic bronchoscopy were submitted for aerobic and anaerobic culture. MAIN OUTCOME MEASURES: Identification of all microorganisms, including anaerobes, and determination of antibiotic susceptibility. RESULTS: A mean of 2.3 bacterial species per patient was isolated, anaerobes alone being isolated in 44% of cases, aerobes alone in 19%, and mixed aerobic and anaerobic isolates in 22%. Aerobic Gram-negative pathogens were uncommon. In seven patients, Mycobacterium tuberculosis was identified; in two it was associated with other bacteria. In four patients, no organisms were isolated. All the nonmycobacterial isolates were susceptible to amoxicillin-clavulanate and in addition the anaerobes were all susceptible to chloramphenicol and almost all to a combination of penicillin and metronidazole. Among the anaerobes, the level of resistance to penicillin, metronidazole, and clindamycin individually was 21%, 12%, and 5%, respectively. CONCLUSIONS: Community-acquired acute lung abscess is usually caused by multiple anaerobic and less frequently aerobic Gram-pos-

itive microorganisms, which should respond to empirical therapy with amoxicillin-clavulanate, chloramphenicol, or a combination of penicillin and metronidazole. Tuberculosis, which may be indistinguishable from an acute lung abscess, occurred in 21% of patients in our study. Most bacterial pathogens are sensitive to conventional antimicrobial therapy and further investigation with percutaneous lung aspiration or bronchoscopy is indicated only when there is lack of early response to therapy or there is the presence of atypical clinical features.

Hanberger H. et al. *New species-related MIC breakpoints for early detection of development of resistance among gram-negative bacteria in Swedish intensive care units.* J Antimicrob Chemother. 1999; 44(5) : 611-9.p Abstract: The frequency of decreased antibiotic susceptibility among 534 Gram-negative aerobic bacilli from patients admitted to intensive care units at eight hospitals in Sweden during 1997 was evaluated. MICs of cefepime, ceftazidime, ceftriaxone, ciprofloxacin, gentamicin, imipenem and piperacillin-tazobactam were determined using Etest. Reduced susceptibility (resistant and intermediate/indeterminate susceptible strains) was defined according to the MIC breakpoints of the British Society for Antimicrobial Chemotherapy (BSAC), the National Committee for Clinical Laboratory Standards (NCCLS) and the new species-related breakpoints of the Swedish Reference Group for Antibiotics (SRGA). The BSAC/NCCLS/SRGA breakpoints for susceptible category (mg/L) of Enterobacteriaceae are: cefepime, not available (NA)/8/0.5; ceftazidime, 2/8/2; ceftriaxone, NA/8/0.5; ciprofloxacin, 1/1/0.12; gentamicin, 1/4/2; imipenem, 4/4/1; and piperacillin-tazobactam, NA/16/16. The most frequently isolated organisms were Escherichia coli (n = 160; 30%), Klebsiella spp. (n = 84; 16%), Enterobacter spp. (n = 77; 14%), Pseudomonas aeruginosa (n = 64; 12%) andProteus spp. (n = 28; 5%). Decreased susceptibility among E. coliusing the BSAC/NCCLS/SRGA respective breakpoints (%) were: cefepime, NA/0/2; ceftazidime, 2/2/2; ceftriaxone, NA/1/2; ciprofloxacin, 2/2/8; gentamicin, 21/0/3; imipenem, 0/0/2; and piperacillin-tazobactam, NA/4/4. Corresponding levels of decreased susceptibility (%) among Klebsiellaspp. were: cefepime, NA/0/5; ceftazidime, 2/1/2; ceftriaxone, NA/1/10; ciprofloxacin, 4/4/19; gentamicin, 25/2/5; imipenem, 0/0/0; and piperacillin-tazobactam, NA/10/10; and among Enterobacter spp. were: cefepime, NA/1/19; ceftazidime, 30/29/30; ceftriaxone, NA/30/36; ciprofloxacin, 3/3/15; gentamicin,18/0/0; imipenem, 0/0/5; and piperacilllin-tazobactam, NA/27/27. In conclusion, the species-related SRGA breakpoints detected Gram-negative isolates with decreased susceptibility in comparison with the native population with higher frequency than did the NCCLS breakpoints. The BSAC breakpoints for susceptible organisms were similar to NCCLS for ciprofloxacin and imipenem, and similar to SRGA for ceftazidime but lower than both NCCLS and SRGA for gentamicin, causing a much higher frequency of decreased susceptibility to gentamicin.

Hand W.L. *Current challenges in antibiotic resistance.* Adolesc Med. 2000; 11(2) : 427-38.p Abstract: The striking, widespread increase in bacterial resistance to antibiotics is an issue of great concern. Worldwide emergence of antibiotic resistances in our common gram-positive coccal pathogens is probably the most serious problem we have in the realm of bacterial infections. The most important of these organisms are penicillin-resistant Streptococcus pneumoniae, vancomycin-resistant Enterococcus, and methicillin- (and now vancomycin-) resistant Staphylococcus aureus. Although known by the above names, all of these organisms are multidrug-resistant. Beta-lactam and vancomycin resistances in gram-positive cocci are caused by altered cell wallnbinding sites with decreased affinity for the drug. Another serious problem is that of resistance in certain gram-negative bacilli due to extended-spectrum beta-lactamase production. These antibiotic resistances in common pathogens have made antimicrobial therapy of many infections extremely difficult or virtually impossible in some instances. The extensive, and often inappropriate, use of antibiotics in the U.S. and worldwide is the major factor in the emergence and spread of antimicrobial resistance. Microbial mechanisms, epidemiology, clinical importance, treatment, and prevention of these antibiotic resistance problems are discussed.

Handal T. et al. *Antimicrobial resistance with focus on oral beta-lactamases.* Eur J Oral Sci. 2000; 108(3) : 163-74.p Abstract: Over the last 10-15 yr antibiotic resistance has increased in the oral microflora. The beta-lactam antibiotics, i.e., penicillins and cephalosporins, are the most frequently used antimicrobial agents. Unfortunately, the efficiency of these drugs is increasingly being challenged by the emergence of resistant bacteria, which is mainly due to their production of beta-lactamases. In this paper, mechanisms of antibiotic resistance are reviewed, with emphasis on beta-lactamases. This review also discusses how the presence of beta-lactamases in oral microorganisms may affect the treatment of oral diseases. Dentists can influence the emerging global crisis of antibiotic resistance by carefully evaluating the indications for antibiotic treatment. General guidelines for when and how to use antibiotics in dentistry are reviewed.

Hanevold C.D. et al. *Effect of rifampin on Staphylococcus aureus colonization in children on chronic peritoneal dialysis.* Pediatr Nephrol. 1995; 9(5) : 609-11.p Abstract: The efficacy of rifampin in eliminating Staphylococcus aureus colonization was evaluated in a pediatric peritoneal dialysis population. Six children with documented nasal colonization were treated for 7 days with rifampin and cloxacillin. Although antimicrobial therapy eliminated nasal carriage in all patients, recolonization occurred in 66%. Exit site colonization proved difficult to eradicate with negative cultures documented in only 3 of 5 children after rifampin/cloxacillin therapy. Although S. aureus carriage is a risk factor for S. aureus infections, efforts to eradicate carriage with rifampin are hindered by rapid recolonization.

Hanley E.M. et al. *Evaluation of an antiseptic triple-lumen catheter in an intensive care unit.* Crit Care Med. 2000; 28(2) : 366-70.p Abstract: OBJECTIVE: To evaluate a decrease in catheter-related bloodstream infection rate in patients with antiseptic triple-lumen catheters in an intensive care unit. DATA SOURCES: Retrospective review of surveillance records, patient medical records, laboratory and microbiological reports, and antibiotic administration records. STUDY SELECTION: Patients admitted to the intensive care unit with triple-lumen catheters. DATA EXTRACTION: A subset of one entry per patient was extracted from 2 yrs of primary bloodstream infection surveillance data. Data collection included risk factors, laboratory and microbiological data, and insertion sites and dates of all intravascular catheters present during triple-lumen catheterization. DATA SYNTHESIS: The catheter-related bloodstream infection rate was 5.4 and 11.3 per 1000 catheter days in antiseptic and nonantiseptic triple-lumen catheter groups, respectively (p =.06). By multivariate analysis using a Cox Proportional Hazards Model, the antiseptic triple-lumen catheters were associated with a significant reduction in catheter-related bloodstream infection (p =.03). Model expansion to include intrajugular site was significant by a likelihood ratio test [2(log likelihood diff) = 4.26 P<.05 chi2(1)] CONCLUSIONS: The use of antiseptic triple-lumen catheters may substantially reduce catheter-related bloodstream infections in an intensive care population and may be subsequently associated with a decrease in length of stay.

Hanna R.M. et al. *Percutaneous catheter drainage in drug-resistant amoebic liver abscess.* Trop Med Int Health. 2000; 5(8) : 578-81.p Abstract: This communication records our experience with the percutaneous catheter drainage (PCD) of 22 amoebic liver abscesses in 19 patients who had failed to respond to amoebicidal therapy. In one patient with a left lobe abscess, imminent rupture was an additional indication for drainage. PCD combined with amoebicidal therapy not only expedited recovery, but was curative in all 19 patients. There were no complications. We conclude that PCD is a most useful adjunct to drug therapy and recommend its routine use in the management of drug-resistant amoebic liver abscesses.

Hansen D.S. et al. *Epidemiology of Klebsiella bacteraemia: a case control study using Escherichia coli bacteraemia as control.* J Hosp Infect. 1998; 38(2) : 119-32.p Abstract: Epidemiological data from 117 episodes of Klebsiella bacteraemia were compared with those from matched controls with Escherichia coli bacteraemia. Cases and controls were obtained from 20,631 blood cultures taken from patients in Hvidovre Hospital between 1990 and 1992. The data studied included: sex and age, risk factors, portal of entry, outcome, nosocomial acquisition and distribution within the hospital. The incidence of Klebsiella bacteraemia was 9.3/10,000 admissions (76% Klebsiella pneumoniae; 24% Klebsiella oxytoca). Patients with Klebsiella and E. coli bacteraemia had many common features, including a high incidence of neoplastic disease, biliary tract disease, and renal failure. Many had undergone surgery or received therapy with steroids, antacids or antibiotics. Klebsiella bacteraemia was more often found in males, in patients with hospital contact within the previous month, and polymicrobial infection. Logistic regression analysis showed that use of invasive plastic devices and diabetes were significantly associated with Klebsiella bacteraemia. The urinary tract was the commonest source, followed by the biliary tract; 27% of patients had no obvious focus of infection, and in many of these an invasive device may have been involved. Forty-five K-serotypes were found—the largest number being nine strains of type K3; only a few strains had acquired resistance characters to antimicrobial agents. There were no differences between community- and hospital-acquired strains; indicating that our hospital does not have a resident strain of Klebsiella.

Hansson C. et al. *The effect of antiseptic solutions on microorganisms in venous leg ulcers.* Acta Derm Venereol. 1995; 75(1) : 31-3.p Abstract: The effect on the microbial ulcer flora of wet gauze dressings soaked in antiseptic solutions used for desloughing leg ulcers is not known. Quantitative cultures were therefore performed in 45 venous leg ulcers, before application and after 15 minutes' treatment with gauze dressings with four different antiseptic solutions: aluminium acetotartrate (Alsol) 1%, potassium permanganate 0.015%, acetic acid 0.25% and chloramine 0.25%. The percentage of ulcers with each type of microorganism did not differ before and after application of the antiseptic solutions. Staphylococcus aureus was found in 79% of the ulcers, gram-negative rods in 39%, S. epidermidis in 21%, Proteus spp in 21%, Pseudomonas spp in 14% and fungi in none. Potassium permanganate reduced the mean number of bacteria per ulcer from 4.4 x 10(6) to 0.9 x 10(6) (ns), chloramine from 2.7 x 10(6) to 2.2 x 10(6) (ns), Alsol from 1.2 x 10(7) to 3.5 x 10(6) (ns) and acetic acid from 6.3 x 10(6) to 2.6 x 10(5) ($p = 0.007$). S. aureus was reduced by acetic acid ($p = 0.002$), gram-negative rods by both chloramine ($p = 0.03$) and acetic acid ($p = 0.03$). The number of Pseudomonas, Proteus, S. epidermidis and Streptococcus haemolyticus group G was not reduced significantly ($p > 0.05$) by any of the solutions.

Hansson C. et al. *The microbial flora in venous leg ulcers without clinical signs of infection. Repeated culture using a validated standardised microbiological technique.* Acta Derm Venereol. 1995; 75(1) : 24-30.p Abstract: The change of ulcer size in relation to the presence of species and quantities of microorganisms was analysed in 58 patients with venous leg ulcers, all without clinical signs of infection. Microbiological samples were taken on the day of inclusion and then repeated 4 times at monthly intervals or until the ulcer had healed or was too small to be cultured from. There was growth of microorganisms in all ulcers, and the numbers were below 10(4) per mm2 of ulcer surface in all cases. No correlation was found between ulcer size change and the species and amounts of microorganisms. Sixty-nine species were isolated. Staphylococcus aureus was found in 88%, Enterococcus faecalis in 74%, Enterobacter cloacae and Peptococcus magnus in 29%, and fungi in 11% of the samples. One or more obligate anaerobe species was found in 41% of the samples and in half of the ulcers and constituted 62% of all bacterial species. The colonising ulcer flora was markedly constant over time in the individual ulcers regardless of change in size. Resident bacterial species were found in 57 of the 58 ulcers. If all samples were considered, the microorganisms were associated with not more than one fifth of the variability in healing rate, as shown by linear multiple regression analysis. The same species of microorganisms were found in ulcers that decreased (or healed) and in those that increased in size. Although an association between the microorganisms and ulcer healing could not be ruled out in this study, there seems to be no indication for routinely performed culture in the absence of clinical signs of infection in venous leg ulcers.

Harbarth S. et al. *Prolonged antibiotic prophylaxis after cardiovascular surgery and its effect on surgical site infections and antimicrobial resistance.* Circulation. 2000; 101(25) : 2916-21.p Abstract: BACKGROUND: Despite evidence supporting short antibiotic prophylaxis (ABP), it is still common practice to continue ABP for more than 48 hours after coronary artery bypass graft (CABG) surgery. METHODS AND RESULTS: To compare the effect of short (<48 hours) versus prolonged (>48 hours) ABP on surgical site infections (SSIs) and acquired antimicrobial resistance, we conducted an observational 4-year cohort study at a tertiary-care center. An experienced infection control nurse performed prospective surveillance of 2641 patients undergoing CABG surgery. The main exposure was the duration of ABP, and main outcomes were the adjusted rate of SSI and the isolation of cephalosporin-resistant enterobacteriaceae and vancomycin-resistant enterococci (acquired antibiotic resistance). Adjustment for confounding was performed by multivariable modeling. A total of 231 SSIs (8.7%) occurred after a median of 16 days, including 93 chest-wound infections (3.5%) and 13 deep-organ-space infections (0. 5%). After 1502 procedures using short ABP, 131 SSIs were recorded, compared with 100 SSIs after 1139 operations with prolonged ABP (crude OR, 1.0; CI, 0.8 to 1.3). After adjustment for possible confounding, prolonged ABP was not associated with a decreased risk of SSI (adjusted OR, 1.2; CI, 0.8 to 1.6) and was correlated with an increased risk of acquired antibiotic resistance (adjusted OR, 1.6; CI, 1.1 to 2.6). CONCLUSIONS: Our findings confirm that continuing ABP beyond 48 hours after CABG surgery is still widespread; however, this practice is ineffective in reducing SSI, increases antimicrobial resistance, and should therefore be avoided.

Harder J. et al. *Isolation and characterization of Human {beta}-Defensin-3, a novel human inducible peptide antibiotic.* J Biol Chem. 2000.p Abstract: The growing public health problem of infections caused by multiresistant Gram-positive bacteria - in particular Staphylococcus aureus (S. aureus) - prompted us to screen human epithelia for endogenous S. aureus- killing factors. A novel 5-kilodalton, non-hemolytic antimicrobial peptide (human -defensin-3, hBD-3) was isolated from human lesional psoriatic scales and cloned from keratinocytes. hBD-3 demonstrated a salt-insensitive broad spectrum of potent antimicrobial activity against many potential pathogenic microbes including multi-resistant S. aureus and Vancomycin-resistent Enterococcus faecium. Ultrastructural analyses of hBD-3-treated S. aureus revealed signs of cell wall perforation. Recombinant hBD-3 (expressed as a His-Tag-fusion protein in E. coli) as well as chemically synthesized hBD-3 were indistinguishable from naturally-occurring peptide with respect to their antimicrobial activity and biochemical properties. Investigation of different tissues revealed skin and tonsils to be major hBD-3 mRNA expressing tissues. Molecular cloning and biochemical analyses of antimicrobial peptides in cell culture supernatants revealed keratinocytes and airway epithelial cells as cellular sources of hBD-3. Tumor necrosis factor alpha and contact with bacteria were found to induce hBD-3 mRNA expression. hBD-3 therefore might be important in the innate epithelial defense of infections by various microorganisms seen in skin and lung, such as cystic fibrosis.

Harnett N. et al. *Molecular characterization of multiresistant strains of Salmonella typhi from South Asia isolated in Ontario, Canada.* Can J Microbiol. 1998; 44(4) : 356-63.p Abstract: Two hundred and fourteen isolates of Salmonella typhi submitted to our laboratory

between 1992 and 1996 were tested for susceptibility to 20 antimicrobial agents. Forty-eight of the 214 isolates (22.4%), recovered from individuals who had travelled in South Asia, were multiresistant. Forty-four of the 48 isolates were resistant to ampicillin, chloramphenicol, tetracycline, streptomycin, sulfamethoxazole, trimethoprim, cotrimoxazole, ticarcillin, and piperacillin; the other four isolates were resistant to four to six agents. Forty-two of the multiresistant isolates belonged to Vi phage type E1, two isolates from the Punjab State belonged to phage type A, another from the Punjab State belonged to phage type E3, one isolate from Pakistan belonged to type M1, and one isolate from India belonged to type J1. Plasmids from 45 of 48 isolates showed a temperature-sensitive mechanism of transfer to Escherichia coli K-12 strains, characteristic of H1 incompatibility group plasmids. The majority of plasmids had an estimated molecular weight of 120 MDa and encoded both citrate utilization and mercury resistance. Plasmids from three isolates had an estimated molecular weight of 112-115 MDa; one of these isolates encoded citrate utilization but not mercury resistance. Analysis of isolates by pulsed-field gel electrophoresis after digestion with XbaI and SpeI indicated that the majority of multiresistant isolates shared a common restriction profile, while four isolates had unique patterns.

Harris J.A. *Antimicrobial therapy of pneumonia in infants and children.* Semin Respir Infect. 1996; 11(3) : 139-47.p Abstract: To provide optimal management for the child with community-acquired pneumonia, the clinician must take multiple factors into consideration. The etiology of pneumonia is difficult to determine and initial choice of therapy is based on the frequency of pathogens in various age groups, local antibiotic resistance patterns of the organisms, clinical presentation, and epidemiological data. Streptococcus pneumoniae and Haemophilus influenzae remain the most common bacterial pathogens outside the newborn period. Increasing numbers of multidrug-resistant strains of S pneumoniae in the United States and Europe, the decline in H influenzae type b because of current vaccination strategies, and increasing recognition of nontypeable H influenzae as etiologic agents of pneumonia have prompted reconsideration of the drug of choice. Amoxicillin and its derivatives or oral cephalosporins are the drugs of choice for initial therapy for mild to moderate disease. For severe disease or if beta-lactamase producing organisms are a concern, extended spectrum cephalosporins are indicated. Pneumococcal pneumonia unresponsive to penicillin therapy may warrant the use of extended spectrum cephalosporins or vancomycin. For older children in whom mycoplasma is a significant cause of pneumonia, the new macrolides have provided additional options for the clinician. Azithromycin and clarithromycin are efficacious, well tolerated, and require less frequent dosing intervals. The introduction of ceftriaxone, a third-generation cephalosporin with a broad spectrum of activity and prolonged half-life, allows once-a-day intramuscular therapy that can be administered on an outpatient basis. With the availability of parenteral outpatient therapy, hospital admission is no longer required for the treatment of most cases of serious community-acquired pneumonia.

Harris M.G. et al. *Survival of contaminating bacteria in over-the-counter artificial tears.* J Am Optom Assoc. 1996; 67(11) : 676-80.p Abstract: BACKGROUND: The use of OTC artificial tears is becoming increasingly widespread. Unintentional contamination of artificial tear products potentiates a risk of developing bacterial keratitis or exacerbating an existing eye infection. Presently, no published study has investigated recovery from bacterial contamination of artificial tear products. METHODS: Four different over-the-counter (OTC) artificial tear products were contaminated with two types of bacteria. Staphylococcus aureus and pseudomonas aeruginosa were analyzed for the survivability of the microorganisms at various times following contamination. RESULTS: In this cross-sectional study, it was found that all the preserved brands showed a significant recovery rate from contamination compared to the preservative-free brand. After 9 hours, the preservative-free brand did not completely regain sterility after contamination with either bacteria. CONCLUSIONS: This study indicates that preserved artificial tears recover from bacterial contamination at a significantly faster rate than preservative-free products. It is likely that the recovery from bacterial contamination is not solely attributed to the preservative, but that other variables may contribute.

Harthug S. et al. *Nosocomial outbreak of ampicillin resistant Enterococcus faecium: risk factors for infection and fatal outcome.* J Hosp Infect. 2000; 45(2) : 135-44.p Abstract: A nosocomial outbreak caused by ampicillin resistant Enterococcus faecium (ARE) was detected at a Norwegian university hospital in January 1995. Prior to this outbreak, ARE were not common in this hospital or other hospitals in Norway. During 1995 and 1996, a total of 149 cases with clinical ARE infection were detected prospectively. A case control study was performed by allocating controls matched for gender, age and ward of admission. Altogether, 123 case control pairs with mean age 70.1 years were included. Isolates from 89 (72.4%) of the cases were identical or related to the defined outbreak strain as determined by pulsed-field gel electrophoresis (PFGE). In 75 of the patients (60.9%), ARE caused urinary tract infection, five (4.1%) had bacteraemia, 33 (26.8%) had wound infection and 10 (8.1%) had other infections. In a logistic regression model for 1:1 matched samples, the following factors were identified as significant risk factors for ARE infection: underlying neurological disease (OR=33.5), prescription of antimicrobial agents for more than 10 days (OR=8.99), prescription of cephalosporins (OR=4.69), underlying gastrointestinal disease (OR=3.36) and length of hospital stay per day (OR=1.04). The intrahospital death rate for the cases was 18.7% compared with 8.9% for the controls, corresponding to an excess mortality attributable to ARE infection of 9.8%. A history of carbapenem prescription was the only independent factor contributing to death (OR=5.64) when comparing ARE patients dying in hospital to those surviving. Copyright 2000 The Hospital Infection Society.

Harthug S. et al. *[Infections caused by multiresistant enterococci in Norway].* Tidsskr Nor Laegeforen. 1998; 118(26) : 4070-3.p Abstract: During the last decade antimicrobial resistant pathogens have become a major medical problem. Internationally, multiresistant enterococci have increased nosocomial morbidity and mortality. Such strains are often resistant to ampicillin, aminoglycosides, and glycopeptides such as vancomycin. The spread of these strains has been shown to correlate to the use of antibiotics and the practice of suboptimal infection control within health care facilities. The current situation in Norwegian hospitals is presented, including the only six cases with infections and the three carriers of vancomycin resistant enterococci found to date. Surveillance in the hospitals shows that such strains are uncommon in non-infected patients. To maintain this favourable situation it is necessary to continue to practice effective methods of infection control and to employ sound antibiotic policies.

Harwell J.I. et al. *The drug-resistant pneumococcus: clinical relevance, therapy, and prevention.* Chest. 2000; 117(2) : 530-41.p Abstract: Streptococcus pneumoniae has been known for > 100 years as the most important bacterial pathogen of the respiratory tract in adults and children. In recent years, the pneumococcus has begun to exhibit increasing resistance to antimicrobial agents. Because of the huge number of infections caused by this organism, the development of resistance has changed the approach to many infectious disease problems, particularly with regard to empiric antibiotic therapy and prophylaxis. In our review of the antibiotic-resistant pneumococcus, we review the microbiologic basis for resistance, risk factors for and clinical relevance of infection by a resistant organism, and infection control measures.

Hasegawa H. et al. *[Combination effect of vancomycin and cefpirome against methicillin-resistant Staphylococcus aureus in vitro—antimicrobial activities in postantibiotic phase].* Kansenshogaku Zasshi. 1996; 70(2) : 151-

60.p Abstract: The antimicrobial activities of vancomycin (VCM) or cefpirome (CPR) at sub- and above-MICs against clinical strains of methicillin-resistant Staphylococcus aureus (MRSA) during the postantibiotic phase (PAE-phase) induced by CPR or VCM were examined. Antimicrobial activities were determined growth suppression (post antibiotic sub-MIC effect: PA SME) at sub-MICs, and bactericidal activity at sub- and above-MICs. During the PAE-phase induced by VCM, growth suppression and bactericidal activity of CPR were enhanced at sub-MICs, compared with the non PAE-phase. On the other hand, during the PAE-phase induced by CPR, not only were growth suppression and bactericidal activity of VCM enhanced at sub-MICs, but bactericidal activity were enhanced at above-MICs compared with non PAE-phase. These suggest that enhancement of growth suppression and bactericidal activity during PAE-phase was a factor of combination effect of VCM and CPR against MRSA.

Hathorn J.W. et al. *Empirical treatment of febrile neutropenia: evolution of current therapeutic approaches.* Clin Infect Dis. 1997; 24 Suppl 2 : S256-65.p Abstract: Administration of empirical antibiotic therapy is now standard practice in the management of febrile neutropenia, but there has been considerable debate about the selection of an efficacious empirical antimicrobial regimen over the past 2 decades. A variety of approaches, including both monotherapeutic and multidrug regimens, have been demonstrated to be effective, although no one regimen has been proven to be superior to another. Changes in the epidemiology of infectious organisms and the growing emergence of highly drug-resistant strains make it necessary to continually reevaluate the therapeutic options. Fortunately, the number of therapeutic options has also been broadening as new antimicrobial agents, including third-generation cephalosporins and carbapenem antibiotics such as imipenem and meropenem, become available. Optimal management is directed by the findings of a clinical evaluation of the patient as well as an awareness of institutional patterns of infection and susceptibility of likely infecting organisms.

Hausdorfer J. et al. *E-test for susceptibility testing of Mycobacterium tuberculosis.* Int J Tuberc Lung Dis. 1998; 2(9) : 751-5.p Abstract: SETTING: Initial isolates should be tested for drug susceptibility to confirm the anticipated effectiveness of chemotherapy. OBJECTIVE: To evaluate E-test strips for susceptibility testing of Mycobacterium tuberculosis. DESIGN: A proportion method using Lowenstein-Jensen medium and the Bactec radiometric system were compared with the E-test (isoniazid [INH], rifampicin [RMP], ethambutol [EMB] and streptomycin [SM]). RESULTS: For 73 of the 81 M. tuberculosis isolates (90.1%) the proportion and E-test methods yielded concordant susceptibility results against all four antimicrobial agents tested. Of these 73 strains, 69 were fully susceptible; the four isolates showing resistance to antimicrobial drugs by both methods were also resistant when tested by Bactec 460TB. While the proportion method indicated susceptibility for the eight remaining strains, E-test results showed mono EMB resistance in five strains, INH resistance for two isolates (including one isolate resistant to EMB plus INH), and for one strain E-test yielded resistance to EMB and SM. Using Bactec as the reference method, the E-test resulted in false resistance in eight strains and no false susceptibility. CONCLUSION: Due to a substantial rate of false resistance, this method cannot be recommended at present for practical use in clinical laboratories.

Haussler S. et al. *Highly resistant Burkholderia pseudomallei small colony variants isolated in vitro and in experimental melioidosis.* Med Microbiol Immunol (Berl). 1999; 188(2) : 91-7.p Abstract: Burkhloderia pseudomallei is the causative agent of melioidosis, a disease in which treatment failures and relapses are common. This study reports on slow growing B. pseudomallei 'small colony variants' (SCVs), isolated either in vitro after exposure to ceftazidime, ciprofloxacin or gentamicin or from the spleen and liver in a mouse model of melioidosis after treatment with ceftazidime. Interestingly, SCVs isolated by either method or antimicrobial agent showed a significant increase in the minimal inhibitory concentrations of various unrelated classes of antimicrobial agents. B. pseudomallei SCVs did not differ from their parental strains in standard biochemical profiles, nor by pulsed field gel electrophoresis or electron microscopy. Although the SCV phenotype was stable throughout numerous passages on antibiotic-free solid media, revertants with the parental colony morphology and, most importantly, with the parental susceptibility pattern occurred. These revertants led to rapid overgrowth of SCVs in liquid media without added antibiotics. Future studies will have to determine the clinical relevance of B. pseudomallei SCVs especially in treatment failure and relapse of infection.

Hawcroft D.M. et al. *The use of a nonradioactively labelled probe system in an electrophoretic ribotyping method for the differentiation of strains of coagulase-negative staphylococci.* Electrophoresis. 1996; 17(1) : 55-7.p Abstract: Bacteria of the genus Staphylococcus are notoriously difficult to classify and identify; many routine hospital laboratories use only simple, older techniques to segregate them into broad groups. Recent studies have demonstrated that subspecific strains vary in their clinical significance and are of increasing importance in hospital-derived infections; this has led to a need for better methods of classification and identification. Restriction fragment length polymorphism analysis of genes for ribosomal RNA ('ribotyping') is potentially very useful since these genes occur in multiple copies in the genome, and are relatively stable. The restriction fragment patterns are sufficiently different to be usable in classification and identification. This paper considers an electrophoretic method for the separation of these restriction fragments which has the advantages of using a nonradioactive probe and a simple colour signal generating system for its evaluation. The technical principles are universal and would allow the procedure to be developed for other groups of microorganisms.

Hawkes C.A. *Antibiotic resistance: a clinician's perspective.* Mil Med. 2000; 165(7 Suppl 2) : 43-5.p Abstract: Since the introduction of antimicrobial agents, resistance has increased steadily across all classes of antibiotics. Organisms vary in susceptibility. Therefore, an antibiogram or susceptibility profile is needed for each infecting organism to determine the most appropriate antibiotic. When the infecting organism has not yet been identified, an informed decision can be made only by obtaining an accurate profile of antibiotic resistance in the hospital, the community, and, in some instances, the world. The appropriate use of antibiotics is correlated with a more favorable clinical outcome and also delays the emergence of resistance. Ensuring such prescribing behavior requires a multidisciplinary approach. Familiarity with the trends and prevalence of antibiotic resistance also facilitates the early identification of individuals harboring resistant organisms. Early isolation can then be initiated, thereby minimizing the risk of nosocomial cross-infection. This article offers a clinician's pragmatic view of antimicrobial resistance.

Hayakawa K. et al. *Microorganism inactivation using high-pressure generation in sealed vessels under sub-zero temperature.* Appl Microbiol Biotechnol. 1998; 50(4) : 415-8.p Abstract: In order to test the possibility of utilizing high pressure in bioscience and biotechnology, a simple method for high-pressure generation and its use for microbial inactivation have been studied. When a pressure vessel was filled with water, sealed tightly and cooled to sub-zero temperatures, high pressure was generated in the vessel. The pressure generation was 60 MPa at -5 degrees C, 103 MPa at -10 degrees C, and 140 MPa at -15 degrees C, -20 degrees C, and -22 degrees C. The high pressure generated inactivated microorganisms effectively: yeasts (Saccharomyces cerevisiae and Zygosaccharomyces rouxii), bacteria (Lactobacillus brevis and Eschericia coli), and fungi (Aspergillus niger and Aspergillus oryzae) were completely inactivated when stored in sealed vessels -20 degrees C for 24 h. However, Staphylococcus aureus was only partly inactivated under the same conditions. This method opens up a new application of high pressure for storing, transporting, and sterilizing of foods and biological materials.

Hayashi H. et al. *Respiratory jugular venodilation: a new landmark for right internal jugular vein puncture in ventilated patients.* J Cardiothorac Vasc Anesth. 2000; 14(1) : 40-4.p Abstract: OBJECTIVE: To report a new technique for right internal jugular vein puncture using respiratory jugular venodilation as a landmark for vein location. DESIGN: Prospective observational study. SETTING: Single community hospital. PARTICIPANTS: Two hundred patients undergoing right internal jugular vein cannulation under general anesthesia. INTERVENTIONS: Catheter placement was attempted using respiratory jugular venodilation as the primary landmark. When it was not applicable, an alternative technique using the carotid pulse as a landmark was used. MEASUREMENTS AND MAIN RESULTS: Visibility of the venodilation, the number of needle passes, the success rate, and the incidence of arterial puncture were analyzed. Respiratory jugular venodilation was observed in 158 patients (79%). In this group of patients, the jugular vein was cannulated at the first attempt in 83.5% of patients, and arterial puncture occurred in one patient (0.6%). In the remaining 42 patients (21%) lacking the visible venodilation, catheter placement was accomplished at the first attempt in 42.9% of patients ($p<0.01$ v. the venodilation-visible group), and 4 patients (9.5%) suffered arterial puncture ($p<0.01$). The overall incidence of arterial puncture was 2.5%. The success rate of cannulation (within four needle passes and no arterial puncture) was 98.1% in the venodilation-visible patients and 73.8% in the others ($p<0.01$), with the overall success rate of 93%. CONCLUSIONS: Respiratory jugular venodilation can be identified in a large proportion of ventilated patients. This experience suggests that respiratory jugular venodilation could be favorably used as the primary landmark for right internal jugular vein puncture in anesthetized patients.

Hayward C.L. et al. *Comparative antimicrobial activity of gatifloxacin tested against Campylobacter jejuni including fluoroquinolone-resistant clinical isolates.* Diagn Microbiol Infect Dis. 1999; 34(2) : 99-102.p Abstract: Campylobacter jejuni is an important pathogen that causes gastroenteritis, as well as other disease states such as meningitis and septic arthritis. In this study, the Etest (AB BIODISK, Solna, Sweden) results were compared to a reference agar dilution method using gatifloxacin, a new 8-methoxyfluoroquinolone. A total of 53 strains of C. jejuni initially isolated from patients in California and Mexico were tested. Results demonstrated a high correlation ($r = 0.88$) between the two utilized in vitro dilution methods. In addition, gatifloxacin activity was compared to that of ciprofloxacin, metronidazole, amoxicillin, erythromycin, chloramphenicol, gentamicin, tetracycline, and trimethoprim/sulfamethoxazole using the Etest. Gatifloxacin (MIC90, 4 micrograms/ml) was approximately eight- to 16-fold more potent than ciprofloxacin (Mic90, > 32 micrograms/ml), a commonly used fluoroquinolone for Campylobacter infections. Eight strains highly resistant to ciprofloxacin (MIC90, > 32 micrograms/ml) were tested for cross resistance against the newer fluoroquinolones (gatifloxacin, levofloxacin, trovafloxacin) and the rank order of potency was: gatifloxacin (MIC50, 16 micrograms/ml) > trovafloxacin = levofloxacin (MIC50, > 32 micrograms/mL). However, only 25% ciprofloxacin-resistant strains were inhibited by < or = 1 microgram/mL of gatifloxacin or trovafloxacin. These results for gatifloxacin against C. jejuni strains must be further assessed in the context of in vivo trials before the clinical role of this new fluoroquinolone can be determined. The Etest appears to be a simple and precise susceptibility test method for testing C. jejuni isolates against fluoroquinolones and other alternative therapeutic agents.

He Z. et al. *Reactions involved in the lower pathway for degradation of 4-nitrotoluene by Mycobacterium strain HL 4-NT-1.* Appl Environ Microbiol. 2000; 66(7) : 3010-5.p Abstract: In spite of the variety of initial reactions, the aerobic biodegradation of aromatic compounds generally yields dihydroxy intermediates for ring cleavage. Recent investigation of the degradation of nitroaromatic compounds revealed that some nitroaromatic compounds are initially converted to 2-aminophenol rather than dihydroxy intermediates by a number of microorganisms. The complete pathway for the metabolism of 2-aminophenol during the degradation of nitrobenzene by Pseudomonas pseudoalcaligenes JS45 has been elucidated previously. The pathway is parallel to the catechol extradiol ring cleavage pathway, except that 2-aminophenol is the ring cleavage substrate. Here we report the elucidation of the pathway of 2-amino-4-methylphenol (6-amino-m-cresol) metabolism during the degradation of 4-nitrotoluene by Mycobacterium strain HL 4-NT-1 and the comparison of the substrate specificities of the relevant enzymes in strains JS45 and HL 4-NT-1. The results indicate that the 2-aminophenol ring cleavage pathway in strain JS45 is not unique but is representative of the pathways of metabolism of other o-aminophenolic compounds.

Hecht D.W. et al. *Susceptibility results for the Bacteroides fragilis group: comparison of the broth microdilution and agar dilution methods.* Clin Infect Dis. 1995; 20 Suppl 2 : S342-5.p Abstract: The antimicrobial susceptibilities of members of the Bacteroides fragilis group were compared using the agar dilution and broth microdilution methods. A total of 455 B. fragilis group isolates were tested against 10 antibiotics. Significant disparity in susceptibility results for most antibiotics was observed between the two methods. Broth microdilution susceptibility results were most similar to agar dilution results when a twofold lower breakpoint was used. In addition, broth microdilution failed to detect resistance to some antibiotics when the recommended agar dilution breakpoint was used. MIC50, MIC90, and geometric mean MIC values for broth microdilution were consistently twofold to fourfold less than those for agar dilution. Susceptibilities of Bacteroides that are determined with use of broth microdilution may more accurately correspond to those determined with use of agar dilution if lower breakpoints are used for interpretation.

Heckmann J.G. et al. *Neurologic manifestations of cerebral air embolism as a complication of central venous catheterization*. Crit Care Med. 2000; 28(5) : 1621-5.p Abstract: OBJECTIVE, PATIENTS, AND METHODS: A severe case of cerebral air embolism after unintentional central venous catheter disconnection was the impetus for a systematic literature review (1975-1998) of the clinical features of 26 patients (including our patient) with cerebral air embolism resulting from central venous catheter complications. RESULTS: The jugular vein had been punctured in eight patients and the subclavian vein, in 12 patients. Embolism occurred in four patients during insertion, in 14 patients during unintentional disconnection, and in eight patients after removal and other procedures. The total mortality rate was 23%. Two types of neurologic manifestations may be distinguished: group A (n = 14) presented with encephalopathic features leading to a high mortality rate (36%); and group B (n = 12) presented with focal cerebral lesions resulting in hemiparesis or hemianopia affecting mostly the right hemisphere, with a mortality rate as high as 8%. In 75% of patients, an early computed tomography indicated air bubbles, proving cerebral air embolism. Hyperbaric oxygen therapy was performed in only three patients (12%). A cardiac defect, such as a patent foramen ovale was considered the route of right to left shunting in 6 of 15 patients (40%). More often, a pulmonary shunt was assumed (9 of 15 patients; 60%). For the remainder, data were not available. CONCLUSION: When caring for critically ill patients needing central venous catheterization, nursing staff and physicians should be aware of this potentially lethal complication.

Hedberg M. et al. *Beta-lactam resistance in anaerobic bacteria: a review.* J Chemother. 1996; 8(1) : 3-16.p Abstract: The majority of the human microflora consists of anaerobic bacteria. Normally these bacteria have low pathogenicity, but under certain conditions, such as destruction of tissues and poor circulation or impaired host defense, they may cause serious infections. Bacteroides species are the most frequently isolated microorganisms from suppurative anaerobic infections and they have the broadest spectrum of resistance to the commonly used antimicrobial agents. Resistance to antimicrobial agents is an increasing problem, especially to beta-lactam compounds. Multiresistant clinical isolates, resistant to beta-lactam antibi-

otics as well as other antimicrobial agents used in the treatment and prophylaxis of anaerobic infections are now occurring. Resistance to beta-lactam antibiotics is usually mediated by beta-lactamase production. A few isolates of Bacteroides fragilis are producing metallo-beta-lactamases which are capable of hydrolyzing beta-lactamase stable compounds such as cefoxitin and imipenem. The enzyme activity in metallo-beta-lactamases is not affected by the clinically used beta-lactamase inhibitors clavulanic acid, sulbactam and tazobactam. Other resistance mechanisms are alterations in the penicillin-binding proteins (PBPs) or a decreased permeability through the outer membrane. Beta-lactam resistance and beta-lactamase production have also been detected in some species of clostridia, fusobacteria, Prevotella, Porphyromonas and in some other anaerobic bacteria.

Hedstrom M. et al. *Urinary tract infection in patients with hip fractures.* Injury. 1999; 30(5) : 341-3.p Abstract: We found that 23% of 435 patients treated for a femoral neck fracture in our department also were treated for a urinary tract infection during their hospital stay. The most common pathogen was Escherichia coli, sensitive for mecillinam in 98% of the cases. The most frequently used antimicrobial agent was a broad-spectrum antibiotic, fluoroquinolon, although the most reasonable choice would have been a non broad-spectrum agent such as mecillinam. Catheterization was not a predisposing factor for urinary tract infection, but a poor medical condition and female sex were. We did not find a higher mortality rate among patients with a urinary tract infection.

Heffelfinger J.D. et al. *Management of community-acquired pneumonia in the era of pneumococcal resistance: a report from the Drug-Resistant Streptococcus pneumoniae Therapeutic Working Group.* Arch Intern Med. 2000; 160(10) : 1399-408.p Abstract : OBJECTIVE: To provide recommendations for the management of community-acquired pneumonia and the surveillance of drug-resistant Streptococcus pneumoniae (DRSP). METHODS: We addressed the following questions: (1) Should pneumococcal resistance to beta-lactam antimicrobial agents influence pneumonia treatment? (2) What are suitable empirical antimicrobial regimens for outpatient treatment of community-acquired pneumonia in the DRSP era? (3) What are suitable empirical antimicrobial regimens for treatment of hospitalized patients with community-acquired pneumonia in the DRSP era? and (4) How should clinical laboratories report antibiotic susceptibility patterns for S pneumoniae, and what drugs should be included in surveillance if community-acquired pneumonia is the syndrome of interest? Experts in the management of pneumonia and the DRSP Therapeutic Working Group, which includes clinicians, academicians, and public health practitioners, met at the Centers for Disease Control and Prevention in March 1998 to discuss the management of pneumonia in the era of DRSP. Published and unpublished data were summarized from the scientific literature and experience of participants. After group presentations and review of background materials, subgroup chairs prepared draft responses, which were discussed as a group. CONCLUSIONS: When implicated in cases of pneumonia, S pneumoniae should be considered susceptible if penicillin minimum inhibitory concentration (MIC) is no greater than 1 microg/mL, of intermediate susceptibility if MIC is 2 microg/ mL, and resistant if MIC is no less than 4 microg/mL. For outpatient treatment of community-acquired pneumonia, suitable empirical oral antimicrobial agents include a macrolide (eg, erythromycin, clarithromycin, azithromycin), doxycycline (or tetracycline) for children aged 8 years or older, or an oral beta-lactam with good activity against pneumococci (eg, cefuroxime axetil, amoxicillin, or a combination of amoxicillin and clavulanate potassium). Suitable empirical antimicrobial regimens for inpatient pneumonia include an intravenous beta-lactam, such as cefuroxime, ceftriaxone sodium, cefotaxime sodium, or a combination of ampicillin sodium and sulbactam sodium plus a macrolide. New fluoroquinolones with improved activity against S pneumoniae can also be used to treat adults with community-acquired pneumonia. To limit the emergence of fluoroquinolone-resistant strains, the new fluoroquinolones should be limited to adults (1) for whom one of the above regimens has already failed, (2) who are allergic to alternative agents, or (3) who have a documented infection with highly drug-resistant pneumococci (eg, penicillin MIC > or =4 microg/mL). Vancomycin hydrochloride is not routinely indicated for the treatment of community-acquired pneumonia or pneumonia caused by DRSP.

Heggers J.P. et al. *Alternate antimicrobial therapy for vancomycin-resistant enterococci burn wound infections.* J Burn Care Rehabil. 1998; 19(5) : 399-403.p Abstract: Survival after a major thermal burn is precarious and fraught with difficult complications associated with hypermetabolism, gut or respiratory dysfunction, and infection. Clinicians must be cognizant of a new threat to the patient with burn injuries—the emergence of vancomycin-resistant enterococci (VRE). In an analysis of 31 clinical isolates obtained during acute burn hospitalization, an optimal antimicrobial therapy for VRE has been identified. All VRE cultures were inoculated to the MicroScan Gram-Positive Breakpoint Combo Panel #8 (Dade Microscan, Inc, Sacramento, Calif), which speciates the enterococci, provides antimicrobial susceptibility patterns (including vancomycin) and a biotype, and examines streptomycin and gentamicin synergy. Eleven (35.5%) of the 31 isolates were identified as E faecium and 20 (64.5%) as E faecalis. All isolates were susceptible to chloramphenicol and tetracycline, whereas only half were sensitive to gentamicin synergy screen. All other antimicrobials screened against VRE were either ineffective or of limited effect. Our preliminary data supports the initiation of chloramphenicol therapy when a VRE burn wound infection is encountered or suspected.

Heifets L.B. *Clarithromycin against Mycobacterium avium complex infections.* Tuber Lung Dis. 1996; 77(1) : 19-26.p Abstract: The turning point in antimicrobial therapy of Mycobacterium avium infections came with the development of two new macrolides, clarithromycin and azithromycin. Controlled clinical trials, the first ever conducted with any agent among patients with M. avium infection, indicated the high efficiency of clarithromycin, in either acquired immune deficiency syndrome (AIDS) patients having a disseminated infection or non-AIDS patients with localized pulmonary disease. Monotherapy with clarithromycin resulted in elimination of bacteremia in almost all patients with disseminated infection, which is inevitably followed by a relapse of bacteremia in patients who survived long enough to reach this event. The strains susceptible to clarithromycin isolated before therapy contained 10(-8) or 10(-9) resistant mutants, and the relapses of bacteremia were caused by multiplication of these pre-existing mutants. Clarithromycin-resistance was associated with a mutation in the 23S rRNA gene. Cross-resistance between clarithromycin and azithromycin was confirmed with laboratory mutants and clinical isolates. At least two methods for determining the susceptibility of the M. avium isolates to clarithromycin are available: one is minimum inhibitory concentration (MIC) determination on Mueller-Hinton agar (pH 7.4) supplemented with 10% Oleic acid-albumin-dextrose catalase, the other is MIC determination in 7H12 broth, also at pH 7.4. The breakpoints for 'susceptible' for these methods are < or = 8.0 micrograms/ml and < or = 2.0 micrograms/ml, respectively. The breakpoints for 'resistant' are > 128 micrograms/ml for the agar method and > 32.0 micrograms/ml for the broth method. The predictability value of MIC determination was confirmed by comparing the test results with the patients' clinical and bacteriological response to therapy. The remaining major problem in the therapy of the M. avium infections is a selection of companion drugs to be used in combination with clarithromycin (or azithromycin) to prevent the emergence of the macrolide-resistance. A number of clinical trials are now in progress to find a solution to this problem.

Heit J.A. et al. *Risk factors for deep vein thrombosis and pulmonary embolism: a population-based case-control study.* Arch Intern Med. 2000; 160(6) : 809-15.p Abstract: BACKGROUND: Reported risk factors for venous thromboembolism (VTE) vary widely, and the magnitude

and independence of each are uncertain. OBJECTIVES: To identify independent risk factors for deep vein thrombosis and pulmonary embolism and to estimate the magnitude of risk for each. PATIENTS AND METHODS: We performed a population-based, nested, case-control study of 625 Olmsted County, Minnesota, patients with a first lifetime VTE diagnosed during the 15-year period from January 1, 1976, through December 31, 1990, and 625 Olmsted County patients without VTE. The 2 groups were matched on age, sex, calendar year, and medical record number. RESULTS: Independent risk factors for VTE included surgery (odds ratio [OR], 21.7; 95% confidence interval [CI], 9.4-49.9), trauma (OR, 12.7; 95% CI, 4.1-39.7), hospital or nursing home confinement (OR, 8.0; 95% CI, 4.5-14.2), malignant neoplasm with (OR, 6.5; 95% CI, 2.1-20.2) or without (OR, 4.1; 95% CI, 1.9-8.5) chemotherapy, central venous catheter or pacemaker (OR, 5.6; 95% CI, 1.6-19.6), superficial vein thrombosis (OR, 4.3; 95% CI, 1.8-10.6), and neurological disease with extremity paresis (OR, 3.0; 95% CI, 1.3-7.4). The risk associated with varicose veins diminished with age (for age 45 years: OR, 4.2; 95% CI, 1.6-11.3; for age 60 years: OR, 1.9; 95% CI, 1.0-3.6; for age 75 years: OR, 0.9; 95% CI, 0.6-1.4), while patients with liver disease had a reduced risk (OR, 0.1; 95% CI, 0.0-0.7). CONCLUSION: Hospital or nursing home confinement, surgery, trauma, malignant neoplasm, chemotherapy, neurologic disease with paresis, central venous catheter or pacemaker, varicose veins, and superficial vein thrombosis are independent and important risk factors for VTE.

Hejnar P. et al. *[Occurrence of gram-negative non-fermenting rods in hemocultures and their sensitivity to antimicrobial agents].* Bratisl Lek Listy. 1998; 99(11) : 573-8.p Abstract: In the period from January 1993 to June 1996 were at the Department of Microbiology of the University Hospital in Olomouc 122 strains of Gram-negative nonfermentative rod-shaped bacteria isolated from haemocultures. The majority represented the group of 51 strains of the genus Acinetobacter (41.8%), complex A. calcoaceticus-baumannii (Acb complex). The second largest group were 21 strains (17.2%) of Pseudomonas aeruginosa. These were followed by 17 strains (13.9%) of Stenotrophomonas maltophilia, 8 strains (6.6%) of non-Acb complex acinetobacters, 6 strains (4.9%) of Pseudomonas putida and 5 strains (4.1%) of Alcaligenes xylosoxidans. The remaining species were represented only by 1-2 strains. In three isolations was the identification impossible. The majority of strains (24.6%) were from the Department of Haematology of the University Hospital in Olomouc. The most frequent diagnoses in patients with positive haemocultures were leukemias and lymphomas (24.6%). The most effective tested antimicrobial agents were ceftazidime (93.4% of sensitive strains) and ofloxacin (91.7%). From the total number of 80 strains detected using the equipment BacT/Alert 120, 22 (27.5%) were isolated repeatedly confirming their role in the etiology of bacteriemic or septic episodes. Because only one blood sample was obtained in 34 cases (58.6%) of the remaining 58 only once detected strains, it was impossible to confirm their etiologic role by repeated isolation. (Tab. 6, Ref. 22.).

Hellinger W.C. *Confronting the problem of increasing antibiotic resistance.* South Med J. 2000; 93(9) : 842-8.p Abstract: Significant increases in prevalence of resistance to antibiotics have been observed in common pathogens of humans in the United States and worldwide. The consequences of the appearance and spread of antibiotic resistance have included increasing morbidity, mortality, and cost of health care. The fundamental cause for the appearance and spread of antimicrobial resistance has been increasing antimicrobial use. However, other factors contribute in both inpatient and outpatient settings. Recognizing the important causes of increasing antibiotic resistance in these settings has led to practical recommendations, which health care facilities and outpatient practitioners will need to review, adapt, and apply for maximum local effectiveness for progress to be made in addressing one of the most challenging problems facing modern medicine.

Hellinger W.C. et al. *Carbapenems and monobactams: imipenem, meropenem, and aztreonam.* Mayo Clin Proc. 1999; 74(4) : 420-34.p Abstract: Imipenem and meropenem, members of the carbapenem class of beta-lactam antibiotics, are among the most broadly active antibiotics available for systemic use in humans. They are active against streptococci, methicillin-sensitive staphylococci, Neisseria, Haemophilus, anaerobes, and the common aerobic gram-negative nosocomial pathogens including Pseudomonas. Resistance to imipenem and meropenem may emerge during treatment of P. aeruginosa infections, as has occurred with other beta-lactam agents; Stenotrophomonas maltophilia is typically resistant to both imipenem and meropenem. Like the penicillins, the carbapenems have inhibitory activity against enterococci. In general, the in vitro activity of imipenem against aerobic gram-positive cocci is somewhat greater than that of meropenem, whereas the in vitro activity of meropenem against aerobic gram-negative bacilli is somewhat greater than that of imipenem. Daily dosages may range from 0.5 to 1 g every 6 to 8 hours in patients with normal renal function; the daily dose of meropenem, however, can be safely increased to 6 g. Infusion-related nausea and vomiting, as well as seizures, which have been the main toxic effects of imipenem, occur no more frequently during treatment with meropenem than during treatment with other beta-lactam antibiotics. The carbapenems should be considered for treatment of mixed bacterial infections and aerobic gram-negative bacteria that are not susceptible to other beta-lactam agents. Indiscriminate use of these drugs will promote resistance to them. Aztreonam, the first marketed monobactam, has activity against most aerobic gram-negative bacilli including P. aeruginosa. The drug is not nephrotoxic, is weakly immunogenic, and has not been associated with disorders of coagulation. Aztreonam may be administered intramuscularly or intravenously; the primary route of elimination is urinary excretion. In patients with normal renal function, the recommended dosing interval is every 8 hours. Patients with renal impairment require dosage adjustment. Aztreonam is used primarily as an alternative to aminoglycosides and for the treatment of aerobic gram-negative infections. It is often used in combination therapy for mixed aerobic and anaerobic infections. Approved indications for its use include infections of the urinary tract or lower respiratory tract, intra-abdominal and gynecologic infections, septicemia, and cutaneous infections caused by susceptible organisms. Concurrent initial therapy with other antimicrobial agents is recommended before the causative organism has been determined in patients who are seriously ill or at risk for gram-positive or anaerobic infection.

Hellyer T.J. et al. *Quantitative analysis of mRNA as a marker for viability of Mycobacterium tuberculosis.* J Clin Microbiol. 1999; 37(2) : 290-5.p Abstract: Numerous assays which use conserved DNA or rRNA sequences as targets for amplification have been described for the diagnosis of tuberculosis. However, these techniques have not been applied successfully to the monitoring of therapeutic efficacy owing to the persistence of amplifiable nucleic acid beyond the point at which smears and cultures become negative. Semiquantitative analysis of rRNA has been used to reduce the time required for antimicrobial susceptibility testing of Mycobacterium tuberculosis, although growth for up to 5 days in the presence of some drugs is still required to discriminate resistant strains. The purpose of the present study was to determine whether quantitative analysis of M. tuberculosis mRNA could be used to assess bacterial viability and to illustrate the application of this technique to rapid determination of drug susceptibility. Levels of mRNA encoding the 85B protein (alpha-antigen), IS6110 DNA, and 16S rRNA were compared in parallel cultures of M. tuberculosis that were treated with either no drug, 0. 2 microg of isoniazid per ml, or 1 microg of rifampin per ml. Exposure of sensitive strains to isoniazid or rifampin for 24 h reduced the levels of 85B mRNA to <4 and <0.01%, respectively, of those present in control cultures without drug. In contrast, the levels of IS6110 DNA and 16S rRNA did not diminish over the same period. Strains which were resistant to either isoniazid or rifampin demonstrated no reduction in 85B mRNA in the presence of the drug to which they were nonre-

sponsive. Quantitative analysis of 85B mRNA offers a potentially useful tool for the rapid determination of M. tuberculosis drug susceptibility and for the monitoring of therapeutic efficacy.

Helttula I. et al. *Central hemodynamics during reamed intramedullary nailing of unilateral tibial fractures.* J Trauma. 2000; 48(4) : 704-10.p Abstract: BACKGROUND: Intramedullary nailing of a long-bone fracture results in intravasation of bone marrow contents into the right atrium and pulmonary vascular bed and, therefore, may alter cardiac and pulmonary hemodynamics. METHODS: Central hemodynamic changes were recorded in 12 healthy adults with a unilateral simple tibial fracture undergoing intramedullary nailing. The patients were cannulated with a pulmonary artery catheter. Reamed intramedullary nailing was performed during general anesthesia. Preoperative and immediate postoperative hemodynamic variables were compared and intraoperative changes studied. RESULTS: During the operation, the right ventricular preload as represented by central venous pressure and the right ventricular afterload as presented by mean pulmonary arterial pressure increased significantly. Preoperative and postoperative arterial oxygen tension values demonstrated hypoxia. Abnormal pulmonary shunting and increased oxygen consumption were observed as well. CONCLUSION: Changes in cardiac and pulmonary hemodynamics are already present after the trauma and before the reamed intramedullary nailing procedure.

Hendershot E.F. *Fluoroquinolones.* Infect Dis Clin North Am. 1995; 9(3) : 715-30.p Abstract: Since the introduction of the floroquinolones for clinical use in the late 1980s, they have been used successfully for a large number of clinical situations. As experience accumulates, the indications and optimal use of these agents gradually become more clear. Unfortunately, two of the pathogens for which these agents were most promising—methicillin-resistant S. aureus and P. aeruginosa—have developed resistance. Currently, the quinolones are excellent agents for the treatment of complicated urinary tract infections, including those caused by P. aeruginosa. In addition, they should be considered as initial therapy for the treatment of severe bacterial gastroenteritis. The quinolones should also be considered when attempting to eradicate the chronic stool carriage of S. typhi. These agents also offer significant advantages in the treatment of osteomyelitis and prostatitis caused by gram-negative bacilli that frequently require prolonged antimicrobial therapy. Treatment of STDs, especially gonorrhea, is another clear indication for their use. Ciprofloxacin should be considered as initial therapy in patients with malignant otitis externa and in cystic fibrosis patients with exacerbations secondary to P. aeruginosa in the sputum. The role of the quinolones for soft tissue and respiratory tract infections is less clear and their use probably should be limited to certain situations in which there is a clear advantage over beta-lactams, macrolides, and trimethoprim-sulfamethoxazole. The new quinolones, fleroxacin, perfloxacin, sparfloxacin, and tosufloxacin, which are being developed and tested for clinical use, will offer advantages in once-a-day dosing and better gram-positive antimicrobial activity. Because the inappropriate or heavy use of the fluoroquinoles has resulted in considerable development of resistance, it is imperative that they be used only when there is a distinct advantage over conventional therapy in terms of efficacy, safety, or cost. Otherwise, the rapid development of resistance will jeopardize the potentially bright future for this entire class of compounds.

Hennequin C. et al. *Possible role of catheters in Saccharomyces boulardii fungemia.* Eur J Clin Microbiol Infect Dis. 2000; 19(1) : 16-20.p Abstract: Four cases of Saccharomyces boulardii fungemia, a very rare side effect of Saccharomyces boulardii therapy, are reported. The clinical impact of Saccharomyces boulardii infection appeared to be moderate. However, even though organ involvement was never demonstrated, septic shock with no other etiology was observed in one of our patients. All patients had an indwelling vascular catheter. Contamination of the air, environmental surfaces, and hands following the opening of a packet suggests that catheter contamination may have been a source of infection. To prevent catheter contamination it is recommended that packets or capsules of Saccharomyces boulardii be opened with gloves, outside the patient's room.

Henrickson K.J. et al. *Prevention of central venous catheter-related infections and thrombotic events in immunocompromised children by the use of vancomycin/ciprofloxacin/heparin flush solution: A randomized, multicenter, double-blind trial.* J Clin Oncol. 2000; 18(6) : 1269-78.p Abstract: PURPOSE: To determine whether an antibiotic flush solution containing vancomycin, heparin, and ciprofloxacin (VHC) can prevent the majority of line infections. PATIENTS AND METHODS: A prospective double-blind study was performed comparing VHC to vancomycin and heparin (VH) to heparin alone in 126 pediatric oncology patients. RESULTS: The 153 assessable lines resulted in 36,944 line days studied. There were 58 blood stream infections (43 gram-positive, 14 gram-negative, and one fungal). Forty were defined as line infections (31 heparin, three VH, six VHC). The time to develop a line infection was significantly increased using either antibiotic flush (VH, P =.011; VHC, P =.036). The rate of total line infections (VH, P =.004; VHC, P =.005), gram-positive line infections (VH, P =. 028; VHC, P =.022), and gram-negative line infections (VH, P =.006; VHC, P =.003) was significantly reduced by either VH or VHC. Sixty-two (41%) of the lines developed 119 occlusion episodes (heparin, 3.99 per 1,000 line days; VHC, 1.75 per 1,000 line days; P =.0005). Neither antibiotic could be detected after flushing, and no adverse events were detected, including increased incidence of vancomycin-resistant Enterococcus colonization or disease. CONCLUSION: The use of either VH or VHC flush solution significantly decreased the complications associated with the use of tunneled central venous lines in immunocompromised children and would save significant health care resources.

Henry C.A. et al. *Phototoxicity of argon laser irradiation on biofilms of Porphyromonas and Prevotella species.* J Photochem Photobiol B. 1996; 34(2-3) : 123-8.p Abstract: Species of Prevotella (Pr.) and Porphyromonas (Po.) and other microorganisms were cultivated as biofilms on agar medium and examined for their susceptibility to argon laser irradiation (continuous mode; wavelengths, 488-514 nm; fluences, 20-200 J cm(-2)). Fluences of 35 to 80 J cm(-2) inhibited biofilm growth in Po. endodontalis, Po. gingivalis, Pr. denticola, Pr. intermedia, Pr. melaninogenica and Pr. nigrescens. A fluence of 70 J cm(-2) did not affect biofilm growth in species of Bacillus, Candida, Enterobacter, Proteus, Pseudomonas, Staphylococcus and Streptococcus. The phototoxic effects of argon laser irradiation against Prevotella and Porphyromonas species were: (1) caused by the radiation alone; (2) modified by biofilm age; (3) dependent on the presence of atmospheric oxygen; (4) influenced by medium supplements of hemin, hemoglobin and blood; (5) greater when compared with other microbial species; (6) demonstrated without augmentation with an exogenous photosensitizer; and (7) apparently unrelated to the protoporphyrin content of the cells. Overall, these in vitro findings suggest that low doses of argon laser radiation may be effective in the treatment and/or prevention of clinical infections caused by biofilm-associated species of Prevotella or Porphyromonas.

Herbin S. et al. *Characteristics and genetic determinants of bacteriocin activities produced by Carnobacterium piscicola CP5 isolated from cheese.* Curr Microbiol. 1997; 35(6) : 319-26.p Abstract: Carnobacterium piscicola CP5, isolated from a French mold-ripened soft cheese, produced a bacteriocin activity named carnocin CP5, which inhibited Carnobacterium, Enterococcus and Listeria spp. strains, and among the Lactobacillus spp. only Lactobacillus delbrueckii spp. [24]. The activity was purified by ammonium sulfate precipitation, anion exchange, and hydrophobic interaction chromatography followed by reverse-phase high-performance liquid chromatography (RP-HPLC). This latter step separated two peaks with anti-listerial activity (CP51 and CP52). Carnocin CP51 was partially sequenced, and

the N-terminal part revealed the presence of the "pediocin-like consensus" sequence-Tyr-Gly-Asn-Gly-Val-. Then, a degenerated 24-mer oligonucleotide probe was constructed from the N-terminal sequence and used to detect the structural gene. It was localized on a plasmid of about 40 kb. Cloning of restriction fragments of this one, followed by DNA sequencing, revealed the presence of the second anti-Listeria bacteriocin gene (CP52). By comparing sequences in data banks and confirming results with PCR reactions, carnocin CP51 shared homologies with carnobacteriocin BM1, and carnocin CP52 was similar to carnobacteriocin B2, both produced by C. piscicola LV17 [2]. However, carnobacteriocin A from C. piscicola LV17 gene was lacking in C. piscicola CP5, and the two microorganisms have been isolated from different ecological environments: C. piscicola CP5 and C. piscicola LV17 were isolated from soft cheese and vacuum-packed meat respectively. This fact could allow different application perspectives for C. piscicola CP5.

Herde J. et al. *[Effect of tonometry and nasolacrimal duct irrigation on bacterial flora of the conjunctiva].* Ophthalmologe. 1995; 92(6) : 817-22.p Abstract: This study was undertaken to assess the influence of preoperative ophthalmological examinations on the microbial flora of the conjunctiva. For this purpose, 112 patients awaiting ocular surgery were included in the study. Conjunctival swabs for microbiological investigation were taken by nurses on the day of admission. In addition, specimens were taken before an ophthalmological examination, after applanation and impression tonometry, after irrigation of the lacrimal duct and 2 h after the end of all examinations. A last swab was taken preoperatively. Comparison of the microbiological results of the first two specimens only showed an agreement in 53% of the cases. The increase after tonometry and irrigation of the lacrimal duct in the number of swabs that were positive was not permanent. Swabs that were primarily germ-free and those that were mostly contaminated also showed strong bacterial fluctuation. Based on the present results, there is no strong evidence that the microorganisms found at the preoperative examinations correlate with a higher risk of postoperative infection. Disinfection of the conjunctival sac and the application of antibiotic drops are necessary on the day before the operation and immediately before it.

Herikstad H. et al. *Emerging quinolone-resistant Salmonella in the United States.* Emerg Infect Dis. 1997; 3(3) : 371-2.p Abstract: We conducted a national survey of antimicrobial resistance in human clinical isolates of Salmonella between July 1, 1994, and June 30, 1995. Every tenth nontyphoidal Salmonella isolate received at state public health laboratories in the United States during this period was tested for resistance to 12 antimicrobial agents, including two quinolones, nalidixic acid, and ciprofloxacin. Emerging quinolone resistance was detected; of 4,008 isolates tested, 21 (0.5%) were resistant to nalidixic acid, and one (0.02%) was resistant to ciprofloxacin. Continued surveillance for quinolone-resistant Salmonella is necessary, particularly after the recent approval of a fluoroquinolone for use in animals intended for food in the United States.

Hernandez-Alles S. et al. *Development of resistance during antimicrobial therapy caused by insertion sequence interruption of porin genes.* Antimicrob Agents Chemother. 1999; 43(4) : 937-9.p Abstract: We have demonstrated by using an in vitro approach that interruption of the OmpK36 porin gene by insertion sequences (ISs) is a common type of mutation that causes loss of porin expression and increased resistance to cefoxitin in Klebsiella pneumoniae. This mechanism also operates in vivo: of 13 porin-deficient cefoxitin-resistant clinical isolates of K. pneumoniae, 4 presented ISs in their ompK36 gene.

Hernández Bustillo M. et al. *Lomefloxacino vs. trimetoprim: Sulfametoxazol en el tratamiento de la prostatitis bacteriana crónica.* Bol. Col. Mex. Urol. 1997; 14(2) : 94-6.p Abstract: Se realizó un estudio multicéntrico, prospectivo y comparativo con distribución al azar para comparar la eficacia y la seguridad de lomefloxacino (LMF) con la de trimetoprim/sulfametoxazol (TMP/SMX) en el tratamiento de la prostatitis bacteriana crónica. El estudio se efectuó en tres centros hospitalarios, y abarcó a un total de 30 pacientes adultos del sexo masculino con diagnósticos clínicos y bacteriológico confirmados. Los pacientes se distribuyeron al azar para recibir LMF a la dosis de 400 mg una vez al día (n = 15), o TMP/SMX a la de 160/800 mg dos veces al día (n = 15) durante seis semanas. Se valoraron los aspectos de seguridad y eficacia antes del tratamiento, durante el mismo y una vez terminado éste mediante cultivos de orina pruebas de laboratorio y valoración clínica, incluso hasta dos y cuatro meses después del tratamiento. Se logró erradicación bacteriológica en 92.3 por ciento de los pacientes tratados. con LMF y en 84.6 por ciento de los que recibieron TMP/SMX (p> 0.05). Se logró un buen resultado clínico en 100 por ciento de los pacientes que recibieron LMF o TMP/SMX. Ambas evaluaciones se realizaron cinco a nueve días después de terminar el tratamiento. Los agentes patógenos que con mayor frecuencia se aislaron fueron Escherichia coli (43.3 por ciento), estafilococo coagulasa negativo (20 por ciento), Staphylococcus saprophiticus (13.3 por ciento) y Enterococcus sp. (13.3 por ciento). Los efectos adversos se consideraron leves, y los experimentaron un paciente que recibió LMF y dos que tomaron TMP/SMX(AU).

Hernandez Garcia A.M. et al. *[In vitro sensitivity of Mycobacterium chelonae strains to various antimicrobial agents].* Microbiologia. 1995; 11(4) : 485-90.p Abstract: The in vitro susceptibility of 32 Mycobacterium chelonae strains to 10 antimicrobial agents was determined. The sources of the different strains were: clinical samples from patients treated at the Hospital Universitario de Canarias and Hospital del Torax (General and Chest facilities) and from environmental sources (water supply, sewage, swimming pools and the sea). The susceptibility tests were performed by a broth microdilution method (Mueller-Hinton Broth). The results showed amikacin as the most effective antimicrobial agent against M. chelonae isolates, then ofloxacin and cefoxitin. However no statistical difference was detected among them. The least effective was imipenem, followed by ciprofloxacin and norfloxacin.

Hernandez Granados J.E. et al. *Resistencia bacteriana en gérmenes nosocomiales en el Hospital General San Juan de Dios, Guatemala.* Rev. med. interna. 1995; 4(1) : :2-11.p Abstract: La resistencia bacteriana a los antibióticos de uso clínico apareció pocos años después de la introducción de la Penicilina en 1941 y se ha convertido en un serio problema a nivel mundial, particularmente en países en vías de desarrollo. Para documentar la presencia de organismos multiresistentes en el Hospital General San Juan de Dios, se revisaron los cultivos realizados de enero a abril de 1993, con ayuda del programa WHONET. Tres organismos con alto grado de resistencia fueron identificados a través del hospital. Pseudomona aeruginosa sensible nicamente a Ceftazidima e Imipenem/Cilastatin est distribuída igualmente en los diferentes departamentos. Salmonella enteritidis y Klebsiella ozaenae sensibles Ónicamente a las quinolonas e Imipenem/Cilastatin, constituyen un serio problema principalmente en el departamento de Pediatría. El uso irracional de antibióticos profil cticos y terapéuticos, la falta de mentalidad sanitaria en el personal médico y paramédico y factores socioeconómicos contribuyen a la selección y persistencia de organismos multiresistentes a nivel hospitalario. Un cambio de actitud en cuanto al uso de antibióticos en la pr ctica médica es necesario para prevenir el retorno a la impotencia terapéutica de la era anterior a la introducción de la penicilina (AU).

Hernandez Rastrollo R. et al. *[Prospective study of infective complications in newborns with fine silicone catheters used for parenteral nutrition infusion].* An Esp Pediatr. 1996; 45(6) : 626-30.p Abstract: OBJECTIVE: Percutaneous silastic central venous catheters have contributed to improve the care of neonates. They are quite safe; however, sometimes complications occur, with infections being the most frequent. A prospective study was undertaken in our NICU to know

the rate of catheter-related sepsis, the influence of the duration of catheterization, the predominant portal of entry and the microorganisms isolated. PATIENTS AND METHODS: Fifty-two catheters were analyzed. Cultures were obtained once a week by aspiration from the catheter hub, the luer-lock connection and parenteral nutrition solution directly from the bag. If sepsis was suspected, blood cultures were obtained from a different vein. The tip was cultured after catheter withdrawal by the semiquantitative technique of Maki. RESULTS: Nineteen catheters (36.5%), 19 luer-lock connections (21.3%) and 7 parenteral nutrition solutions were colonized. We found a significant increase of the rate of colonization after the catheter had been in place 3 weeks or more ($p < 0.05$). Coagulase negative Staphylococcus was isolated in 75.7% of the samples. The rate of catheter related sepsis was 15.4% (7/8 caused by coagulase negative Staphylococcus). CONCLUSIONS: Catheter related sepsis may be more frequent than expected it colonization of the catheter were analyzed systematically. Screening catheter colonization allows an earlier diagnosis of pathogens if sepsis develops. Finally, we believe that the use of sterile techniques to handle the catheter and connections will further decrease catheter related infections.

Herrera A. N. et al. *Relaciones fenotípicas y moleculares entre cepas de vibrio cholerae 01 aisladas en Chile, Perú y Bolivia: comparación con cepas de reservorios ambientales.* Rev. méd. Chile. 1996; 124(12) : 1431-7.p Abstract: The phenotype, biotype and susceptibility to nine antimicrobials was determined for each isolated strain. Also, the genes of cholera and termolabile toxins were determined using DNA probes and a chromosomal restriction profile was done using HindIII, EcoRI and NotI enzymes. Features studied were similar in the 53 strains isolated from patients. Those isolated from environmental reservoirs had different antimicrobial susceptibility, showing ampicillin resistance and the GT gene was detected in one of 20 strains, compared to clinical samples were it was present in all. Strains isolated from patients and envirinment had similar chromosomal restriction profiles. The chromosomal restriction profile gives an image of bacterial genome and it is a useful and reliable tool for the epidemiological surveillance of cholera (AU).

Herrera-Insua I. et al. *The effect of antibiotic exposure on adherence to neutrophils of Enterococcus faecium resistant to phagocytosis.* J Antimicrob Chemother. 1997; 39 Suppl A : 109-13.p Abstract: Many clinical isolates of Enterococcus faecium are resistant to neutrophil-mediated phagocytosis and killing. As antibiotic exposure may alter bacterial surface properties and promote phagocytosis, we used a fluorescence microscopy assay to examine the effect of antibiotic pretreatment on the resistance to phagocytosis of six strains of E. faecium. Using two antimicrobial agents with good in-vitro activity against E. faecium, namely quinupristin/ dalfopristin and sparfloxacin, we found that exposure to quinupristin/dalfopristin at concentrations both below and above the MIC promoted bacterial adherence to neutrophils (PMNs) for all of three strains of vancomycin-susceptible E. faecium, while sparfloxacin was similarly effective in two of these three strains. In contrast, neither antibiotic was effective in promoting PMN adherence for three vancomycin-resistant strains of E. faecium. The variability amongst strains in response to antibiotic exposure suggests that either the mechanisms of resistance to phagocytosis, or its regulation, may be different amongst different strains of E. faecium.

Herrera M. et al. *Antibacterial activity of glass-ionomer restorative cements exposed to cavity-producing microorganisms.* Oper Dent. 1999; 24(5) : 286-91.p Abstract: The antibacterial activity of the glass-ionomer restorative cements Ketac-Fil, Ketac-Silver, Fuji II LC, and Vitremer was studied in vitro, in conjunction with a total of 32 strains of five bacterial genera that may be associated with dental caries: Streptococcus spp, Lactobacillus spp, Actinomyces spp, Porphyromonas spp, and Clostridium spp. Agar plate diffusion was the method used for the bacterial cultures, which included a chlorhexidine control. All four glass-ionomer cements were found to inhibit bacterial growth, though with noteworthy differences in their spheres of action. Vitremer was the cement determined to have the greatest antibacterial effects, whereas Ketac-Silver presented the least inhibitory action.

Herrera N. et al. *[Phenotypic and molecular features of Vibrio cholerae isolated in Chile, Peru and Bolivia. Comparison with environmental reservoirs].* Rev Med Chil. 1996; 124(12) : 1431-7.p Abstract: BACKGROUND: Since 1991, a massive cholera epidemic started in Peru and involved most Central and South American Countries. In Chile, 147 cases were registered, the last one in 1995. AIM: To study the phenotypic and molecular features of Vibrio cholerae strains isolated from patients in Peru, Bolivia and Chile and from environmental reservoirs in Santiago, Chile. MATERIALS AND METHODS: The phenotype, biotype and susceptibility to nine antimicrobials was determined for each isolated strain. Also, the genes of cholera and termolabile toxins were determined using DNA probes and a chromosomal restriction profile was done using HindIII, EcoRI and NotI enzymes. RESULTS: Features studied were similar in the 53 strains isolated from patients. Those isolated from environmental reservoirs had different antimicrobial susceptibility, showing ampicillin resistance, and the GT gene was detected in one of 20 strains, compared to clinical samples were it was present in all. Strains isolated from patients and environment had similar chromosomal restriction profiles. CONCLUSIONS: The chromosomal restriction profile gives an image of bacterial genome and it is a useful and reliable tool for the epidemiological surveillance of cholera.

Herruzo-Cabrera R. et al. *Antimicrobial effectiveness of 2% glutaraldehyde versus other disinfectants for hospital equipment, in an in vitro test based on germ-carriers with a high microbial contamination.* Rev Stomatol Chir Maxillofac. 1999; 100(6) : 299-305.p Abstract: 2% glutaraldehyde is the reference disinfectant for hospital instruments. However, its high environmental toxicity makes desirable to search for alternatives. We compare the antimicrobial activity of 2% glutaraldehyde with 0.44% N-duopropenide (NDP), 0.66% NDP in 48 degrees alcoholic solution (NDP-alc), 0.13% glutaraldehyde-phenate, 1% or 3% persulphate (Virkon) and 0.1% or 0.5% chlorhexidine, using a model that mimics non-regular surface instruments contaminated with microbial strains (44 bacteria, 6 of which were Mycobacterium). The contaminated carrier is soaked in the disinfectant solution. After 5 or 20 minutes contact the disinfectant is neutralized. The overall results on all microorganisms in 20 minutes, show similar antibacterial activity for 2% glutaraldehyde and 0.66% NDP-alc, followed by 0.44% NDP and after by the two concentrations of Virkon and 0.5% chlorhexidine. The 0.13% glutaraldehyde-phenate and 0.1% chlorhexidine exhibited significantly less effect than any other disinfectant. 0.66% NDP-alc was faster antimicrobial activity than 2% glutaraldehyde, destroying totally the inoculum in 5 minutes. Activity on Mycobacterium showed great differences between 2% glutaraldehyde and the rest of products (> 5 log versus < 3 log reduction in 20 minutes), with an exception: NDP-alc, with similar and faster activity (> 5 log in 5 minutes) than 2% glutaraldehyde. With human blood, the survival microorganisms increase 0.3 log (average) in all the disinfectants used. The aggressiveness on metallic devices was greater in Virkon than in the other disinfectants. We conclude that NDP (alone or in alcoholic solution) may be a good alternative to glutaraldehyde in hospital instruments disinfection.

Herwaldt L.A. *Control of methicillin-resistant Staphylococcus aureus in the hospital setting.* Am J Med. 1999; 106(5A) : 11S-18S; discussion 48S-52S.p Abstract: Methicillin-resistant Staphylococcus aureus (MRSA) is a common cause of nosocomial infections. Healthcare professionals in the United States should develop programs to prevent transmission of this organism within their institutions. Aggressive control efforts are justified for several reasons: (1) the incidence of nosocomial MRSA reflects the general effectiveness of

infection control practice; (2) MRSA do not replace susceptible strains but instead increase the overall rate of nosocomial S. aureus infections; (3) MRSA infections cause substantial morbidity and mortality; (4) serious MRSA infections must be treated with vancomycin. Thus, in hospitals with high rates of MRSA, use of this antimicrobial agent increases, which in turn may increase the risk for selecting vancomycin-resistant enterococci. Hospitals have used numerous different approaches to control nosocomial spread of MRSA. Staff should choose a control method based on the prevalence of MRSA in their institution and in their referring facilities, the rate of nosocomial transmission of MRSA in their hospital, the risk factors present in their patient population, the reservoirs and modes of transmission specific to their hospital, and their resources. Any MRSA control plan must stress adherence to basic infection control measures, such as hand washing and contact isolation precautions. In addition, decolonization of patients and staff, control of antimicrobial use, surveillance cultures, and molecular typing may be helpful adjuncts.

Herwaldt L.A. et al. *The positive predictive value of isolating coagulase-negative staphylococci from blood cultures.* Clin Infect Dis. 1996; 22(1) : 14-20.p Abstract: We used four criteria to define true bloodstream infections after isolation of coagulase-negative staphylococci (CNS) from Isolator (Wampole Laboratories, Cranbury, NJ) blood cultures: (1) the patient's temperature was > or = 38 degrees C, (2) appropriate treatment was administered, (3) the physician diagnosed bloodstream infection or criteria for nosocomial bloodstream infection were met, and (4) at least one clinical sign or laboratory value was consistent with infection. Sixty (26.4%) of 227 episodes met these four criteria. By logistic regression, variables associated with meeting the definition of infection were admission to a service other than the surgical intensive care unit, the biotype of the Staphylococcus epidermidis isolates, the log of the weighted average of the total number of bacteria per milliliter of blood in all positive cultures, resistance to at least six antimicrobial agents, and the positivity of a BACTEC blood culture specimen that was drawn with the first positive Isolator culture specimen. In a high-risk population, 26% of Isolator blood cultures positive for CNS represented infections, a rate two to four times greater than that reported in the literature. Information regarding the species, biotype, antibiogram, and number of organisms per milliliter of blood might help physicians distinguish between CNS bloodstream infections and contamination.

Herzum M. et al. *Restenosis after percutaneous coronary interventions and infection.* Herz. 2000; 25(2) : 91-4.p Abstract: Infectious agents may directly or indirectly (through the response of the host's immune system) modulate the growth of vascular cells. Local and/or systemic increase of cytokines could influence the extent of (re-)stenosis in the vascular tree. Further studies in this field may identify patients at a high risk for atherogenesis and restenosis. Their results should be helpful in treating restenosis after percutaneous coronary interventions.

Heurlin N. et al. *Lack of T-helper lymphocytes in BAL fluid from a HIV-negative patient with recurrent non-tuberculous mycobacterial lung infections.* Scand J Infect Dis. 1996; 28(6) : 625-8.p Abstract: We describe here a previously healthy, 42 year old, HIV-negative woman. Following a seemingly successful 2-year antimycobacterial regimen for a lung infection caused by Mycobacterium avium/intracellulare she acquired a lung infection caused by M. chelonei. Characterization of alveolar cells from bronchoalveolar lavage fluid using flow cytometry revealed a total lack of T-cell subset CD4+ helper lymphocytes in spite of a normal proportion of the CD3+ and CD4+ T-cells in peripheral blood. The levels of Th2 cytokines such as IL-4, TGF-beta and G-CSF were higher in the patient's alveolar cells than in the cells of 4 healthy controls. This imbalance of cells and cell cytokines may contribute to the patient's susceptibility for non-tuberculous mycobacteria and her failure to eradicate these microorganisms.

Heyrman J. et al. *The use of fatty acid methyl ester analysis (FAME) for the identification of heterotrophic bacteria present on three mural paintings showing severe damage by microorganisms.* FEMS Microbiol Lett. 1999; 181(1) : 55-62.p Abstract: Mural paintings in Carmona (Spain), Herberstein (Austria) and Greene (Germany), showing visible deterioration by microorganisms, were sampled to investigate the biodiversity of the heterotrophic bacteria present. Four hundred twenty-eight bacterial strains were isolated from which 385 were characterized by fatty acid methyl ester analysis (FAME). The isolates were grouped into 41 clusters on the basis of their FAME profiles, 20 isolates remained ungrouped. The majority (94%) of the isolates comprised the gram-positive bacteria and the main clusters were identified as Bacillus sp., Paenibacillus sp., Micrococcus sp., Arthrobacter sp. and Staphylococcus sp. Other clusters contain nocardioform actinomycetes and gram-negative bacteria, respectively. A cluster of the latter contained extreme halotolerant bacteria isolated in Herberstein. The FAME profiles of this cluster showed a high similarity with Halomonas.

Hibbert-Rogers L.C. et al. *Molecular epidemiology of ceftazidime resistant Enterobacteriaceae from patients on a paediatric oncology ward.* J Antimicrob Chemother. 1995; 36(1) : 65-82.p Abstract: Between the autumn of 1989 and January 1990, 21 of the 44 children on the paediatric oncology ward of St. James's University Hospital, Leeds, UK were infected or colonised with Enterobacteriaceae producing extended-spectrum beta-lactamases. This represents 48% of the patients on the ward. Only six patients (14%) had microbiologically proven septicaemia caused by such bacteria during this period. Eighty-one isolates of Enterobacteriaceae producing extended-spectrum beta-lactamases derived from blood culture (7 isolates from 6 patients) or faecal samples (74 isolates) were available for examination. These comprised 28 Escherichia coli, 28 Klebsiella oxytoca, 11 Klebsiella pneumoniae, 10 Citrobacter freundii, 3 Enterobacter spp. and 1 Serratia marcescens. Clinical isolates were resistant to penicillins and to ceftazidime. Strains isolated in this study also showed multiple resistance to a range of antimicrobial agents. Transfer to a nalidixic acid resistant laboratory strain of E. coli UB5201 was attempted, but transfer of the ceftazidime resistance determinant was only successful in 25 isolates (31%). Examination of plasmid DNA revealed sequences in each isolate that hybridised with the TEM beta-lactamase gene probe used on a variety of plasmids ranging in size from 2.5- > 150 kb, sometimes found on several replicons in a single isolate. The TEM gene probe also hybridised with chromosomal DNA in a large number of isolates. Nucleotide sequence analysis demonstrated the presence of three extended-spectrum beta-lactamases: TEM-10B produced by two isolates, TEM-12B produced by 37 isolates and TEM-26B produced by 40 isolates. In two cases, isolates produced two beta-lactamases, and it proved impossible to identify these enzymes unequivocally. The genes encoding TEM-10B and TEM-26B both differ from TEM-12B by single nucleotide substitutions. Analysis of the ribotype patterns derived from the clinical isolates provided evidence for cross-colonisation between patients, and this was confirmed by analysis of the plasmid profiles. Four years after discontinuing ceftazidime and other extended-spectrum cephalosporins on this ward, patients were still colonised with bacteria that produced extended-spectrum beta-lactamases.

Hidaka T. *[Current status and perspectives on the development of rifamycin derivative antibiotics].* Kekkaku. 1999; 74(1) : 53-61.p Abstract: Rifampicin (RFP) was developed as one of the anti-tuberculosis drugs in 1966 and has been used for almost 30 years. Establishment of combination therapy using RFP has been contributing to the treatment/eradication of tuberculosis. A number of rifamycin derivatives, as post RFPs, have been synthesized/developed over the the years. Chemical modification of rifamycins has largely been concentrated on the moiety of naphthalene ring because modification of the ansa chain moiety reduces the activity. In 1992, rifabutin was approved as a preventive drug for MAC infection in AIDS patients in the United States and in European countries. It is noteworthy that

rifapentine (RPT) was approved as an anti-tuberculosis drug in 1998 by FDA in the United States. A newly synthesized rifamycin derivative (KRM-1648, rifalazil) possesses a potent activity against both M. Tuberculosis and MAC, and it is now under clinical trial for the treatment of Tuberculosis in the United States. KRM-1648 is metabolized to 30-hydroxy KRM and 25-deacetyl KRM in the body, and its 30-hydroxylation is caused by liver cytochrome P450 3A. It is well known that RFP, RFB and RPT induce liver cytochrome P450 in animals and human, and these accelerate the metabolism of concomitant drugs such as HIV protease inhibitors resulting in lowering their blood levels. While KRM-1648 did not induce liver P450 in animals, but it is not examined yet in human. Clinical study of DOT with intermittent therapy of RPT in combination with INH resulted in the preferable therapeutic effect comparable to the RFP therapy. Since KRM-1648 has a potent activity, a high tissue distribution and a long half-life, it may be also suitable for intermittent therapy. For the future novel anti-tuberculosis drugs and therapy for tuberculosis, it is prerequisite to develop new drugs with a preferable antimicrobial activity, to shorten further the treatment period, and to be effective against multi-drug resistant bacilli. It is expected that more effective novel rifamycin derivatives can be developed with the above view points.

Hidalgo E. et al. *Silver nitrate: antimicrobial activity related to cytotoxicity in cultured human fibroblasts.* Skin Pharmacol Appl Skin Physiol. 1998; 11(3) : 140-51.p Abstract: The aims of this study were to ascertain whether silver nitrate (AgNO3) concentrations below those used in clinical practice inhibit bacterial growth, and in parallel study the cytotoxic effects on human fibroblasts. The cytoprotective effects of fetal calf serum (FCS) were also evaluated. The cytotoxic effects of eight different silver nitrate concentrations were determined by assessing mitochondrial activity of viable cells capable of cleaving tetrazolium salts. Antimicrobial activity of AgNO3, range: 7-550 x 10(-5)%, was tested against Staphylococcus aureus, Citrobacter freundii, and Pseudomonas aeruginosa. Silver nitrate concentrations exerting antimicrobial effects were: S. aureus, >70 x 10(-5)%; P. aeruginosa, >/=270 x 10(-5)%, and C. freundii, >/=550 x 10(-5)%. With 2% FCS, the lowest AgNO3 concentration studied (7 x 10(-5)%) showed cytotoxic effects (cell survival 71 +/- 19%) at only 2 h of incubation. Under these conditions AgNO3 cytotoxicity was time- and concentration-dependent in all exposure periods. Cytotoxicity was greatly enhanced causing 76% fibroblast growth inhibition at concentrations of 14 x 10(-5)% and contact time of 2 h. The AgNO3 concentration of 7 x 10(-5)% was also cytotoxic with 5% FCS in the media compared with controls, although cell survival was higher than with 2% FCS. The cytoprotective action of FCS was clearly shown at the concentration of 10% at which AgNO3 cytotoxicity of 7 x 10(-5)% to 28 x 10(-5)% was partially or completely inhibited. Our results show that AgNO3 at concentrations 100-700 times more diluted than that normally used in clinical practice retained effective inhibitory activity against some of the above-mentioned microorganisms. However, even these concentrations are cytotoxic for cultured fibroblasts. Thus, silver nitrate concentrations up to 100 times more diluted can be used, since they possess bacterial growth-inhibiting power, are less cytotoxic and therefore favour wound healing.

Higaki S. et al. *Characterization of Peptostreptococcus species in skin infections.* J Int Med Res. 2000; 28(3) : 143-7.p Abstract: We examined the characteristics of Peptostreptococcus species in infectious skin diseases. P. magnus was the species identified most frequently, followed by P. asaccharolyticus. Peptostreptococcus species were mainly isolated from infected atheroma and secondary infections due to ulcers; their resistance to five antimicrobial agents was generally low. The resistance of the three predominant Peptostreptococcus species to the antimicrobials was similar to that of all of the Peptostreptococcus species. The predominant Peptostreptococcus species isolated from infected atheroma might be pathogenic. It was considered that the presence of anaerobes as well as aerobes was important to induce the infectious condition.

Higaki S. et al. *Distribution and antimicrobial susceptibility of coagulase-negative staphylococci from skin lesions.* J Int Med Res. 1999; 27(4) : 191-5.p Abstract: The distribution and antimicrobial susceptibility of coagulase-negative staphylococci from skin lesions were investigated. Staphylococcus epidermidis was found on all areas of the body, whereas S. capitis, S. haemolyticus and S. hominis were mainly found on the face/head or arm/leg. The distribution of coagulase-negative staphylococci in skin lesions and at the same location on normal skin was similar. Staphylococcus lugdunensis was the most susceptible to the nine tested antimicrobials (benzylpenicillin, ampicillin, piperacillin, cefazolin, erythromycin, minocycline, gentamicin, vancomycin and ofloxacin) and S. epidermidis the least susceptible. S. haemolyticus also showed low susceptibility to all nine antimicrobials. Low susceptibility to penicillins may be explained by beta-lactamase production. The existence of coagulase-negative staphylococci, especially concerning their potential pathogenicity and multiple drug resistance, should not be neglected.

Hii C.S. et al. *Role of the extracellular signal-regulated protein kinase cascade in human neutrophil killing of Staphylococcus aureus and Candida albicans and in migration.* Infect Immun. 1999; 67(3) : 1297-302.p Abstract: Killing of Staphylococcus aureus and Candida albicans by neutrophils involves adherence of the microorganisms, phagocytosis, and a collaborative action of oxygen reactive species and components of the granules. While a number of intracellular signalling pathways have been proposed to regulate neutrophil responses, the extent to which each pathway contributes to the killing of S. aureus and C. albicans has not been clearly defined. We have therefore examined the effect of blocking one such pathway, the extracellular signal-regulated protein kinase (ERK) cascade, using the specific inhibitor of the mitogen-activated protein kinase/ERK kinase, PD98059, on the ability of human neutrophils to kill S. aureus and C. albicans. Our data demonstrate the presence of ERK2 and a 43-kDa form of ERK but not ERK1 in human neutrophils. Upon stimulation with formyl methionyl leucyl phenylalanine (fMLP), the activities of both ERK2 and the 43-kDa form were stimulated. Despite abrogating the activity of both ERK forms, PD98059 only slightly reduced the ability of neutrophils to kill S. aureus or C. albicans. This is consistent with our finding that PD98059 had no effect on neutrophil adherence or degranulation, although pretreatment of neutrophils with PD98059 inhibited fMLP-stimulated superoxide production by 50%, suggesting that a change in superoxide production per se is not strictly correlated with microbicidal activity. However, fMLP-stimulated chemokinesis was markedly inhibited, while random migration and fMLP-stimulated chemotaxis were partially inhibited, by PD98059. These data demonstrate, for the first time, that the ERK cascade plays only a minor role in the microbicidal activity of neutrophils and that the ERK cascade is involved primarily in regulating neutrophil migration in response to fMLP.

Hill B.C. et al. *A simplified method for testing Bordetella pertussis for resistance to erythromycin and other antimicrobial agents.* J Clin Microbiol. 2000; 38(3) : 1151-5.p Abstract: Present methods of antimicrobial susceptibility testing of Bordetella pertussis are time consuming and require specialized media that are not commercially available. We tested 52 isolates of B. pertussis for resistance to erythromycin, trimethoprim-sulfamethoxazole, chloramphenicol, and rifampin by agar dilution with Bordet-Gengou agar (BGA) containing 20% horse blood (reference method), Etest using BGA and Regan-Lowe agar without cephalexin (RL-C), and disk diffusion using BGA and RL-C. The organisms tested included four erythromycin-resistant isolates of B. pertussis from a single patient, a second erythromycin-resistant strain of B. pertussis from an unrelated patient in another state, and 47 nasopharyngeal surveillance isolates of B. pertussis from children in the western United States. The results of agar dilution testing using direct inoculation of the organisms suspended in Mueller-Hinton broth were within +/-1 dilution of those obtained after overnight passage of the inoculum in Stainer-Scholte medium, which is the traditional method of testing B. pertussis. The Etest

method produced MICs similar to those of the agar dilution reference method for three of the four antimicrobial agents tested; the trimethoprim-sulfamethoxazole results were lower with Etest, particularly when the direct suspension method was used. Most of the Etest MICs, except for that of erythromycin, were on scale. Disk diffusion testing using RL-C medium was helpful in identifying the erythromycin-resistant strains, which produced no zone of inhibition around the disk; susceptible isolates produced zones of at least 42 mm. Thus, the antimicrobial susceptibility testing of B. pertussis can be simplified by using the Etest or disk diffusion on RL-C to screen for erythromycin-resistant isolates of B. pertussis.

Hill R.L. et al. *Bactericidal and inhibitory activity of quinupristin/dalfopristin against vancomycin- and gentamicin-resistant Enterococcus faecium*. J Antimicrob Chemother. 1997; 39 Suppl A : 23-8.p Abstract: There is a need for new agents, or combinations of agents, for the treatment of infections caused by vancomycin- and gentamicin-resistant Enterococcus faecium (VGREF) that may be resistant to all available antimicrobial agents. The early in-vitro activity of quinupristin/dalfopristin (30:70)—an injectable streptogramin—encouraged us to test this agent against VGREF. By broth dilution, the MICs of quinupristin/dalfopristin against 38 isolates of VGREF ranged from 0.06 mg/L to 2.0 mg/L (mode 0.12 mg/L). The addition of 0.5 mg/L of ciprofloxacin significantly reduced the modal MIC of quinupristin/dalfopristin to 0.015 mg/L (P = 5.75 x 10(-8)). Although the addition of 8.0 mg/L of teicoplanin or 4 mg/L of tetracycline did not significantly reduce the modal MIC, the lowest concentration of the MIC range was reduced from 0.06 to 0.015 mg/L. In broth, quinupristin/dalfopristin had slow bactericidal activity against the four strains tested over 48 h, with a 1-2 log10 cfu/mL reduction after 24 h in > 1 mg/L of quinupristin/dalfopristin for two strains and > 8 mg/L for the two other strains. A mixture of quinupristin/dalfopristin in a 70:30 ratio was more bactericidal: against one of the four strains 4-32 mg/L of the combination produced a further 0.5-1.0 log10 reduction in cfu/mL after 24 h and there was a reduction of 6.0 log10 cfu/mL after 48 h for another. By ultracentrifugation, the binding of 32 mg/L quinupristin/dalfopristin to human plasma protein was 90%, and in plasma broth, 32 mg/L of quinupristin/dalfopristin maintained bacteriostatic but not bactericidal activity. There is some useful synergy with ciprofloxacin and tetracycline, and the activity of quinupristin/dalfopristin may be enhanced against some strains by reversing the concentrations of its two components, quinupristin and dalfopristin, as that may occur in vivo.

Hillberg R.E. *The role of infection in acute exacerbations of chronic obstructive pulmonary disease.* Am J Manag Care. 2000; 6(8 Suppl) : S427-36.p Abstract: Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death in the United States and the second leading cause of work disability. Extensive data indicate that bacterial infection has an important role in acute exacerbations of COPD. Antibiotic therapy has been shown to benefit patients with exacerbations of COPD by improving clinical outcomes and hastening clinical and physiologic recovery. Antibiotics also provide long-term benefits such as preventing the progression of disease, minimizing secondary colonization with resistant organisms, and prolonging the time between exacerbations. Classifying an episode of COPD as uncomplicated, complicated, or at risk for Pseudomonas is useful in determining antibiotic therapy for patients with an acute exacerbation. Although patients with less severe uncomplicated disease can be treated with older antimicrobial agents, those with serious comorbid conditions or advanced structural lung disease require treatment with new more potent agents. Knowing the patterns of antimicrobial resistance in the respiratory pathogens, antibiotic pharmacokinetics, and factors influencing patient compliance is necessary to prevent treatment failures.

Hillier S.L. et al. *Role of bacterial vaginosis-associated microorganisms in endometritis.* Am J Obstet Gynecol. 1996; 175(2) : 435-41.p Abstract: OBJECTIVE: Our goal was to define the role of bacterial vaginosis and bacterial vaginosis-associated microorganisms in endometritis. STUDY DESIGN: Endometrial biopsies were obtained for histologic and microbiologic study from 178 consecutive women with suspected pelvic inflammatory disease, and 85 of them underwent laparoscopy to diagnose salpingitis. RESULTS: Histologic endometritis was confirmed in 117 (65%) of the women. Among women who underwent laparoscopy, salpingitis was present in 68% of those with and 23% of those without endometritis. Some but not all bacterial vaginosis-associated microorganisms were linked with endometritis. By logistic regression analysis, after adjustment for bacterial vaginosis and isolation of Neisseria gonorrhoeae and Chlamydia trachomatis, endometritis was associated with endometrial N. gonorrhoeae (odds ratio 5.7, 95% confidence interval 1.8 to 17.5), C. trachomatis (odds ratio 4.8, 95% confidence interval 1.3 to 18.2), anaerobic gram-negative rods (odds ratio 2.6, 95% confidence interval 1.1 to 5.7), and nonwhite race (odds ratio 2.3, 95% confidence interval 1.1 to 4.8). CONCLUSIONS: The association of anaerobic gram-negative rods with endometritis, after adjustment for bacterial vaginosis, N. gonorrhoeae, and C. trachomatis, supports the role of these microorganisms in the etiology of histologic endometritis among women with clinically suspected pelvic inflammatory disease.

Hipólito, M. *Estudo da resistência a antimicrobianos das principais bactérias isoladas de mastite bovina, no estado de São Paulo, no período de 1980 a 1993, e sua relação com a saúde pública* 1996. 88 p. ilus, tab. São Paulo. s.n. 1996.p Abstract: Estuda a resistência bacteriana frente a antimicrobianos utilizados no tratamento da mastite bovina no período de 1980 a 1993; a significância das diferenças percentuais e a relação com a Saúde Pública. O teste de sensibilidade (antibiograma) foi de difusão em ágar com uso de discos, testando os antimicrobianos ampicilina, cloranfenicol, gentamicina, kanamicina, penicilina e tetracicina frente aos agentes etiológicos Staphylococcus sp, Streptococcus sp e Escherichia coli. Os resultados são apresentados a cada 2 anos, com 7 sub-períodos, e analisados estatisticamente pelo teste de duas proporções, com aproximação normal e significância de "t"alfa 0,05. Nas séries históricas, as tendências foram, na sua grande maioria, de queda dos percentuais de resistência. Para o Staphylococcus sp, a gentamicina apresentou os menores porcentuais de resistência e poucas diferenças significativas, seguido pelo cloranfenicol, kanamicina e tetraciclina. A penicilina apresentou altos percentuais de resistência. Para o Streptococcus sp, os menores percentuais de resistência foram frente ao cloranfenicol e penicilina, com o cloranfenicol apresentando os menores números de diferenças significativas. Para a E. coli, os menores percentuais de resistência foram frente … gentamicina e cloranfenicol, sendo a gentamicina, o antimicrobiano com menor número de diferenças significativas. As diferenças significativas tanto ocorreram pela queda como pelo aumento dos percentuais de resistência. Os resultados indicaram uma grande variação dos percentuais de resistência para estes agentes etiológicos, permitindo destacar a importância do conhecimento epidemiológico para o uso de antimicrobianos (AU).

Hirakata Y. et al. *In vitro susceptibility studies and detection of vancomycin resistance genes in clinical isolates of enterococci in Nagasaki, Japan*. Epidemiol Infect. 1997; 119(2) : 175-81.p Abstract: Glycopeptide resistance in enterococci is now a cause of clinical concern in the United States and Europe. However, details of vancomycin resistance in enterococci in Japan have been unknown. We measured minimum inhibitory concentrations (MICs) of various antimicrobial agents for a total of 218 clinical strains of enterococci isolated in our hospital in 1995-6 in addition to 15 strains with known genotypic markers of resistance. We also screened vancomycin resistance genes using a single step multiplex-PCR. In clinical isolates, only two strains of Enterococcus gallinarum were of intermediate resistance to vancomycin (MIC, 8 micrograms/ml), while the others were all susceptible. Glycopeptides (vancomycin and teicoplanin) and streptogramins (RP 58500 and RPR 106972) showed potent antimicro-

bial effects for the isolates. In addition, ampicillin was also potent for Enterococcus faecalis, while ampicillin, minocycline and gentamicin were potent for Enterococcus avium. No vanA or vanB genes were detected, while vanC1 and vanC23 genes were detected from two and four strains, respectively. Our results suggest that incidence of VRE in Japan may be estimated as still very low at this time.

Hirata D. et al. *Preferential binding with Escherichia coli hsp60 of antibodies prevalent in sera from patients with rheumatoid arthritis.* Clin Immunol Immunopathol. 1997; 82(2) : 141-8.p Abstract: One hundred thirty-two patients with various connective tissue disorders, including 60 with rheumatoid arthritis (RA), had antibodies against human as well as Escherichia coli hsp60 in titers significantly higher than those of normal controls. There was a correlation between titers of antibody to human hsp60 and those to E. coli hsp60. Levels of antibodies against human and E. coli hsp60 were lower in joint fluids than in sera, indicating little production of antibodies in the joint. Antibodies affinity-purified with E. coli hsp60 bound strongly with the homologous hsp60, but weakly with human hsp60. However, antibodies affinity-purified with human hsp60 bound comparably with both E. coli hsp60 and human hsp60. Antibodies affinity-purified with Mycobacterium tuberculosis hsp65 bound to human hsp60 with a reactivity similar to the reactivity of those affinity-purified with human hsp60. The reactivity to the three hsp60 species was lost when sera were absorbed with E. coli hsp60, while the reactivity to E. coli hsp60 remained after extensive absorption with M. tuberculosis hsp65 or human hsp60. These results indicate that anti-hsp60 antibodies in patients with RA and other connective tissue disorders are raised by infection with intestinal microorganisms such as E. coli. They may represent another example of autoimmune responses triggered by antigenic mimicry of host proteins to microbes and suggest that the reactivity of antibodies from RA patients with M. tuberculosis hsp65 might have been a cross-reaction with the E. coli homologue.

Ho M. *Current outlook of infectious diseases in Taiwan.* J Microbiol Immunol Infect. 1998; 31(2) : 73-83.p Abstract: The "emerging" infectious diseases have received global attention. Taiwan is a country which is going through the process of becoming "developed" from being "developing". If we compare five leading causes of death in 1952 and in 1993, three were infectious diseases in 1952 and there was none in 1993. And yet today, infectious diseases remain a major problem in this country as well in every country in the world, whether developing or developed. Some of the problems Taiwan faces are old problems with old faces. They have never been adequately solved because the societal and environmental sanitary infrastructure does not ensure proper sewage disposal, safe potable water and freedom from dangerous vectors. Examples are the diarrheal diseases, parasitic diseases, scrub typhus and Japanese encephalitis. Some of the Taiwan's problems are caused by old agents which present a new face. Mortality from tuberculosis took a dramatic and gratifying plunge in the last fifty years. Yet tuberculosis is ever present and a constant public health threat. Dengue has become a problem again because of a world breakdown in the control of the mosquito, Aedes egypti, and it is partly contributed to by increased urbanization and world travel. The problem of antibiotic resistant bacteria causing hospital acquired and community acquired infections is probably the most serious "new" problem. The most important cause is excessive and indiscriminate use of antibiotics in the community and in hospitals. We propose the establishment of "Bacterial Infections Reference Laboratory" at the National Health Research Institutes to be a national facility to study the epidemiology and control of antibiotic resistance. All infectious diseases require a rigorous system of surveillance, and precise etiological diagnosis before they can be treated or prevented. This should be kept clearly in mind when one considers the changing role of the infectious disease physician in Taiwan in the face of unsolved disease problems and a new health care system. There is inadequate attention to precise microbiological definition of most infectious diseases in Taiwan. The community of infectious disease specialists may well redirect its attention to improving the competence and utilization of microbiological laboratory diagnosis.

Ho M. et al. *Surveillance of antibiotic resistance in Taiwan, 1998.* J Microbiol Immunol Infect. 1999; 32(4) : 239-49.p Abstract: For the first national surveillance of antibiotic resistance in Taiwan, we collected in 1998 from 22 hospitals (6 medical centers, 15 regional hospitals, and 1 local hospital) 3,211 isolates in all parts of the country. Besides 50 random successive isolates from inpatients, each hospital was requested to collect 25 isolates each from positive blood cultures, hospital-acquired infections, outpatients and the pediatric department. We re-speciated all the submitted specimens and determined their antibiotic susceptibility patterns. The most common isolates were Enterobacteriaceae (Escherichia coli, Klebsiella pneumoniae), Staphylococcus aureus, and Pseudomonas aeruginosa. Among hospital-acquired infections, Acinetobacter spp. were among those which accounted for over 10% of the isolates. The oxacillin resistance of S. aureus was 82% in isolates from hospital-acquired infections, and 40% from outpatients. Among Enterococcus spp., 85% were either E. faecalis or E. faecium. They were 14% resistant to vancomycin. Among gram-negative bacteria, K. pneumoniae and Acinetobacter baumanii were hospital-acquired isolates that were most clearly more resistant than community acquired isolates. This difference was less apparent in the case of Enterobacter cloacae, Serratia marcescens, and P. aeruginosa. These bacteria were generally more resistant from all sources. Fifty-one percent of Salmonella were resistant to ampicillin; however, these were all sensitive to ciprofloxacin. Isolates from the East were least resistant. Plotting the disc zone diameters of antibiotics within the susceptible range, we identified subpopulations with smaller diameters in the case of vancomycin against S. aureus, ciprofloxacin against E. coli, and ciprofloxacin against Salmonella spp. These findings represent one of the purposes of this surveillance as they may portend developing resistances which bear careful watching in the future.

Ho P. et al. *Changing patterns of susceptibilities of blood, urinary and respiratory pathogens in Hong Kong.* J Hosp Infect. 1995; 31(4) : 305-17.p Abstract: The incidence and antimicrobial susceptibility of organisms isolated from blood, urine and respiratory specimens at a teaching hospital in Hong Kong were studied retrospectively from 1986-1993. The incidence of Gram-positive bacteraemia, particularly coagulase-negative staphylococci (CNS), increased significantly from 33.6 to 47.3% ($P < 0.001$) while that of Gram-negative bacteraemia fell from 60.0 to 47.0% ($P < 0.001$). Among blood isolates, methicillin resistance of CNS increased from 17.0 to 58.0% ($P < 0.001$) and cefuroxime resistance of Enterobacter spp. increased from 21.0 to over 50% ($P < 0.01$). Among urinary isolates, cefuroxime resistance of Klebsiella spp. (11.0 to 24.0%, $P < 0.001$) and Enterobacter spp. (32.0 to 75.0%, $P < 0.001$) increased. Nalidixic acid resistance among Gram-negative urinary isolates, except Proteus mirabilis, rose by three- to sixfold. For Streptococcus pneumoniae, isolated from the respiratory tract, penicillin resistance increased dramatically (2 to 18%, $P < 0.001$). For respiratory isolates of Haemophilus influenzae, ampicillin resistance increased from 17.0 to 29.0% ($P < 0.001$). These data are useful in guiding empirical treatment of nosocomial infections.

Ho P.L. et al. *Emergence of fluoroquinolone resistance among multiply resistant strains of Streptococcus pneumoniae in Hong Kong.* Antimicrob Agents Chemother. 1999; 43(5) : 1310-3.p Abstract: The MICs of 17 antimicrobial agents for 181 Streptococcus pneumoniae strains were determined by the E-test. Overall, 69.1% were penicillin resistant (MIC > 0.06 microgram/ml). Resistance to ciprofloxacin (MIC > 2 microgram/ml), levofloxacin (MIC > 2 microgram/ml), or trovafloxacin (MIC > 1 microgram/ml) was found in 12.1, 5.5, or 2.2% of the strains, respectively. These high rates of resistance raise concerns for the future.

Hoefnagels-Schuermans A. et al. *Origin and transmission of methicillin-resistant Staphylococcus aureus in an endemic situation: differences between geriatric and intensive-care patients.* J Hosp Infect. 1997; 36(3) : 209-22.p Abstract: Imported vs. hospital-acquisition of MRSA was assessed in > 6000 patients at a large tertiary care teaching hospital. About five percent (5.1%) of patients carried MRSA on admission, mostly without clinical symptoms; the highest percentage (11.6%) being in geriatric patients. Hospital-acquisition of MRSA occurred in 1.7% of patients and was particularly high in intensive-care units (5.2%). Phenotype and genotype analysis of 158 MRSA strains isolated from 61 patients revealed a cluster of closely related strains in the hospital-acquired MRSA infections and the close relationship of this cluster to the regional epidemic MRSA strain. The MRSA strains imported by geriatric patients were genetically different, did not spread between geriatric patients and were only a minor source of nosocomial infection.

Hoeper M.M. et al. *Long-term treatment of primary pulmonary hypertension with aerosolized iloprost, a prostacyclin analogue.* N Engl J Med. 2000; 342(25) : 1866-70.p Abstract: BACKGROUND: Continuous intravenous infusion of epoprostenol (prostacyclin) is an effective treatment for primary pulmonary hypertension. This approach requires the insertion of a permanent central venous catheter, with the associated risk of serious complications. Recently, aerosolized iloprost, a stable prostacyclin analogue, has been introduced as an alternative therapy for severe pulmonary hypertension. METHODS: We evaluated the effects of aerosolized iloprost on exercise capacity and hemodynamic variables over a one-year period in patients with primary pulmonary hypertension. RESULTS: Twenty-four patients with primary pulmonary hypertension received aerosolized iloprost at a daily dose of 100 or 150 microg for at least one year. The mean (+/-SD) distance covered in the six-minute walk test increased from 278+/-96 m at base line to 363+/-135 m after 12 months (P<0.001). During the same period, the mean pulmonary arterial pressure before the inhalation of iloprost declined from 59+/-10 mm Hg to 52+/-15 mm Hg (P=0.006), cardiac output increased from 3.8+/-1.4 liters per minute to 4.4+/-1.3 liters per minute (P=0.02), and pulmonary vascular resistance declined from 1205+/-467 dyn x sec x cm(-5) to 925+/-469 dyn x sec x cm(-5) (P<0.001). The treatment was generally well tolerated, except for mild coughing, minor headache, and jaw pain in some patients. CONCLUSIONS: Long-term treatment with aerosolized iloprost is safe and has sustained effects on exercise capacity and pulmonary hemodynamics in patients with primary pulmonary hypertension.

Hofer E. et al. *[The emergence of multiple antimicrobial resistance in Vibrio cholerae isolated from gastroenteritis patients in Ceara, Brazil].* Rev Soc Bras Med Trop. 1999; 32(2) : 151-6.p Abstract: Of 7058 Vibrio cholerae strains recovered from patients suspected of cholera in the State of Ceara between December 1991 and September 1993, two were resistant to antimicrobials (Ampicillin, erythromycin, trimethoprim-sulfamethoxazole, tetracycline) and to vibriostatic agent O/129 (2,4-diamino-6,7-diisopropylpteridine). From the bacteriological standpoint, one strain was identified as V. cholerae serogroup O:1, biotype El Tor, serovar Inaba, and another as V. cholerae serogroup O:22, biochemically classified as Heiberg type II. It was shown that only in the serogroup O:1 strain, multiple resistance was encoded by a plasmid transferrable by conjugation to Escherichia coli K12 and a sensitive strains of V. cholerae O1 and non-O1, with at a frequency between 8 x 10(-2) and 5 x 10(-6). The plasmid, with a molecular weight of 147 Kb, encoded both multiple resistance to antimicrobials and the vibriostatic compound (O/129), compatible with descriptions reported in other parts of world.

Hofer E. et al. *Emergência da múltipla resistência a antimicrobianos em Vibrio cholerae isolados de pacientes com gastroenterite no Ceará, Brasil.* Rev. Soc. Bras. Med. Trop. 1999; 32(2) : 151-6.p Abstract: Das 7058 amostras de Vibrio cholerae isoladas de pacientes com suspeita de síndrome coleriforme, no período de 1991 a 1993, no Estado do Ceará, foram detectadas duas com as características de múltipla resistência aos antimicrobianos (tetraciclina, ampicilina, sulfametoxazol-trimetoprima) e ao composto vibriostático O/129 (2,4-diamino-6, 7-diisopropilpteridina). Do ponto de vista bacteriológico uma amostra foi identificada como V.cholerae sorogrupo O:1, biotipo El Tor e sorovar Inaba e a outra, caracterizada como V. cholerae sorogrupo O:22, classificada bioquimicamente no tipo II de Heiberg. Foi demonstrado que apenas na amostra do sorogrupo O:1, a multirresistência era codificada por um plasmídio, transferível por conjugação para Escherichia coli K12 e amostras sensíveis de V. cholerae O1 e não O1, numa frequência entre 8x10-_ a 5x10-(6). O plasmídio responsável pela multirresistência apresentou um peso molecular de 147 Kb, compatível com as descrições em outras partes do mundo (AU).

Hoffman J.S. *Pharmacological therapy of Helicobacter pylori infection.* Semin Gastrointest Dis. 1997; 8(3) : 156-63.p Abstract: Helicobacter pylori has been associated with several diseases including peptic ulcer disease and gastric cancer. Eradication of H pylori not only results in ulcer healing, but reduces recurrences essentially curing peptic ulcer disease. Eradicating H pylori can be difficult. There are several reasons for antimicrobial failure, and the resistance rates for several antibiotics are increasing. The most common drugs used to treat this infection include amoxicillin, clarithromycin, tetracycline, bismuth, and omeprazole and lansoprazole. Dual therapy using a proton pump inhibitor and a single antibiotic gives a suboptimal eradication rate. Triple therapy using at least two antibiotics and either bismuth or a proton pump inhibitor gives satisfactory eradication rates of 90%. However, these regimens are complicated and have significant side effects and compliance problems. The ideal regimen has yet to be developed. In the future, we will prevent infection with immunization. Several vaccines are being developed.

Hoffman P.S. *Antibiotic resistance mechanisms of Helicobacter pylori.* Can J Gastroenterol. 1999; 13(3) : 243-9.p Abstract: Infection with Helicobacter pylori is most frequently associated with gastritis and peptic ulcer disease. Antimicrobial intervention, together with proton pump inhibitors, has become the standard therapy for treating this disease. Resistance to clarithromycin and metronidazole, two of the most commonly used antimicrobials for treatment of H pylori infections, is often associated with treatment failures and relapse of infection. Clarithromycin resistance arises through mutations leading to base changes in 23S ribosomal RNA subunits, while resistance to metronidazole is due to mutations in the rdxA gene, which encodes a novel nitroreductase that is responsible for reductive activation of the drug. Products of metronidazole activation are mutagenic and can be demonstrated to increase both the mutation frequency and the frequency at which antibiotic resistance arises in H pylori.

Hofling J.F. et al. *Salivary counts of mutans streptococci and lactobacilli in children ageing 6-8 year old having a socioeconomic background in Brazil.* Indian J Dent Res. 1998; 9(3) : 91-7.p Abstract: Saliva samples from students aged 6 to 8 year-old were analysed in order to determine the incidence of Streptococcus group mutans and Lactobacillus. Two hundred children were examined, distributed in five socioeconomic categories (A to E). Stimulated saliva samples were collected and inoculated into the SB20 and Rogsa agar culture medium for the Streptococcus and Lactobacillus cultivation. After growth, the number of these microorganisms (CUF/mL) was determined after identification of the representative colonies by biochemical methods on the basis of carbohydrate fermentation. A significative part of the population, particularly among the lower socioeconomic categories (D/E) was considered a high risk group in developing dental caries because of the high number of Streptococcus group mutans and Lactobacillus.

Hofmann J. et al. *The prevalence of drug-resistant Streptococcus pneumoniae in Atlanta.* N Engl J Med. 1995; 333(8) : 481-6.p Abstract: BACKGROUND. Streptococcus pneumoniae is a major cause of illness,

and the emergence of drug-resistant strains threatens to complicate the management of pneumococcal infections. We conducted a laboratory-based surveillance for drug-resistant S. pneumoniae among patients with invasive pneumococcal infections in Atlanta. METHODS. From January through October 1994, pneumococcal isolates from 431 patients with invasive disease in metropolitan Atlanta were serotyped and tested to determine their susceptibility to various antimicrobial agents. Susceptibility to the antimicrobial agents was defined according to guidelines established by the National Committee for Clinical Laboratory Standards. RESULTS. The annual incidence of invasive pneumococcal infection was 30 cases per 100,000 population. Isolates from 25 percent of the patients were resistant to penicillin (7 percent were highly resistant), and isolates from 26 percent were resistant to trimethoprim-sulfamethoxazole (7 percent highly resistant). Fifteen percent of the isolates were resistant to erythromycin, 9 percent to cefotaxime (4 percent were highly resistant), and 25 percent to multiple drugs. Drug-resistant pneumococci were found in both children and adults. Children under six years of age were more likely than older children and adults to have isolates resistant to multiple drugs or cefotaxime. Whites were more likely than blacks to have invasive pneumococcal infections caused by drug-resistant organisms. Among white children younger than six years, 41 percent of the S. pneumoniae isolates were resistant to penicillin. CONCLUSIONS. Drug-resistant strains of S. pneumoniae are common among both children and adults in Atlanta. Although blacks had a higher incidence of invasive pneumococcal infections than whites, whites were more likely to be infected with a drug-resistant isolate. Control of drug-resistant pneumococci will require more judicious use of antimicrobial agents and wider use of the pneumococcal polysaccharide vaccine.

Hogardt M. et al. *Specific and rapid detection by fluorescent in situ hybridization of bacteria in clinical samples obtained from cystic fibrosis patients.* J Clin Microbiol. 2000; 38(2) : 818-25.p Abstract: We report on the rapid and specific detection of bacteria commonly isolated from clinical specimens from cystic fibrosis (CF) patients by fluorescent in situ hybridization (FISH). On the basis of comparative sequence analysis, we designed oligonucleotide probes complementary to species-specific 16S rRNA regions of these microorganisms and demonstrated the specificities of the probes by hybridization of different remotely related as well as closely related reference strains. Furthermore, in a pilot project we investigated 75 sputum samples and 10 throat swab specimens from CF patients by FISH and detected Pseudomonas aeruginosa, Burkholderia cepacia, Stenotrophomonas maltophilia, Haemophilus influenzae, and Staphylococcus aureus within these specimens. The specificity of FISH was 100% in comparison to the results of conventional microbial culture. In contrast, the sensitivity of standard laboratory cultivation was moderately higher, since the limit for microscopic detection of bacteria within sputum samples by FISH was approximately 4 x 10(5) CFU/ml of sputum (resulting in a 90% sensitivity for FISH). Moreover, we demonstrated that FISH will be useful for the rapid detection of bacteria that cause acute pulmonary exacerbations in CF patients, as demonstrated in patients with H. influenzae, S. aureus, and P. aeruginosa exacerbations. Therefore, FISH is a valuable additional method for the rapid and specific detection of bacteria in clinical samples from CF patients, in particular, patients with pulmonary exacerbations.

Hoi L. et al. *Evaluation of a simplified semi-quantitative protocol for the estimation of Vibrio vulnificus in bathing water using cellobiose-colistin agar: a collaborative study with 13 municipal food controlling units in Denmark*. J Microbiol Methods. 2000; 41(1) : 53-7.p Abstract: A simplified semi-quantitative method using pre-enrichment in alkaline peptone water supplemented with polymyxin B and plating onto cellobiose-colistin (CC) agar for the estimation of Vibrio vulnificus in bathing water was evaluated. This protocol was tested in a collaborative study with 13 food controlling laboratories in Denmark during the 1999 bathing season in periods when water temperatures exceeded 20 degrees C. The average percentage of yellow colonies larger than 1 mm in diameter on CC agar that could be identified as V. vulnificus by colony hybridization with a species-specific DNA probe was 79%. This high percentage of specificity demonstrated that by using CC agar in estimating the level of V. vulnificus in bathing water, recognition of yellow colonies larger than 1 mm is sufficient for the identification of V. vulnificus with no further characterization needed. The simplified protocol may be included in the routine control of the microbial quality of bathing water done by the local food controlling laboratories, since it involves simple traditional and low-cost microbiological methods with no use of molecular skills or sophisticated equipment.

Holanda M.A. et al. *Silicose em cavadores de poços: história natural, epidemiologia e medidas de controle.* J. pneumol. 1995; 21(1) : 27-33.p Abstract: A silicose em cavadores de poços temàse apresentado como grave problema de saΔde ocupacional, despertando, desde sua descoberta, em 1984, no Piauí, e em 1986, no Ceará, o interesse de médicos pneumologistas e de outras disciplinas não médicas com relação ao seu conhecimento e controle. No presente estudo, são abordados: a história natural da doença, apresentando peculiaridades próprias, pouco encontradas em outras atividades, como o processo primitivo de escavação de poços, os riscos aos quais os cavadores estão sujeitos, as caracterísiticas anatomopatológicas e a classificaçã do tipo acelerada quanto … forma de apresentação; os dados epidemiológicos que revelam prevalência de silicose e provável silicose em 180 (26,4 por cento) dos 687 cavadores examinados, prevalência de silicotuberculose em 13 (7,2 por cento) dos 180 diagnosticados e elevada freqência de óbitos, 34 (39,5 por cento) de 86 silicóticos diagnosticados entre 1986 e 1989. As medidas de controle que poderão ser capazes de interromper o ciclo natural da doença são discutidas (AU).

Holder I.A. et al. *Formulation of 'idealized' topical antimicrobial mixtures for use with cultured skin grafts.* J Antimicrob Chemother. 1996; 38(3) : 457-63.p Abstract: In order to develop antimicrobial mixtures which provide broad-spectrum antimicrobial activity for use with cultured cell autografts, several individual antimicrobial agents, in concentrations non-toxic for cells in culture, were tested against a variety of bacteria and Candida spp. isolated from burn patients. An agar well diffusion topical assay was used. Antimicrobials active against Gram-positive and Gram-negative bacteria and antifungal agents, individually, were uniformly effective against their respective spectra of organisms. Broad-spectrum antibacterials were uniformly effective against Gram-negative bacteria but their activity varied against Gram-positive bacteria. Adding an agent active against Gram-positive bacteria to all broad spectrum antibacterial agents conferred uniform Gram-positive activity to the mixture. One mixture consisting of specific Gram-negative, Gram-positive and broad spectrum antibacterial agents, was uniformly active against all bacteria tested and the addition of antifungal agents extended the activity to cover Candida spp. without interfering with the mixture's overall antibacterial activity. Another mixture showed either additive or antagonistic activities against the battery of microorganisms tested. Thus, these methods can be used to identify mixtures of antimicrobials, in concentrations non-toxic for cells in culture, that have very broad spectra of antimicrobial activity. Such mixtures should be evaluated in patients when cultured skin grafts are used.

Hollander R. et al. *[Microbiological public health aspects in the use of rain water as water reservoirs for toilet flushing, garden irrigation and laundry].* Gesundheitswesen. 1996; 58(5) : 288-93.p Abstract: From a total of 102 rain water cisterns in use for toilet flushing, garden irrigation and laundering washing about 1,600 water samples were collected and subjected to microbiological analysis. The assays included aerobic heterotrophic microorganisms growing at 20 and 37 degrees C, respectively, as well as the identification of Escherichia coli, coliform organisms, faecal streptococci, Pseudomonas aeruginosa, staphylococci, yersiniae, salmonellae, shigellae, legionellae and yeasts. The median of the total number of cells per ml was 1,200 at 20 degrees

C and 230 at 37 degrees C, respectively. Approximately 26 E. coli cells and 198 coliform organisms (median values) were found per 100 ml. In the case of cisterns manufactured of plastic the total number of cells was generally found to be lower than in samples collected from concrete or brick-made storage tanks. With the exception of the ubiquitously distributed organism Pseudomonas aeruginosa (found in 11.8% of the samples) and salmonella in only one sample, no other pathogens were detected. More than 95% of all analysed samples met the quality standards for bathing waters as set by the European Community. Provided certain precautions are taken, such as strict separation of mains for drinking water and rain water, as well as correct labelling of pipelines and collection sites, the use of rain water for toilet flushing, garden irrigation and laundry washing presents no unacceptable risk to public health.

Holloway J. et al. *Positive urine nitrite test: an accurate predictor of absence of pure enterococcal bacteriuria.* South Med J. 2000; 93(7) : 681-2.p Abstract: BACKGROUND: The aim of this study was to determine the potential ability of the urine nitrite test (NT) to predict the class of organism causing urinary tract infection. METHODS: We retrospectively reviewed the records of all adult patients with a positive urine culture over a 6-month period. The infecting microorganisms and the urine NT results were recorded. RESULTS: A total of 729 positive cultures met inclusion criteria. Twenty-one (11%) of the 190 gram-positive organisms and 199 (46%) of the 429 gram-negative organisms yielded a positive NT. Only 5.3% of samples with pure growth of enterococcus yielded a positive NT. The predictive value that a sample yielding a positive NT would show pure growth of enterococcus was low at 2.3%. CONCLUSION: A positive NT is highly predictive of the absence of pure enterococcal bacteriuria.

Holloway Y. et al. *Inexpensive 4-hour micro-agar dilution susceptibility determination method.* Antimicrob Agents Chemother. 1996; 40(12) : 2792-5.p Abstract: Using a micro-agar dilution (MAD) method in which microscope slides are covered with a thin film of agar, and MICs are read microscopically after a 4-h incubation, 18 antibiotics were tested against 29 to 32 microorganisms each. Identical MICs were obtained for microscopic MAD MICs performed in duplicate in 87.1% of the antibiotic-microorganism combinations, and 97.9% were identical within one dilution. When read macroscopically after an 18-h incubation, identical duplicate MICs were obtained in 86.8% of the cases, and 98.4% were identical within one dilution. Using agar dilution as the "gold standard," the correlation obtained with MAD slides read microscopically at 4 h was 94.3%, and macroscopic correlation at 18 h was 97.6%. The correlation of MAD slides with agar dilution for the groups of microorganisms most frequently used was as follows (microscopic/macroscopic): Staphylococcus aureus 96%/98%; Streptococcaceae 97%/98%; Enterobacteriaceae 98%/99%; and Pseudomonadaceae 95%/98%. At the present rate of exchange (fl 1.60 = $1.00f1p4he cost of a MAD slide, including labor, is $1.28 (20 microorganisms tested) or $0.06 per microorganism-antibiotic combination tested. This method is easy to perform, rapid, and inexpensive. It is suitable for use in routine and research laboratories.

Holm C. et al. *Intrathoracic blood volume as an end point in resuscitation of the severely burned: an observational study of 24 patients.* J Trauma. 2000; 48(4) : 728-34.p Abstract: BACKGROUND: Treatment of burn shock according to empirical resuscitation formulas is still considered the gold standard, and the burn community does not advocate the use of invasive cardiorespiratory monitoring in general. As a consequence, data dealing with early postburn hemodynamics are sparse, and only few studies have paid attention to the topic of end-point burn shock resuscitation. However, recent studies have suggested that burn survival may be improved when invasive monitoring is used to guide fluid therapy during the shock phase. MATERIALS AND METHODS: In an observational study of 24 patients with severe burns, the transpulmonary double indicator dilution technique was used for semi-invasive hemodynamic monitoring. The clinical utility of the intrathoracic blood volume (ITBV) as an end-point variable for fluid resuscitation was evaluated, comparing correlation of filling pressure obtained by a pulmonary artery catheter and intrathoracic blood volume to cardiac index and oxygen delivery. In addition fluid volume predicted by the Parkland burn formula was compared with the actual fluid volume given when ITBV was used as end point for resuscitation. RESULTS: ITBV-guided resuscitation was associated with restoration of preload and peripheral delivery of oxygen within 24 hours in the majority of patients. Augmentation of ITBV was significantly correlated with changes in cardiac index and oxygen transport rate. No such correlation could be demonstrated for the conventional preload parameters such as central venous pressure and pulmonary capillary wedge pressure. Thus, ITBV seemed in burned, hypovolemic patients a better indicator of the preload component of the cardiac output than the conventional preload parameters obtained with the pulmonary artery catheter. Significantly larger volumes of crystalloids than predicted by the Parkland formula were administered when ITBV was used as end point for resuscitation. The extravascular lung water remained normal during this extraordinary high volume load. CONCLUSION: ITBV may be a reliable preload indicator to guide volume therapy in life-threatening burns, and end-point-fixed resuscitation to this parameter seems to be associated with significantly higher fluid administration than calculated compared with traditional burn formulas. The effects of burn resuscitation to fixed end points on survival and multiple organ failure should be evaluated in future randomly assigned trials.

Holmes A.R. et al. *Binding properties of Streptococcus gordonii SspA and SspB (antigen I/II family) polypeptides expressed on the cell surface of Lactococcus lactis MG1363.* Infect Immun. 1998; 66(10) : 4633-9.p Abstract: The oral bacterium Streptococcus gordonii expresses two cell wall-associated polypeptides, designated SspA (1,542 amino acid residues) and SspB (1,462 amino acid residues), that have 70% sequence identity. These polypeptides are members of the antigen I/II family of oral streptococcal adhesins and mediate the binding of streptococci to salivary glycoproteins, collagen, and other oral microorganisms such as Actinomyces naeslundii. To determine if SspA and SspB have differential binding properties, the coding sequences of the sspA and sspB genes were cloned into expression plasmid vector pTREX1-usp45LS to generate pTREX1-sspA and pTREX1-sspB, respectively, and the Ssp polypeptides were displayed on the cell surface of Lactococcus lactis MG1363. Lactococcal cells expressing similar levels of surface SspA or SspB polypeptide were then compared for their abilities to adhere to a range of antigen I/II polypeptide substrates. More than twice as many L. lactis cells expressing SspA bound to immobilized salivary agglutinin glycoprotein (SAG) as did L. lactis cells expressing SspB. In contrast, lactococci expressing SspB adhered twice as well as lactococci producing SspA to collagen type I and to Candida albicans. The binding of A. naeslundii to lactococci was only weakly enhanced by surface expression of Ssp polypeptides. L. lactis(pTREX1-sspB) cells bound in greater numbers to SAG than did Enterococcus faecalis JH2-2 cells expressing SspB from pAM401EB-5. The results suggest that SspA and SspB have markedly different binding affinities for their oral substrates and thus may function to promote site diversity in colonization by S. gordonii.

Holt D.E. et al. *The myelotoxicity of chloramphenicol: in vitro and in vivo studies: I. In vitro effects on cells in culture.* Hum Exp Toxicol. 1997; 16(10) : 570-6.p Abstract: 1 Chloramphenicol is used extensively in non-industrialized countries for the treatment of life-threatening infections because it is cheap and effective, despite its known hemotoxicity and linkage to fatal aplastic anaemia. It is important to define the mechanism of toxicity so that means can be devised to ameliorate the toxic effects in order to produce safer usage. 2 Chloramphenicol, at concentrations from 5 mM to 2 mM initiated apoptosis in dividing cells from a monkey kidney-derived cell line and in haematopoietic progenitor cells from human neonatal cord blood. 3 Growth of progenitor cells was suppressed at concentrations of chloramphenicol

which would be considered less than therapeutic during patient treatment. 4 These effects could be ameliorated in progenitor cells by co-culture with the antioxidant mercaptoethylamine and in monkey kidney cells by co-culture with vitamin C. 5 This is the first report of apoptosis in chloramphenicol toxicity and suggests a possible link between a metabolic event i.e. the production of free radicals; a morphological effect, apoptosis; and a clinical effect, bone marrow suppression and aplastic anaemia.

Holt H.M. et al. *Infections following epidural catheterization.* J Hosp Infect. 1995; 30(4) : 253-60.p Abstract: Seventy-eight patients with culture-positive epidural catheters, were studied. Fifty-nine had symptoms of exit site infection and 11 patients had clinical meningitis, two of whom also had an epidural abscess. This corresponds to a local infection incidence of at least 4.3% and an incidence of central nervous system infection of at least 0.7% at Odense University Hospital. This degree of infection is of the same magnitude as that reported for intravascular devices. We found that the patients with generalized symptoms of infection had been catheterized for a longer time, and were older than patients with only local symptoms of infection. The microorganisms isolated from the tips of the epidural catheters were coagulase-negative staphylococci (41%), Staphylococcus aureus (35%), Gram-negative bacilli (14%) and others (10%). The Gram-negative bacilli and S. aureus caused serious infections more frequently than the others. We discuss the symptoms and diagnosis of spinal epidural abscess and suggest a proposal for prophylactic and diagnostic guidelines for epidural catheter-related infections.

Holt H.M. et al. *[Infections in connection with epidural catheterization].* Ugeskr Laeger. 1996; 158(31) : 4403-5.p Abstract: Seventy-eight patients with culture-positive epidural catheters were studied. Fifty-nine had symptoms of exit site infection and 11 patients had clinical meningitis, two of whom also had en epidural abscess. This corresponds to a local infection incidence of at least 4.3% and an incidence of central nervous system infection of at least 0.7% at Odense University Hospital. The patients with generalized symptoms of infection had been catheterized for a longer time, and were older than patients with only local symptoms of infection. The microorganisms isolated from the epidural catheters were coagulase- negative staphylococci (41%), Staphylococcus aureus (35%), Gram-negative bacilli (14%) and other bacteria (10%). The Gram-negative bacilli and S. aureus caused serious infections more frequently than the others. We discuss the symptoms and diagnosis of spinal epidural abscess and propose prophylactic and diagnostic guidelines for epidural catheter-related infections.

Honderlick P. et al. *[Microbiological diagnosis of bacteremia from a catheter: a simple method? Results of a retrospective study].* Pathol Biol (Paris). 2000; 48(5) : 467-9.p Abstract: Diagnosing catheter-related bloodstream infections is important but not always easy and a failure to make the diagnosis may have serious consequences. A high rate of unnecessary catheter removal is noted. We retrospectively compared the clinical and usual methods of microbiological diagnoses of catheter-related sepsis to the speed of detection of the catheter versus peripheral blood cultures using the Bact-Alert system. We analyzed 50 files of patients with central indwelling devices: 16 single lumen catheters and 34 implanted ports. Twenty-one catheters were classified as infected, and we observed an earlier positivity of catheter versus peripheral blood in all cases, but significant for 19 patients. According to standard diagnosis methods, 29 catheters were estimated non-infected, a more rapid detection of peripheral culture was reported for 17 specimens and, for another eight patients, the time of detection was equal to blood culture drawn from the catheter. In this group, four discrepancies were recorded with a differential time in favor of sepsis related to catheters ranging from 0.5 to 2 hours. Because of its simplicity and low cost, we believed that this method could be the first step of a diagnosis of catheter-related sepsis and could, therefore, avoid unjustified removal, in particular for the implanted ports for which the diagnostic methods are less codified than for catheters. A prospective study is ongoing; the design of the study focuses only on implanted ports.

Hong J. et al. *Structure and organization of hemolytic and nonhemolytic diastereomers of antimicrobial peptides in membranes.* Biochemistry. 1999; 38(51) : 16963-73.p Abstract: Recently, we reported on a new group of diastereomers of short-model peptides (12 amino acids long) composed of leucine and lysine with varying ratios, possessing several properties that make them potentially better than native or de novo-designed all L-amino acid antimicrobial peptides. Preliminary studies have revealed that modulating the hydrophobicity and positive charges of these diastereomers is sufficient to confer antibacterial activity and cell selectivity. However, the relationship between their biological function, structure, and mode of action was not investigated. Here we synthesized and investigated three types of linear model diastereomers (12 amino acids long) with varying lysine:leucine (or tryptophan) ratios (i.e., K(3)L(8)W, K(5)L(6)W, and K(7)L(4)W), which confer different levels of lytic activities. For each K:L ratio, tryptophan was introduced in the middle or the N- or C-terminus of the peptides, as an intrinsic fluorescent probe. Only the hemolytic peptide K(3)L(8)W binds to both negatively charged and zwitterionic phospholipid membranes. K(5)L(6)W and K(7)L(4)W bind similarly, but only to negatively charged membranes, despite the fact that K(5)L(6)W is substantially more lytic to bacteria than K(7)L(4)W. Interestingly, although K(3)L(8)W contains 33% D-amino acids, ATR-FTIR spectroscopy revealed a structure of approximately 90% alpha-helix in both types of membranes. In addition, K(5)L(6)W contains approximately 40% 3(10)-helix and K(7)L(4)W is predominantly a random coil in membranes. Polarized ATR-FTIR and tryptophan-quenching experiments, using brominated phospholipids, revealed a similar depth of penetration and an orientation that was parallel to the membrane surface for all the peptides, but with K(3)L(8)W affecting the lipid order more than the others. The results provide insight into the mode of action of this group of diastereomeric peptides, and the effect of hydrophobicity and positive charges on their membrane structure, function, and cell selectivity. Moreover, this research should assist in the development of suitable diastereomeric peptide antibiotics for therapeutic use that would overcome the problem the increasing resistance of bacteria to conventional antibiotics.

Hood S.K. et al. *Adherence to stainless steel by foodborne microorganisms during growth in model food systems.* Int J Food Microbiol. 1997; 37(2-3) : 145-53.p Abstract: Biofilm formation on stainless steel by Salmonella typhimurium, Listeria monocytogenes, Escherichia coli O157:H7, Pseudomonas fragi and Pseudomonas fluorescens during growth in model food systems was studied. Test growth media included tryptic soy broth (TSB), diluted TSB (dTSB), 1% reconstituted skim milk (RSM) and diluted meat juice (DMJ). Adherent cells were stained with acridine orange and enumerated using epifluorescent microscopy and computerized image analysis. Cells were observed on the stainless steel surface after 1 h in all of the media. However, the increases in the number of adherent cells over time was seen only with S. typhimurium in DMJ, E. coli O157:H7 in TSB, dTSB and DMJ, P. fragi in RSM and P. fluorescens in RSM. The medium which produced the highest observed level of adherent cells was different for each microorganism.

Hoogkamp-Korstanje J.A. et al. *Comparative in vitro activity of moxifloxacin against Gram-positive clinical isolates.* J Antimicrob Chemother. 2000; 45(1) : 31-9.p Abstract: The in vitro activity of moxifloxacin was compared with that of 15 antibacterial agents against 513 Gram-positive microorganisms. The MIC(90) (mg/L) of moxifloxacin was 0.06 for quinolone-susceptible Staphylococcus aureus and Staphylococcus epidermidis, 0.12 for Streptococcus pyogenes and Streptococcus agalactiae; 0.25 for Streptococcus pneumoniae, Streptococcus mitis, Streptococcus bovis, Streptococcus anginosus and Actinomyces pyogenes; 0.5 for Streptococcus sanguis and

Listeria monocytogenes, 2 for Corynebacterium jekeium and Bifidobacterium bivius. Over 50% of Enterococcus faecalis, Enterococcus faecium, quinolone-resistant staphylococci, Nocardia steroides and Clostridium difficile were susceptible to 2 mg/L moxifloxacin. Moxifloxacin and trovafloxacin demonstrated comparably high activity towards Gram-positive cocci; moxifloxacin and clinafloxacin were most active against Gram-positive bacilli.

Hooke C. *Recombinant tissue plasminogen activator for central venous access device occlusion.* J Pediatr Oncol Nurs. 2000; 17(3) : 174-8.p Abstract: Maintaining and restoring the function of central venous access devices (CVAD) is an important component of pediatric oncology nursing care. Until 1999, Abbokinase Open Cath (urokinase; Abbott, Abbott Park, IL), a thrombolytic agent was the product primarily used to resolve thrombotic occlusions in intravascular devices. Changes in the manufacturing process mandated by the FDA have resulted in a lack of availability of Abbokinase Open Cath. Recombinant tissue plasminogen activator (TPA) has provided an alternative solution for clearing occluded intravascular devices. This article reviews the literature supporting the use of TPA for CVAD clearance and discusses the process of how to administer the medication. Future implications for research about the use of TPA, and its role in the care of CVADs are discussed.

Hoosen A.A. et al. *Sexually transmitted diseases including HIV infection in women with Bartholin's gland abscesses.* Genitourin Med. 1995; 71(3) : 155-7.p Abstract: OBJECTIVES—The aim of this study was to establish the prevalence of sexually transmitted infections including human immunodeficiency virus (HIV) infection in women with Bartholin's gland abscess. SETTING—Gynaecology Clinic of King Edward VIII Hospital, a large urban, referral hospital for the province of Kwa-Zulu Natal, serving an underprivileged population. METHODS—Thirty consecutive women presenting with unruptured Bartholin's gland abscesses were studied. Prior to surgical drainage, aspirates from the abscess cavity and swab specimens from the vagina and endocervix were collected for microbiological investigations. In addition peripheral venous blood samples were obtained for syphilis and HIV antibody testing. RESULTS—Antibody to HIV was detected in 9 of the 30 (30%) patients studied. Recognised sexually transmitted pathogens were detected in both aspirates and endocervical specimens: Chlamydia trachomatis was detected in 3 aspirate and 2 endocervical specimens whilst Neisseria gonorrhoeae was cultured in 5 aspirate and 7 endocervical specimens. When comparing microorganisms isolated from HIV antibody positive and negative women, only Bacteroides species yielded a significantly higher growth ($p = 0.01$) in the antibody positive women. CONCLUSION—Our findings show that women with Bartholin's gland abscesses have a high prevalence of HIV antibody. Furthermore, this is the only study that demonstrates a role for C trachomatis in the aetiology of Bartholin's gland abscesses. Health workers should be aware of the need for appropriate counselling, and comprehensive treatment of sexually transmitted infections including C trachomatis in women with Bartholin's gland abscesses.

Hooton T.M. et al. *Diagnosis and treatment of uncomplicated urinary tract infection.* Infect Dis Clin North Am. 1997; 11(3) : 551-81.p Abstract: Acute uncomplicated urinary tract infection is one of the most common problems for which young women seek medical attention and accounts for considerable morbidity and health care costs. Acute cystitis or pyelonephritis in the adult patient should be considered uncomplicated if the patient is not pregnant or elderly, if there has been no recent instrumentation or antimicrobial treatment, and if there are no known functional or anatomic abnormalities of the genitourinary tract. Most of these infections are caused by E. coli, which are susceptible to many oral antimicrobials, although resistance is increasing to some of the commonly used agents. Review of the published data suggests that a 3-day regimen is more effective than a single-dose regimen for all antimicrobials tested. Regimens with trimethoprim-sulfamethoxazole seem to be more effective than those with beta lactams, regardless of the duration. Because of increasing resistance to trimethoprim-sulfamethoxazole, an alternative regimen such as nitrofurantoin (in a 7-day regimen), a fluoroquinolone, or an oral third-generation cephalosporin may be a better empiric choice in some areas. Acute pyelonephritis caused by highly virulent uropathogens in an otherwise healthy woman may be considered an uncomplicated infection. The optimal treatment duration for acute uncomplicated pyelonephritis has not been established, but 10- to 14-day regimens are recommended. We prefer to use antimicrobials that attain high renal tissue levels, such as a fluoroquinolone, trimethoprim-sulfamethoxazole, or an aminoglycoside, for pyelonephritis. Acute uncomplicated cystitis or pyelonephritis in healthy adult men is uncommon but is generally caused by the same spectrum of uropathogens with the same antimicrobial susceptibility profile as that seen in women.

Hopkins B. et al. *Reducing nosocomial pressure ulcers in an acute care facility.* J Nurs Care Qual. 2000; 14(3) : 28-36.p Abstract: In 1996, a nursing committee at an acute care facility organized the first pressure ulcer point prevalence survey for that hospital. In 1996, hospital-acquired pressure ulcers were 90 percent of the predicted prevalence rate; in 1997, the rate dropped to 59 percent of the predicted prevalence and in 1998, to 53 percent of the predicted prevalence. The severity index decreased markedly from 291 (1996) to 98 (1997) then to 62 (1998). These improvements are attributed to the purposeful addition of multidimensional interventions, including best practices and research-based protocols, to prevent and treat nosocomial pressure ulcers.

Hopkins R.J. *Current FDA-approved treatments for Helicobacter pylori and the FDA approval process.* Gastroenterology. 1997; 113(6 Suppl) : S126-30.p Abstract: U.S. Food and Drug Administration (FDA) approval of new drugs expands treatment options and serves as a "safety net" of well-documented efficacy and safety. The information provided in the package insert facilitates physician education and provides some assurance that marketing information is accurate. As of February 1997, three Helicobacter pylori regimes have been FDA-approved for eradication of H. pylori in infected patients with active duodenal ulcers. Regimen 1, omeprazole + clarithromycin (O/C), was supported by two multicenter, controlled studies with a 6-month follow-up. Eradication rates were 74% (n = 53; 95% confidence interval [CI], 62-85) and 64% (n = 61; 95% CI, 52-76). Twenty-five of 26 patients with failed eradication therapy who were taking O/C with clarithromycin-susceptible strains before treatment and who had pretreatment and posttreatment susceptibility tests performed developed clarithromycin resistance after treatment. Regimen 2, ranitidine-bismuth-citrate + clarithromycin, was supported by two multicenter, placebo-controlled studies with a 6-month follow-up. Eradication rates were 84% (n = 19; 95% CI, 60-96) and 73% (n = 22; 95% CI, 50-88). Insufficient pretreatment and posttreatment susceptibility data were collected to assess antimicrobial resistance. Regimen 3, bismuth subsalicylate + metronidazole + tetracycline + an H2-receptor antagonist, was supported by two pivotal literature-based studies. Eradication rates in patients with duodenal ulcer were 82% (n = 51; 95% CI, 70-92) and 77% (n = 39; 95% CI, 61-89), respectively. When extrapolating the results of these three FDA-approved regimens to the clinical setting, particular aspects of the clinical trial should be kept in mind. These include the type of controls, primary end points used, population studied, and number and type of dropouts.

Hoppe H.L. et al. *Otitis media: focus on antimicrobial resistance and new treatment options.* Am J Health Syst Pharm. 1998; 55(18) : 1881-97; quiz 1932-3.p Abstract: Antimicrobial resistance among organisms that cause acute otitis media (AOM) and new approaches in the prevention and treatment of AOM are discussed. Organisms commonly responsible for causing AOM include Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis. The evolution of pneumococcal resistance to penicillins, erythromycin, trimetho-

prim-sulfamethoxazole, and oral cephalosporins may require treatment with agents such as vancomycin or rifampin in certain patients. H. influenzae and M. catarrhalis are becoming increasingly resistant to penicillins, trimethoprim-sulfamethoxazole, oral cephalosporins, and macrolides. Mechanisms of resistance include changes in penicillin-binding proteins, production of beta-lactamase, alterations in target enzymes, and inhibition of drug access to the site of action. Because of changing resistance patterns and the limited spectra of activity of many currently available antimicrobials, new antimicrobials have been developed in the hope of improving therapy. While amoxicillin and trimethoprim-sulfamethoxazole are appropriate first-line agents, children at risk for resistant infections may be treated initially with cefuroxime axetil, cefpodoxime proxetil, cefprozil, or amoxicillin-clavulanate. After local resistance patterns, patient adherence to therapy, in vitro data, and cost factors have been weighed, other agents to consider include loracarbef, clarithromycin, azithromycin, and ceftriaxone. Along with the efforts to improve treatment, research is focusing on the prevention of otitis media with bacterial and viral vaccines. The emergence of resistant strains of organisms causing AOM has complicated its treatment.

Hordnes K. et al. *[What is the purpose of mucosal antibodies? Relevance to colonization with group B streptococci].* Tidsskr Nor Laegeforen. 1997; 117(28) : 4109-13.p Abstract: The surface area of the mucosae is extremely large and its contact with the external environment is of vital importance. Most infectious agents use the mucosae as their portal of entry. Some microorganisms, however, colonize the mucosal surfaces without causing disease, and may even be beneficial by contributing to the digestion of food or by excluding pathogens. An important part of the immune system operates in the mucosae, the principal mediator substance of this local immune system being secretory IgA. Other antibody isotypes are usually found in small amounts in exocrine fluids, but IgG predominates in secretions of the uterine cervix. These mucosal antibodies may eliminate microbes, or they may coexist with persistent colonization. In a recent study, we found increased levels of IgA and IgG antibodies to group B streptococci in the cervical secretions of women colonized with these bacteria. Group B streptococci are often transmitted to the infant during delivery, and are a major cause of severe infection in newborns. We have used this study as a background for discussing the role of mucosal antibodies. Presumably, group B streptococci may be eradicated by reenforcing the local antibody response, and a mucosal vaccine will be evaluated in the near future.

Horowitz M.B. et al. *The use of stents in the management of neurovascular disease: a review of historical and present status.* Neurosurgery. 2000; 46(6) : 1335-42; discussion 1342-3.p Abstract: In the mid-1960s, radiologists began experimenting with stents for use in the peripheral vasculature in the hope of treating vascular insufficiency resulting from vessel stenosis in a nonsurgical manner. The 1990s saw stents move into the neurovascular arena for the management of a variety of disease processes, including arterial and venous sinus stenosis, arterial dissection, arterial aneurysms, and arteriovenous fistulae. This article reviews the current status of stenting in regard to the management of neurovascular maladies.

Hortal M. et al. *Ten-year review of invasive pneumococcal diseases in children and adults from Uruguay: clinical spectrum, serotypes, and antimicrobial resistance.* Int J Infect Dis. 2000; 4(2) : 91-5.p Abstract: OBJECTIVES: Since 1987, the Reference Laboratory of the Ministry of Health of Uruguay has been monitoring infections due to Streptococcus pneumoniae in patients under 5 years of age, in those between 5 to 14 years of age, and in adults. The purpose of the present study was to retrospectively analyze a 10-year collection of invasive S. pneumoniae isolates from children 5 to 14 years of age and adults. METHODS: The Reference Children's Hospital, Pasteur Hospital, and two private hospitals in Montevideo as well as four hospitals located in other representative areas of the country participated in the pneumococcal surveillance program. Based on the information available at the Microbiology Department of the Central Public Health Laboratory (demographic data, date and site of isolate, and clinical diagnosis), all patients with an invasive pneumococcal disease were recorded. Pneumonia was clinically and radiologically diagnosed and etiology was assessed by isolation of S. pneumoniae from blood or pleural fluid. All specimens were collected at the Emergency Service. Capsular serotyping and antimicrobial susceptibilities were determined for each isolate. RESULTS: During the 10-year period, 228 invasive S. pneumoniae were identified and included in the study (blood, n = 129; cerebrospinal fluid [CSF], n = 73; pleural fluid, n = 20; peritoneal fluid, n = 3; synovial fluid, n = 1; pericardic fluid, n = 1; abscess, n = 1). The most frequent clinical presentations were pneumonia (n = 71) and meningitis (n = 69). Thirty-five adults had an underlying condition including, four with malignancies, four with lupus, two with human immunodeficiency virus (HIV)-infected, and two patients in hemodialysis among others. Eighteen of the 228 patients died (7.9% fatality rate), but only four of these had an underlying condition. Eleven fatal cases were attributable to meningitis (2 children, 9 and 11 years old; 9 adults, mean age, 59 y). Four patients with pneumonia and three with sepsis died, including a splenectomized woman. Nine different capsular serotypes (1, 5, 7, 9, 12, 15, 19A, 20, and 23A) were identified among the 18 fatal cases. Resistance to penicillin, generally combined with trimethoprim-sulfamethoxazole, fluctuated annually, not surpassing 10%. CONCLUSIONS: The study results indicated that 96% of the serotypes involved in severe pneumococcal diseases were included in the 23-valent vaccine and that S. pneumoniae resistance to penicillin was moderate.

Horvath R. et al. *[Detection of DNA specific for Mycobacterium tuberculosis in archeological material using the polymerase chain reaction].* Epidemiol Mikrobiol Imunol. 1997; 46(1) : 9-12.p Abstract: The paleopathological diagnosis of bone tuberculosis in archeological findings may be confirmed by the polymerase chain reaction (PCR). If the M. tuberculosis-specific DNA fragment is amplified, then the presence of this microorganism in the sample is demonstrated. The pilot study presented investigated whether our molecular biology laboratory can collaborate with anthropologists in paleopathological analyses and to verify the use of the commercial diagnostic kit Cleanmix (Talent, Italy), for DNA isolation from archeological samples. The results were compared with the conclusions of anthropologists. Successful amplification of specific DNA fragments was achieved in a specimen from the period of the 13th to 15th century. The specimen consists of four thoracic vertebrae modified by osseous tuberculosis (gibbus). The PCR result was also positive in a five-year-old femur sample of a patient with chronic pulmonary tuberculosis. All other specimens of various ages but without macroscopic symptoms of osseous tuberculosis, were PCR negative. These results suggest that it is possible to detect former infections with pathogenic microorganisms in archeological bones find.

Horvathova Z. et al. *Bacteremia due to methicillin-resistant staphylococci occurs more frequently in neutropenic patients who received antimicrobial prophylaxis and is associated with higher mortality in comparison to methicillin-sensitive bacteriemia.* Int J Antimicrob Agents. 1998; 10(1) : 55-8.p Abstract: Bacteriemia due to coagulase-negative staphylococci (CNS) resistant to methicillin and sensitive only to glycopeptides in 220 cancer patients was prospectively analyzed for risk factors and outcome. A group of 33 cases of bacteriemia with CNS-sensitive only to glycopeptides was compared with a group of 187 cases with CNS sensitive to methicillin. All cases appeared in two affiliated major cancer institutes in Bratislava with the same antibiotic policy. Univariate analysis showed differences in recorded risk factors: acute leukemia (48 vs. 33%, $P < 0.05$), neutropenia (57 vs. 32%, $P < 0.045$), previous prophylaxis with quinolones (30 vs. 11%, $P < 0.01$) and penicillin-V (15 vs. 3%, $P < 0.02$) and previous colonisation with CNS (27 vs. 3%, $P < 0.01$) were more frequently associated with bacteriemia resistant to methicillin and sensitive only to glycopeptides. Attributable mortality was also higher in this subgroup in

comparison to bacteriemias with CNS sensitive to methicillin (12 vs. 3%, P < 0.05) however, overall mortality was similar. Bacteriemias due to CNS caused by sensitivity only to glycopeptides occurred more frequently in neutropenic patients (1), with acute leukemia (2), receiving quinolone and penicillin prophylaxis (3), and previously colonized (4), patients and had worse prognosis in comparison to those with methicillin-sensitive staphylococcal bacteriemias.

Hoshino K. et al. *[Antimicrobial activity of macrolides against clinical isolates].* Jpn J Antibiot. 1998; 51(4) : 249-71.p Abstract: Antimicrobial activity of 6 macrolides was determined using a micro-broth dilution method, against 535 clinical isolates of 22 species, which were isolated in 1996 from 325 facilities in Japan. Results were as follows. 1. In general, antimicrobial activities of 14-membered macrolides were higher than those of 16-membered macrolides. The antimicrobial activities of 14-membered macrolides were in the order of clarithromycin (CAM), erythromycin (EM), roxithromycin (RXM). Among 16-membered macrolides, rokitamycin (RKM) was the most potent, josamycin (JM) was next potent followed by midecamycin (MDM). More numbers of highly-resistant strain of > 100 micrograms/ml were recognized in 14-membered macrolides than in 16-membered macrorides. 2. Most of S. pyogenes (group A) strains were distributed in the susceptible range and almost none was found in the resistant range. 3. S. pneumoniae strains were distributed widely from the susceptible range to the highly resistant range, and as high as 37.1% fell into the high resistance of > 100 micrograms/ml range. 4. Against Peptostreptococcus spp. and MRSA, 16-membered macrolides were more effective than 14-membered macrorlides, and their antibacterial activities were in the order of RKM, JM, MDM. Ratio of high-resistant strains of > 100 micrograms/ml against 14-membered macrolides was much higher than that against 16-membered macrolies. 5. Most of M. (B.) catarrhalis strains were distributed in the susceptible range of < or = 1.56 micrograms/ml, and most of H. influenzae strains were distributed within the moderately resistant and the resistant ranges. 6. In M. (B.) catarrhalis and H. influenzae, no correlation between macrolide resistance and beta-lactamase production was recognized. 7. Most of C. jejuni strains were susceptible to all macrolides used in this study.

Houben M.H. et al. *A systematic review of Helicobacter pylori eradication therapy—the impact of antimicrobial resistance on eradication rates.* Aliment Pharmacol Ther. 1999; 13(8) : 1047-55.p Abstract: BACKGROUND: We systematically reviewed all available data in the literature to determine the overall eradication rates of currently advised Helicobacter pylori eradication regimens and to resolve conflicting evidence on the impact of antimicrobial resistance on the eradication rates. METHODS: A comprehensive search of all published trials on H. pylori eradication therapy was carried out via an electronic database search, hand-searching and checking reference lists of pharmaceutical companies and other reviews. Full papers and abstracts in the English language which study currently advised eradication regimes were included. RESULTS: 770 study-arms were analysed. Mean eradication rates for bismuth based triple, proton pump inhibitor triple, quadruple and ranitidine bismuth citrate combination therapies vary from 65 to 92%. In case of nitroimidazole resistance, a drop in efficacy of up to 50% was found for bismuth-based triple and proton pump inhibitor-based triple therapies. For quadruple therapy, a significant difference in efficacy was found in the equal-effects analysis; however, this could not be confirmed in the random-effects analysis. In case of clarithromycin resistance, a mean drop in efficacy of 56% was found for one- and two-week clarithromycin containing proton pump inhibitor-triple therapies and of 58% for two-week ranitidine bismuth citrate combined with clarithromycin therapies. For ranitidine bismuth citrate combined with clarithromycin and nitroimidazole, no difference in efficacy was found in case of nitroimidazole or clarithromycin resistance, but data are still scarce. CONCLUSIONS: The cure rate with most regimens dropped significantly, in case of nitroimidazole-resistant strains, compared to nitroimidazole-susceptible strains. In case of clarithromycin resistance, the efficacy of most regimens is also decreased; however, data are still scarce. These data should allow physicians to make a better choice of an appropriate therapy for their patients.

Houndt T. et al. *Long-term shifts in patterns of antibiotic resistance in enteric bacteria.* Appl Environ Microbiol. 2000; 66(12) : 5406-9.p Abstract: Several mechanisms are responsible for the ability of microorganisms to tolerate antibiotics, and the incidence of resistance to these compounds within bacterial species has increased since the commercial use of antibiotics became widespread. To establish the extent of and changes in the diversity of antibiotic resistance patterns in natural populations, we determined the MICs of five antibiotics for collections of enteric bacteria isolated from diverse hosts and geographic locations and during periods before and after commercial application of antibiotics began. All of the pre-antibiotic era strains were susceptible to high levels of these antibiotics, whereas 20% of strains from contemporary populations of Escherichia coli and Salmonella enterica displayed high-level resistance to at least one of the antibiotics. In addition to the increase in the frequency of high-level resistance, background levels, conferred by genes providing nonspecific low-level resistance to multiple antibiotics, were significantly higher among contemporary strains. Changes in the incidence and levels of antibiotic resistance are not confined to particular segments of the bacterial population and reflect responses to the increased exposure of bacteria to antimicrobial compounds over the past several decades.

Howden C.W. *Use of proton-pump inhibitors in complicated ulcer disease and upper gastrointestinal tract bleeding.* Am J Health Syst Pharm. 1999; 56(23 Suppl 4) : S5-11.p Abstract: The use of proton-pump inhibitors in the management of complicated peptic ulcer disease and upper gastrointestinal bleeding is described. Treatment of peptic ulcers in patients who are Helicobacter pylori positive should include antimicrobial therapy to eradicate the infection; based on considerations of primary antimicrobial resistance and safety, one recommended regimen is the combination of a proton-pump inhibitor (lansoprazole 30 mg or omeprazole 20 mg), clarithromycin 500 mg, and amoxicillin 1 g, each twice daily for 14 days. The proportion of H. pylori-negative ulcers has increased in the United States, now accounting for 39% of patients with ulcers who report no intake of nonsteroidal anti-inflammatory drugs (NSAIDs). Compared with H. pylori-positive ulcers, H. pylori-negative ulcers are more aggressive, characterized by high recurrence rates and increased risk of bleeding and perforation. Long-term therapy with a proton-pump inhibitor may be useful in these patients. Acid suppressants may also have a role in the initial treatment of patients who have a bleeding ulcer, including those associated with NSAID use. For patients who require continuous NSAID therapy, proton-pump inhibitors have been shown to heal a significantly higher percentage of peptic ulcers in eight weeks than histamine H2-receptor antagonists, and maintenance therapy with either lansoprazole or omeprazole reduces ulcer recurrence. Preliminary data suggest a role for proton-pump inhibitors in the prevention of stress ulcers among critically ill patients. Proton-pump inhibitors play an important role in the treatment of both H. pylori-negative and H. pylori-positive peptic ulcers, as well as in upper gastrointestinal tract bleeding. Further study is needed regarding their role in preventing stress ulcers in critically ill patients.

Howe R.A. et al. *Cotrimoxazole. Rationale for re-examining its indications for use.* Drug Saf. 1996; 14(4) : 213-8.p Abstract: Trimethoprim was specifically developed in the late 1960s as a sulphonamide potentiator and was launched in combination with sulfamethoxazole as cotrimoxazole. Laboratory data showed synergy of antimicrobial action for the combination and suggested that the use of both agents would delay the emergence of resistance. However, the tissue distribution of trimethoprim and sulfamethoxazole does not favour synergy, and resistance among common pathogens to sulfamethoxazole is high. Clinical studies comparing trimethoprim alone with cotrimoxazole

for the treatment of respiratory tract and urinary tract infections have failed to show any benefit from the combination. The development of delayed resistance by use of the combination has not been substantiated. The common adverse effects seen with cotrimoxazole are gastrointestinal disturbances and skin rashes which are well described adverse effects of sulphonamides. Comparative studies suggest that these are less common with trimethoprim alone. Serious adverse effects such as liver disorders and Stevens-Johnson syndrome appear more common with cotrimoxazole. Where there is little evidence for benefit from the use of the combination, the exposure of patients to the additional risk from the adverse effects and drug interactions of 2 drugs cannot be justified. Therefore use of cotrimoxazole should be restricted to those situations such as Pneumocystis carnii pneumonia where the combination has been shown to be beneficial.

Howe R.A. et al. *Expression and detection of hetero-vancomycin resistance in Staphylococcus aureus.* J Antimicrob Chemother. 1999; 44(5) : 675-8.p Abstract: Isolates of Staphylococcus aureus resistant to vancomycin have been reported but appear to be extremely rare. However, isolates displaying hetero-resistance to vancomycin (hVRSA) are reportedly common in parts of Japan (9.3% of MRSA isolated from a group of university hospitals). We have investigated the reliability of the proposed method for detection of hetero-resistant isolates and the ability of clinical S. aureus isolates to express vancomycin resistance. The original method for identification of hVRSA was found to have poor reproducibility and may select for, rather than detect, vancomycin resistance. There appears to be a spectrum of heterogeneity in the expression of resistance to vancomycin among S. aureus. Until there is a clearer understanding of the mechanism and control of vancomycin resistance in S. aureus, and reliable tests are devised, the clinical relevance of different degrees of hetero-resistance cannot be assessed.

Hoyos A. et al. *[Pattern of antimicrobial susceptibility of enterococci strains].* Rev Med Chil. 1995; 123(4) : 473-8.p Abstract: Enterococci resistance to antimicrobials has increased lately. We studied the susceptibility to 12 antimicrobials of 150 enterococci strains coming from hospitalized and outpatients, using the agar dilution method. Teicoplanin, followed by imipenem and amoxicilin-clavulanic acid had the lower minimal inhibitory concentrations. No strains of E faecalis was resistant to ampicillin, whereas 14% of E faecium had minimal inhibitory concentrations over 8 micrograms/ml. The high minimal inhibitory concentrations of cefpirome (64 micrograms/ml) renders this antimicrobial useless in the treatment of enterococcal infections. Betalactamase production and resistance to glucopeptides were not detected. Antimicrobial susceptibility of strains coming for hospitalized or outpatients were similar.

Hoyos L. A. et al. *Patrón de susceptibilidad a los antimicrobianos de cepas de enterococos.* Rev. méd. Chile. 1995; 123(4) : 473-8.p Abstract: Enterococci resistance to antimicrobials has increased lately. We studied the susceptibility to 12 antimicrobials of 150 enterococci strains coming from hospitalized and outpatients, using the agar dilution method. Teicoplanin, followed by imipenem and amoxicilin-clavulanic acid had the lower minimal inhibitory concentrations. No strains of E faecalis was resistant to ampicillin, whereas 14 percent of E faecium had minimal inhibitory concentrations over 8 æg/ml. The high minimal inhibitory concentrations of cefpirone (64æg/ml) renders this antimicrobial useless in the treatment of enterococcal infections. Betalactamase production and resistance to glycopeptides were not detected. Antimicrobial susceptibility of strains coming for hospitalized or outpatients were similar (AU).

Hryniewicz W. et al. *Susceptibility patterns of Enterococcus spp. isolated in Poland during 1996.* Int J Antimicrob Agents. 1998; 10(4) : 303-7.p Abstract: Susceptibility of Enterococcus spp. isolated from various clinical specimens to different antimicrobial agents was evaluated. Of the 346 enterococcal isolates obtained from four regional Polish hospitals during 6 months of 1996, 261 (75.4%) were identified as Enterococcus faecalis, 75 (21.7%) as Enterococcus faecium and ten (2.9%) as other enterococcal species. High-level resistance to gentamicin was expressed by 33.4% of E. faecalis and 86.5% of E. faecium strains and corresponding streptomycin resistance by 43.9 and 82.4%, respectively. Over 80% of E. faecium isolates were resistant to ampicillin. None of the isolates was resistant to teicoplanin, however 7.9% of E. fecalis and 1.4% of E. faecium strains were moderately susceptible to vancomycin.

Hsieh P.C. et al. *Bacteria lacking a multidrug pump: a sensitive tool for drug discovery.* Proc Natl Acad Sci U S A. 1998; 95(12) : 6602-6.p Abstract: Microorganisms express multidrug resistance pumps (MDRs) that can confound antibiotic discovery. We propose the use of mutants deficient in MDRs to overcome this problem. Sensitivity to quinolones and to amphipathic cations (norfloxacin, benzalkonium chloride, cetrimide, pentamidine, etc.) was increased 5- to 30-fold in a Staphylococcus aureus mutant with a disrupted chromosomal copy of the NorA MDR. NorA was required both for increased sensitivity to drugs in the presence of an MDR inhibitor and for increased rate of cation efflux. This requirement suggests that NorA is the major MDR protecting S. aureus from the antimicrobials studied. A 15- to 60-fold increase in sensitivity to antimicrobials also was observed in wild-type cells at an alkaline pH that favors accumulation of cations and weak bases. This effect was synergistic with a norA mutation, resulting in an increase up to 1,000-fold in sensitivity to antimicrobials. The usefulness of applying MDR mutants for natural product screening was demonstrated further by increased sensitivity of the norA- strain to plant alkaloid antimicrobials, which might be natural MDR substrates.

Hsu R.M. et al. *Histologic, microbiologic, and clinical correlates of the diagnosis of sarcoidosis by transbronchial biopsy.* Arch Pathol Lab Med. 1996; 120(4) : 364-8.p Abstract: OBJECTIVE—To determine the frequency of positive microbiologic cultures in patients with epithelioid granulomas and negative histochemical stains for microorganisms in transbronchial biopsy specimens. Secondary objectives were to compare the histologic features of sarcoidosis with those of infectious granulomas and to assess the reliability of histology in establishing the diagnosis of sarcoidosis. DESIGN—Retrospective study. Specific histologic features of transbronchial biopsy specimens were correlated with clinical and microbiologic data, final diagnosis, and an estimate of the probability, on admission, that the patient had sarcoidosis. SETTING—A large, urban, tertiary-care, university-affiliated hospital. PATIENTS—Ninety-two adult patients in whom epithelioid granulomas, negative for microorganisms on Ziehl-Neelsen and Gomori methemaine silver stain, were found in transbronchial biopsy specimens. Patients were identified through a search of surgical pathology files from 1975 to 1987. RESULTS—Ten patients (10.9%) had mycobacterial or fungal granulomas, while 82 had sarcoidosis. In all patients with a high clinical probability of sarcoidosis, the diagnosis was confirmed. Transbronchial biopsy specimens from patients with infectious granulomas had fewer granulomas (2.0 +/- 1.7 (SD) versus 7.1 +/- 6.6; P<.01), which involved a smaller proportion of lung tissue per case (9.5 +/- 10.0% versus 26.6 +/- 24.0%; P<.01). Sarcoid granulomas often exhibited Schaumann bodies (69.5% versus 10%; P<.01). Necrosis tended to predominate in infectious granulomas (19.5 versus 40%; not significant). CONCLUSIONS—Numerous granulomas, Schaumann bodies, and a high clinical probability of sarcoidosis are significantly associated with that diagnosis. Necrosis does not exclude sarcoidosis. Clinicopathologic assessment of transbronchial biopsy specimens is useful in predicting the final diagnosis of sarcoidosis but does not obviate the need for microbiologic cultures, which were positive in 10.9% of patients in this study.

Hsueh P.R. et al. *Antimicrobial resistance and serotype distribution of Streptococcus pneumoniae strains isolated in southern Taiwan.* J Formos Med Assoc. 1996; 95(1) : 29-36.p Abstract: The antimicrobial sus-

ceptibilities and serotypes of 115 Streptococcus pneumonia strains isolated in southern Taiwan from January 1990 to December 1993 were determined. All isolates were susceptible to cephalothin, cefotaxime, trimethoprim/sulfamethoxazole and vancomycin, and 14 of the isolates were resistant to penicillin G. The oxacillin disk method for presumptive detection of resistance to penicillin had a sensitivity of 85.7% and specificity of 97.0%. Resistance rates were as follows: erythromycin 62.2%, tetracycline 71.3%, clindamycin 46.1% and chloramphenicol 19.1%. Eighty-four percent of the isolates were resistant to one or more of the antibiotic tested. Multiple resistance (to three or more classes of antibiotics) was identified in 40.9% of all the isolates and 100% of penicillin-resistant isolates. The predominant serotypes were: 14 (19.1%), 3 (17.4%), 23 (15.7%), 6 (10.4%), and 15 (6.1%). Serotypes 14 and 63 most commonly caused childhood infections, while serotypes 3 and 23 were frequently encountered in adults. The proportion of coverage in 23-valent pneumococcal polysaccharide vaccine was 92.2%, if vaccine-related serotypes were considered to be cross-protecting. Seven (58%) of 12 typable penicillin-resistant isolates belonged to serotype 23 and two (16.7%) to serotype 6. All isolates of serotype 14, 23, 15 and 19 were resistant to one or more antibiotics. Multiple drug resistance was frequently associated with serotype 23 (31.9%), 14 (23.4%) and 6 (17.0%). Sixty-five percent of isolates of serotype 3 were susceptible to all antibiotics tested. The high level of antimicrobial resistance in S. pneumoniae mandates the continuous surveillance of resistance and the strict control of antibiotic use in Taiwan.

Hsueh P.R. et al. *Flavobacterium indologenes bacteremia: clinical and microbiological characteristics.* Clin Infect Dis. 1996; 23(3) : 550-5.p Abstract: To our knowledge, Flavobacterium indologenes has never been reported as a cause of bacteremia in humans. F. indologenes bacteremia was diagnosed in 12 patients at a tertiary referral center in southern Taiwan between 1 January 1992 and 31 December 1994. Six of these patients had ventilator-associated pneumonia, two had primary bacteremia, and one patient each had pyonephrosis, peritonitis, biliary tract infection, and surgical wound infection. Five patients (42%) had malignancies, and three (25%) had multiple burns. Polymicrobial bacteremia was diagnosed in eight patients (67%). Two (17%) of the patients in this study died; both had polymicrobial bacteremia. Antimicrobial susceptibility testing of the blood isolates from the 12 patients showed that > 90% of the isolates were susceptible to piperacillin, cefoperazone, ceftazidime, and minocycline. The chromatograms of esterified fatty acids for the isolates were identical. F. indologenes should be considered an etiologic agent of bloodstream infection, especially in hospitalized patients with severe underlying diseases.

Hsueh P.R. et al. *Report of invasive Rhodococcus equi infections in Taiwan, with an emphasis on the emergence of multidrug-resistant strains.* Clin Infect Dis. 1998; 27(2) : 370-5.p Abstract: From November 1995 to October 1997, seven patients with invasive infections due to Rhodococcus equi were treated in Taiwan. Four patients had pulmonary lesions, and one each of the remaining three patients had a recurrent Port-A-Cath (Kabi-Pharmacia, North Ryde, New South Wales, Australia)-related bacteremia, a primary bacteremia, and a brain abscess. Three patients had underlying hematologic malignancies, and one each of the remaining four patients had diabetes mellitus, Waldenstrom's macroglobulinemia, long-term use of steroids, and AIDS. The 13 isolates of R. equi recovered from these patients were identified by using API Coryne System (bioMerieux, Marcy l'Etoile, France), VITEK GPI card (bioMerieux Vitek, Hazelwood, MO), supplemental biochemical tests, and cellular fatty acid chromatograms. Susceptibilities of these isolates to 16 antimicrobial agents, with use of the agar dilution method, varied; among them, amikacin and trimethoprim-sulfamethoxazole were the most active agents. Different random amplified polymorphic DNA (RAPD) patterns of isolates from different patients documented the lack of epidemiological relatedness of the causative organisms of these infections. This study confirms the emergence of multidrug-resistant R. equi infection in Taiwan and documents the relapsing or reactivating nature of this infection.

Hsueh P.R. et al. *Multicenter surveillance of antimicrobial resistance of Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis in Taiwan during the 1998-1999 respiratory season.* Antimicrob Agents Chemother. 2000; 44(5) : 1342-5.p Abstract: A susceptibility surveillance study of 276 isolates of Streptococcus pneumoniae, 301 of Haemophilus influenzae, and 110 of Moraxella catarrhalis was carried out from November 1998 to May 1999 in Taiwan. High rates of nonsusceptibility to penicillin (76%), extended-spectrum cephalosporins (56%), azithromycin (94%), clarithromycin (95%), and trimethoprim-sulfamethoxazole (TMP-SMX) (65%) for S. pneumoniae isolates and high rates of nonsusceptibility to amoxicillin (58%) and TMP-SMX (52%) for H. influenzae isolates were found. Higher percentages of S. pneumoniae isolates nonsusceptible to aminopenicillins, extended-spectrum cephalosporins, macrolides, and TMP-SMX were observed among penicillin-intermediate and -resistant isolates. All quinolones tested were active in vitro against these three organisms.

Hsueh P.R. et al. *Clinical and microbiological characteristics of Flavobacterium indologenes infections associated with indwelling devices.* J Clin Microbiol. 1996; 34(8) : 1908-13.p Abstract: Clinical infections caused by Flavobacterium indologenes have never been documented. Thirteen isolates derived from seven patients with indwelling device-associated F. indologenes infections were identified from 1 April through 30 November 1995. The antimicrobial susceptibilities to 20 antimicrobial agents of the isolates, the cellular fatty acid chromatograms for the isolates, and the random amplified polymorphic DNA (RAPD) patterns generated by arbitrarily primed PCR of the isolates were studied. The antibiotypes and RAPD patterns differed among the isolates recovered from different patients. However, both antibiotypes and RAPD patterns were identical among the five isolates from one patient with multiple episodes of central venous catheter-associated bacteremia within a 1.5-month period and between the two isolates from another patient suffering from two episodes of catheter-related bacteriuria at an interval of 14 days. It is documented that the recurrent infections in each of these two patients were caused by a single F. indologenes clone, respectively. Identical antibiotypes and RAPD patterns were also demonstrated between two isolates from a patient with ventilator-associated pneumonia, one recovered from an endotracheal aspirate and the other derived from a blood specimen 10 days later, indicating the invasive nature of F. indologenes. Two cellular fatty acid chromatograms were identified among these isolates. All of the isolates showed in vitro resistance to cephalothin, cefotaxime, ceftriaxone, moxalactam, aztreonam, aminoglycosides, erythromycin, clindamycin, vancomycin, and teicoplanin. F. indologenes should be included as an etiologic agent of infections associated with the use of indwelling devices.

Hsueh P.R. et al. *Dissemination of high-level penicillin-, extended-spectrum cephalosporin-, and erythromycin-resistant Streptococcus pneumoniae clones in Taiwan.* J Clin Microbiol. 1999; 37(1) : 221-4.p Abstract: Sixty-seven clinical isolates of Streptococcus pneumoniae (40 of serotype 23F, 19 of serotype 19F, and 8 of serotype 6B) with decreased susceptibilities to penicillin and erythromycin were characterized by antimicrobial susceptibility patterns; DNA restriction endonuclease cleavage profiles of the penicillin-binding protein genes pbp1a, pbp2b, and pbp2x; random amplified polymorphic DNA (RAPD) patterns generated by arbitrarily primed PCR; and chromosomal macrorestriction profiles based on pulsed-field gel electrophoresis. A total of 22 clones (identical or closely related pulsotypes and identical RAPD patterns) were identified; 14 clones of 23F, 6 of 19F, and 2 of 6B. Three 23F clones (26 isolates) and one 19F clone (9 isolates) expressed high-level resistance to penicillin, cefotaxime, and erythromycin (MICs >/= 256 microg/ml). These data strongly suggest that multiple high-level penicillin-, extended-spectrum cephalosporin-, and macrolide-resistant clones of S. pneumoniae

have been disseminated in Taiwan.

Hsueh P.R. et al. *Extremely high incidence of macrolide and trimethoprim-sulfamethoxazole resistance among clinical isolates of Streptococcus pneumoniae in Taiwan*. J Clin Microbiol. 1999; 37(4) : 897-901.p Abstract: From January 1996 to December 1997, 200 isolates of Streptococcus pneumoniae recovered from 200 patients treated at National Taiwan University Hospital were serotyped and their susceptibilities to 16 antimicrobial agents were determined by the agar dilution method. Sixty-one percent of the isolates were nonsusceptible to penicillin, exhibiting either intermediate resistance (28%) or high-level resistance (33%). About two-fifths of the isolates displayed intermediate or high-level resistance to cefotaxime, ceftriaxone, cefepime, imipenem, and meropenem. Extremely high proportions of the isolates were resistant to erythromycin (82%), clarithromycin (90%), and trimethoprim-sulfamethoxazole (TMP-SMZ) (87%). Among the isolates nonsusceptible to penicillin, 23.8% were resistant to imipenem; more than 60% displayed resistance to cefotaxime, ceftriaxone, cefepime, and carbapenems; 96.7% were resistant to erythromycin; and 100% were resistant to TMP-SMZ. All isolates were susceptible to rifampin and vancomycin. The MICs at which 50% and 90% of the isolates were inhibited were 0.12 and 1 microgram/ml, respectively, for cefpirome, and 0.12 and 0.25 microgram/ml, respectively, for moxifloxacin. Six serogroups or serotypes (23F, 19F, 6B, 14, 3, and 9) accounted for 77.5% of all isolates. Overall, 92.5% of the isolates were included in the serogroups or serotypes represented in the 23-valent pneumococcal vaccine. The incidence of macrolide and TMP-SMZ resistance for S. pneumoniae isolates in Taiwan in this study is among the highest in the world published to date.

Hsueh P.R. et al. *Persistence of a multidrug-resistant Pseudomonas aeruginosa clone in an intensive care burn unit*. J Clin Microbiol. 1998; 36(5) : 1347-51.p Abstract: Long-term colonization of various body sites with a multidrug-resistant Pseudomonas aeruginosa clone (resistant to piperacillin, cefoperazone, ceftazidime, aztreonam, imipenem, cefepime, cefpirome, ofloxacin, ciprofloxacin, minocycline, and aminoglycosides) with subsequent severe infections in burn patients has not been reported previously. Thirty-nine isolates of multidrug-resistant P. aeruginosa (resistant to ceftazidime and at least three of the agents listed above) recovered from various clinical samples from three patients in an intensive care burn unit from April 1997 to May 1997 and seven preserved isolates recovered from six patients in other medical wards at National Taiwan University Hospital from April 1996 to May 1997 were studied for their epidemiological relatedness. The epidemic could be attributed to a multidrug-resistant P. aeruginosa clone belonging to serogroup O:F (serogroup O:4) by means of antimicrobial susceptibility testing, O serogrouping, and analysis of the randomly amplified polymorphic DNA patterns generated by arbitrarily primed PCR of the isolates. The epidemic strain persisted in the three patients for weeks to months; in the meantime, these patients had received multiple antimicrobial agents for the management of intervening episodes of invasive infections (bacteremia, ventilator-associated pneumonia, and/or catheter-related sepsis) caused by this strain, as well as concomitant infections due to other organisms. The strain had been isolated only once previously, from a burn patient who was on the unit in December 1996. The present report, describing a small outbreak due to P. aeruginosa, documents the fact that a single clone of multidrug-resistant P. aeruginosa can cause long-term persistence in different body sites of burn patients and that the colonization can subsequently result in various severe infections.

Hsueh P.R. et al. *Invasive Streptococcus pneumoniae infection associated with rapidly fatal outcome in Taiwan*. J Formos Med Assoc. 1996; 95(5) : 364-71.p Abstract: We observed 42 cases of invasive Streptococcus pneumoniae infections from 1991 through 1993 in southern Taiwan. The antimicrobial susceptibilities and distribution of serotypes of the 42 isolates from these invasive infections were determined. Serotypes 14, 3, 6, 23, 15 and 4 were most commonly identified. Serotypes 14 and 6 most frequently caused infections in pediatric patients, while serotypes 3, 14 and 23 were commonly encountered in adults. Overall, 85.7% of the isolates were included in the serotypes represented in the 23-valent pneumococcal vaccine. Three isolates were intermediately resistant to penicillin and none were fully resistant. Resistance rates were: erythromycin, 61.9%; clindamycin, 47.6%; chloramphenicol, 19%; and tetracycline, 73.8%. Resistance to three or more classes of antibiotics was found in 33.3% of the isolates, in which the majority were serotypes 14 and 6 and nontypeable isolates. Bacteremic pneumonia and primary bacteremia accounted for 64.3% of the infections. Mortality was 42.6%. Factors associated with higher mortality included age of > 16 years, the presence of underlying diseases, development of one or more septic complications, bacteremic pneumonia and the presence of serotype 3 isolates. Rapidly fatal outcome (the illness developed less than 48 hours prior to admission and the death occurred within 48 hours of hospitalization) occurred in 12 (66.7%) of the 18 patients who died. All these patients received adequate antibiotic treatment and aggressive intensive care, indicating the fulminant nature of this infection. Mucoid serotype 3 isolates caused rapidly fatal outcomes. Given the severity of these infections despite adequate antibiotic therapy and the vulnerability of patients with altered immune responses, there is a dire need for introduction of new therapeutic options and preventive measures to prevent mortality due to invasive S. pneumoniae infections.

Huang A.H. et al. *Impact of Helicobacter pylori antimicrobial resistance on the outcome of 1-week lansoprazole-based triple therapy.* J Formos Med Assoc. 2000; 99(9) : 704-9.p Abstract: PURPOSE: To determine the effect of Helicobacter pylori antimicrobial resistance on the efficacy of different proton pump inhibitor (PPI)-based triple therapies. METHODS: One-hundred and twelve dyspeptic patients with H. pylori infection, as demonstrated by positive histology and culture, were randomized to receive one of the three PPI-based triple therapies. The regimens included lansoprazole (L) plus any two of the following three antibiotics: amoxicillin (A), metronidazole (M), and clarithromycin (C); patients were allocated to ALC, MLC, and ALM subgroups. Six weeks after the start of triple therapy, the 13C-urea breath test (UBT) was performed to evaluate the success of H. pylori eradication. Patients with positive UBT results underwent endoscopy for H. pylori culture. The pre- and post-treatment H. pylori isolates were analyzed for initial and acquired resistance using the E-test. RESULTS: One hundred patients completed the study. The H. pylori eradication rates were 70% (21/30) in the ALM subgroups, 79% (26/33) in the MLC subgroup, and 89% (33/37) in the ALC subgroup. The frequencies of pretreatment H. pylori antimicrobial resistance were 0% for amoxicillin resistance (AR), 32% for metronidazole resistance (MR), and 6% for clarithromycin resistance (CR). For H. pylori isolates with initial MR, the eradication rates in the ALM (40%) and MLC (67%) subgroups were apparently lower than that in the ALC (92%) subgroup. In the ALM and MLC subgroups (i.e., patients who received metronidazole), the eradication failure rate was significantly higher for patients with MR isolates than for patients with metronidazole-susceptible isolates (47% vs 16%, $p < 0.05$). In the ALC and MLC subgroups (i.e., patients who received clarithromycin), the eradication failure rate was significantly higher for patients with CR isolates than for those with clarithromycin-susceptible isolates (100% vs 11%, $p < 0.05$). CONCLUSIONS: The results indicate that H. pylori antimicrobial resistance is relevant to the success of eradication. The high MR but low CR and AR prevalence among H. pylori isolates in this study suggests that PPI-based triple therapy including amoxicillin and clarithromycin may achieve the most favorable eradication rate.

Huang D.F. et al. *Reiter's syndrome caused by Streptococcus viridans in a patient with HLA-B27 antigen*. Clin Exp Rheumatol. 2000; 18(3) : 394-6.p Abstract: A 26-year-old male patient with mitral valve prolapse and HLA-B27 antigen received endodontic treatment for dental caries. Two weeks later fever, dysuria, diarrhea, sterile inflam-

matory arthritis of lower limbs, enthesitis, dactylitis, conjunctivitis, and uveitis consecutively developed. Blood culture performed at the time of active arthritis yielded Streptococcus viridans. He did not have any history of psoriasis, acute infectious diarrhea, chronic inflammatory bowel diseases, or sexually transmitted diseases. Laboratory studies also excluded the possibility of infections by human immunodeficiency virus, hepatitis B or C virus, chlamydia, and streptococci from the upper airway. This report indicates that Streptococcus viridans can be the triggering microorganisms of Reiter's syndrome in some circumstances.

Huang J.J. et al. *Emphysematous pyelonephritis: clinicoradiological classification, management, prognosis, and pathogenesis.* Arch Intern Med. 2000; 160(6) : 797-805.p Abstract: BACKGROUND: Emphysematous pyelonephritis (EPN) is a rare, severe gas-forming infection of renal parenchyma and its surrounding areas. The radiological classification and adequate therapeutic regimen are controversial and the prognostic factors and pathogenesis remain uncertain. OBJECTIVES: To elucidate the clinical features, radiological classification, and prognostic factors of EPN; to compare the modalities of management (ie, antibiotic treatment alone, percutaneous catheter drainage combined with antibiotic treatment, or nephrectomy) and outcome among the various radiological classes of EPN; and to clarify the gas-forming mechanism and pathogenesis of EPN by gas analysis and pathological findings. PATIENTS AND METHODS: Forty-eight EPN cases from our institution were enrolled between August 1,1989, and November 30, 1997. According to the radiological findings on computed tomographic scan, they were classified into the following classes: (1) class 1: gas in the collecting system only; (2) class 2: gas in the renal parenchyma without extension to extrarenal space; (3) class 3A: extension of gas or abscess to perinephric space; class 3B: extension of gas or abscess to pararenal space; and (4) class 4: bilateral EPN or solitary kidney with EPN. The clinical manifestations, management, and outcome were compared. The gas contents of specimens from 6 patients were analyzed. The pathological findings from 8 patients who received nephrectomy were reviewed. The statistical methods consisted of the Fisher exact test (2 tailed) for categorical variables and Wilcoxon rank sum test for continuous variables to test the predictors of poor prognosis. RESULTS: Forty-six patients (96%) had diabetes mellitus, and 10 (22%) of the 46 also had urinary tract obstruction in the corresponding renoureteral unit. The other 2 nondiabetic patients (4%) had severe hydronephrosis. Twenty-one (72%) of the 29 patients with diabetes mellitus also had a glycosylated hemoglobin A(1c) level higher than 0.08. Escherichia coli (69%) and Klebsiella pneumoniae (29%) were the most common pathogens. The mortality rate in patients who received antibiotic treatment alone was 40% (2 of 5 patients). The success rate of management by percutaneous catheter drainage (PCD) combined with antibiotic treatment was 66% (27 of 41 patients). In classes 1 and 2 EPN, all the patients who were treated using a PCD or ureteral catheter combined with antibiotic treatment survived. In extensive EPN (classes 3 and 4), 17 (85%) of the 20 patients with fewer than 2 risk factors (ie, thrombocytopenia, acute renal function impairment, disturbance of consciousness, or shock) were successfully treated using PCD combined with antibiotic treatment; and the patients with 2 or more risk factors had a significantly higher failure rate than those with no or only 1 risk factors (92% vs 15%, P<.001). Eight of the 14 patients who had an unsuccessful treatment using a PCD underwent subsequent nephrectomy, 7 of whom survived. Only 2 patients were managed by direct nephrectomy and survived. The overall success rate of nephrectomy was 90% (9 of 10 patients). The total mortality was 18.8% (9 of 48 patients). Five of the 6 gas samples contained hydrogen (average, 12.8%), and all had carbon dioxide (average, 14.4%). The pathological findings from 8 of 10 who underwent nephrectomy revealed poor perfusion in most cases (ie, infarction, 5 patients; vascular thrombosis, 3 patients; and arteriosclerosis and/or glomerulosclerosis, 4 patients). CONCLUSION: Acute renal infection with E coli or K pneumoniae in patients with diabetes mellitus and/or urinary tract obstruction is the cornerstone for the development of EPN. Mixed acid fermentation of glucose by Enterobacteriaceae is the major pathway of gas formation. For localized EPN (classes 1 and 2), PCD combined with antibiotic treatment can provide a good outcome. (ABSTRACT TRUNCATED).

Huang W.H. et al. *New one-week, low-dose triple therapy for the treatment of duodenal ulcer with Helicobacter pylori infection*. Chung Hua I Hsueh Tsa Chih (Taipei). 1998; 61(8) : 448-55.p Abstract: BACKGROUND: Antimicrobial therapy is the recommended treatment for duodenal ulcer associated with Helicobacter pylori infection. The eradication of bismuth-based triple therapy with bismuth subcitrate, metronidazole and amoxicillin is limited by low compliance, drug resistance and side-effects. Two-week proton pump inhibitor (PPI)-based triple therapy has a higher eradication rate but is costly. This study was designed to compare the efficacy, patient compliance and cost of short-term PPI-based triple therapy with those of bismuth-based triple therapy. METHODS: Ninety patients with active duodenal ulcer disease and H pylori infection, proven with the 13C-urea breath test and CLO test (Campylobacter-like organism test) were treated randomly in three therapeutic groups: Group A, DeNol 120 mg, amoxicillin 500 mg and metronidazole 250 mg four times a day orally for 14 days; Group B, omeprazole 20 mg plus clarithromycin 500 mg twice a day and amoxicillin 500 mg four times a day for 14 days; Group C, omeprazole 20 mg, clarithromycin 250 mg and metronidazole 500 mg twice a day for seven days. Nizatidine 150 mg twice a day was given continuously following the end of anti-H pylori therapy for each group. Two months later, endoscopy, the CLO test and 13C-urea breath test were repeated to assess the eradication rate of H pylori and the ulcer-healing rate. Drug tolerance was evaluated by patients themselves by daily recording of any side-effects. RESULTS: Eighty-four patients completed the entire course of therapy and evaluation for H pylori infection. The H pylori eradication rates in Groups A, B and C were 75% (21/28), 93% (26/28) and 89% (25/28), respectively ($p = 0.466$). The ulcer healing rate was 86% (24/28) in Group A and 89% (25/28) in Groups B and C ($p = 0.764$). A total of 74 patients (88%) were free from symptoms at the end of the triple therapy. Symptom relief was faster in patients with PPI-based triple therapy (Groups B and C) (days 3 and 4) than for patients with bismuth-based triple therapy (day 5). The cost of Group C therapy was lower than that for Groups A and B. There were no major side-effects in any of the patients. CONCLUSIONS: One-week triple therapy with omeprazole, clarithromycin and metronidazole is highly effected for the eradication of H pylori. A therapeutic regime of one week's duration with lower cost, good compliance and mild side-effects may offer a good choice for treatment of duodenal ulcer associated with H pylori infection in clinical practice.

Hubert S.K. et al. *Glycopeptide-intermediate Staphylococcus aureus: evaluation of a novel screening method and results of a survey of selected U.S. hospitals.* J Clin Microbiol. 1999; 37(11) : 3590-3.p Abstract: Isolates of Staphylococcus aureus with decreased susceptibilities to glycopeptide antimicrobial agents, such as vancomycin and teicoplanin, have emerged in the United States and elsewhere. Commercially prepared brain heart infusion agar (BHIA) supplemented with 6 microg of vancomycin per ml was shown in a previous study to detect glycopeptide-intermediate S. aureus (GISA) with high sensitivity and specificity; however, this medium, when prepared in-house, occasionally showed growth of vancomycin-susceptible control organisms. This limitation could significantly impact laboratories that prepare media in-house, particularly if they wished to conduct large surveillance studies for GISA. Therefore, a pilot study to detect GISA was performed with vancomycin-containing Mueller-Hinton agar (MHA) prepared in-house in place of commercially prepared BHIA. MHA was selected for this study because this medium is widely available and well standardized. The results of the pilot study showed that supplementation of MHA with 5 microg of vancomycin per ml was both a sensitive and a specific method for screening for GISA isolates. This method was used to screen for GISA among 630 clin-

ical isolates of methicillin-resistant S. aureus collected during 1997 from 33 U.S. hospitals. Although 14 S. aureus isolates grew on the screening agar, all were vancomycin susceptible (MICs were </=1 microg/ml) by broth microdilution testing. Population analyses of five isolates revealed two with a subpopulation for which vancomycin MICs were 8 microg/ml. In summary, the MHA screen plate containing 5 microg of vancomycin per ml prepared in-house provides a sensitive and cost-effective method for large-scale screening for GISA for which vancomycin MICs are 8 microg/ml. However, confirmation of isolates as vancomycin resistant is critical. This study suggests that GISA was not a widespread problem in the United States in 1997.

Huebner J. et al. *Coagulase-negative staphylococci: role as pathogens.* Annu Rev Med. 1999; 50 : 223-36.p Abstract: Coagulase-negative staphylococci have long been regarded as apathogenic but their important role as pathogens and their increasing incidence have been recognized and studied in recent years. Although specific virulence factors are not as clearly established as they are in Staphylococcus aureus, it seems clear that factors such as bacterial polysaccharide components are involved in attachment and/or persistence of bacteria on foreign materials. Coagulase-negative staphylococci are by far the most common cause of bacteremia related to indwelling devices. Most of these infections are hospital-acquired, and studies over the past several years suggest that they are often caused by strains that are transmitted among hospitalized patients. Other important infections due to coagulase-negative staphylococci include central nervous system shunt infections, native or prosthetic valve endocarditis, urinary tract infections, and endophthalmitis. Intravenous treatment of systemic infections is usually required because coagulase-negative staphylococci have become increasingly resistant to multiple antibiotics.

Huebner R.E. et al. *Nasopharyngeal carriage and antimicrobial resistance in isolates of Streptococcus pneumoniae and Haemophilus influenzae type b in children under 5 years of age in Botswana.* Int J Infect Dis. 1998; 3(1) : 18-25.p Abstract: OBJECTIVES: A prospective survey was conducted to determine the prevalence of asymptomatic nasopharyngeal carriage of Streptococcus pneumoniae and Haemophilus influenzae type b in children under 5 years of age in Botswana and to determine the antibiotic resistance patterns of these organisms to commonly used antimicrobial agents. METHODS: Children 2 months to 5 years of age (n = 249) were recruited from outpatient clinics in Gaborone and Francistown, and 29 were sampled from the pediatric wards at Princess Marina (Gaborone) and Nyangabgwe (Francistown) Hospitals. Nasopharyngeal specimens were collected and the carriage and antibiotic resistance of S. pneumoniae and H. influenzae type b were determined. Analyses of risk factors associated with carriage and resistance were performed. RESULTS: Streptococcus pneumoniae was isolated from 69% of the outpatient children in Gaborone and 85% of the children in Francistown; the carriage rate in hospitalized children was 36% and 33% in Gaborone and Francistown, respectively. Approximately half of the isolates at both sites were resistant to at least one antibiotic, the most common being cotrimoxazole and penicillin. Resistance to three or more antibiotics (multiple resistance) was found in less than 10% of the isolates. Most penicillin resistance at both sites was at the intermediate level; however, almost 20% of the isolates demonstrated high-level resistance to cotrimoxazole. The most prevalent serogroups or serotypes of antibiotic-resistant isolates were 14, 19F, 19A, 6A, 6B, and 4. No risk factors for antibiotic resistance were identified. Haemophilus influenzae type b was isolated from 8% of the children in Gaborone and from 3% of the children in Francistown. Almost a third of the isolates were resistant to ampicillin. CONCLUSIONS: The high levels of antibiotic resistance in pneumococci isolated from children in Botswana suggest that the clinical management of meningitis and otitis media with a b-lactam antibiotic may fail in a significant proportion of cases and that empiric first-line use of cefotaxime or ceftriaxone for meningitis and higher dose amoxicillin (90 mg/kg/day) for otitis media is recommended. The levels of penicillin resistance in this study would not impact on the management of pneumonia with amoxicillin.

Hughes J.M. et al. *Approaches to limiting emergence of antimicrobial resistance in bacteria in human populations.* Clin Infect Dis. 1997; 24 Suppl 1 : S131-5.p Abstract: Infectious diseases continue to be major threats to human health around the world. Within the past few years, several divergent groups of organisms have emerged as significant causes of morbidity and mortality. Included among these are bacteria that are refractory to therapy because of the development of resistance to multiple antimicrobial agents. Multidrug resistance in strains of Mycobacterium tuberculosis, Streptococcus pneumoniae, Shigella dysenteriae, Salmonella typhi, and Enterococcus faecium has been reported. Surveillance of resistant microorganisms in the United States and abroad is fragmentary and targets relatively few organisms. Surveillance is further hampered by the fact that detection of some novel resistance mechanisms is difficult by means of current laboratory methods. Both clinicians and public health officials are likely to continue to face a variety of challenges regarding surveillance, treatment, prevention, and control of drug-resistant infections.

Hunfeld K.P. et al. *New colorimetric microdilution method for in vitro susceptibility testing of Borrelia burgdorferi against antimicrobial substances.* Eur J Clin Microbiol Infect Dis. 2000; 19(1) : 27-32.p Abstract: A newly developed colorimetric microdilution method was used to analyze the activity of 12 antimicrobial agents against nine Borrelia burgdorferi isolates, including all three genospecies pathogenic for humans. In addition, in vitro antimicrobial resistance patterns of Borrelia valaisiana and Borrelia bissettii tick isolates were investigated. The applied test system is based upon color changes that occur in the presence of phenol red and result from the accumulation of nonvolatile acid produced by actively metabolizing spirochetes. After 72 h of incubation, minimal inhibitory concentrations (MICs) were determined from the decrease of absorbance by software-assisted calculation of growth curves. MIC values were lowest for azlocillin (MIC, < or = 0.125 microg/ml), ceftriaxone (MIC range, < or = 0.015-0.06 microg/ ml), and azithromycin (MIC range, < or = 0.015-0.06 microg/ml). Whereas tobramycin (MIC range, 8-64 microg/ml) exhibited little activity, spectinomycin (MIC range, 0.25-2 microg/ml) showed in vitro antimicrobial activity against Borrelia burgdorferi. The MICs of penicillin G for Borrelia afzelii isolates were ten times higher than those for Borrelia burgdorferi, Borrelia valaisiana, and Borrelia bissettii isolates ($P<0.05$) and 100 times higher than those for isolates belonging to the genospecies Borrelia garinii ($P < 0.05$). Further significant differences with respect to the MIC values of the other antimicrobial agents tested were not noted. The colorimetric microdilution method offered the advantages of reliability, reproducibility, and convenience and could handle large numbers of isolates and antibiotics.

Hunt C.P. *The emergence of enterococci as a cause of nosocomial infection.* Br J Biomed Sci. 1998; 55(2) : 149-56.p Abstract: Enterococci have traditionally been regarded as low-grade pathogens but have emerged as an increasingly important cause of nosocomial infection. The rise in hospital-acquired enterococcal infection has been in part due to the increased use of broad-spectrum antibiotics and the rising number of severely ill patients. The intrinsic resistance of enterococci to many antimicrobial agents, and the acquisition of resistance to the few antibiotics available for treatment, has led to real therapeutic difficulties. The microbiological laboratory has an important role to play in the control of enterococcal infection through surveillance, and should be able to identify antibiotic-resistant strains likely to cause a problem. Infection control measures, such as source isolation of infected or colonised patients, should be considered. The possibility that vancomycin-resistant strains of enterococci are entering the community via the food chain indicates the need for greater control of the use of glycopeptide antibiotics in animal feed.

Hunt J.P. et al. *Acinetobacter calcoaceticus pneumonia and the formation of pneumatoceles.* J Trauma. 2000; 48(5) : 964-70.p Abstract: Pneumatoceles are cystic lesions of the lungs often seen in children with staphylococcal pneumonia and positive-pressure ventilation. Acinetobacter calcoaceticus is an aerobic, short immobile gram-negative rod, or coccobacillus, which is an omnipresent saprophyte. The variant anitratus is the most clinically significant pathogen in this family, usually presenting as a lower respiratory tract infection. Acinetobacter has been demonstrated to be one of the most common organisms found in the ICU. We present three critically ill surgery patients with Acinetobacter pneumonia, high inspiratory pressures, and the subsequent development of pneumatoceles. One of these patients died from a ruptured pneumatocele, resulting in tension pneumothorax. Treatment of pneumatoceles should center on appropriate intravenous antimicrobial therapy. This should be culture directed but is most often accomplished with Imipenem. Percutaneous, computed tomographic-guided catheter placement or direct tube thoracostomy decompression of the pneumatocele may prevent subsequent rupture and potentially lethal tension pneumothorax.

Hunt R.H. *Peptic ulcer disease: defining the treatment strategies in the era of Helicobacter pylori.* Am J Gastroenterol. 1997; 92(4 Suppl) : 36S-40S; discussion 40S-43S.p Abstract: Peptic ulcer disease continues to be a major health care problem costing the public billions of dollars each year. Recent evidence confirms a major role for Helicobacter pylori infection in the natural history of most cases of peptic ulcer disease. The most established and effective antibiotic treatment for the eradication of H. pylori has been the classic bismuth "triple therapy" regimen containing bismuth, metronidazole, and tetracycline. However, pretreatment resistance to metronidazole, poor compliance, and side effects have limited the widespread acceptance of bismuth triple therapy for routine use. Recent studies suggest that the combination of one or two antibiotic agents and a proton pump inhibitor offers a better tolerated regimen than bismuth triple therapy. Efficacy is similar with respect to eradication of H. pylori, and the combined use of a proton pump inhibitor assures rapid symptom relief and ulcer healing. Although the mechanisms by which H. pylori eradication is effected, the optimal dosing schedules, and the specific antimicrobial agents to be administered require further study, the combination of a proton pump inhibitor and one or two antibiotics promises to be an appropriate first-line treatment for peptic ulcer disease.

Huovinen P. et al. *The relationship between erythromycin consumption and resistance in Finland. Finnish Study Group for Antimicrobial Resistance.* Ciba Found Symp. 1997; 207 : 36-41; discussion 41-6.p Abstract: Because the discovery of new antimicrobial agents cannot be expected in the near future, we will have to manage with the antimicrobials currently available at least for the next decade or two. Therefore, attempts to prevent development of antimicrobial resistance are of major importance. The relationship of local antimicrobial consumption and antimicrobial resistance has been shown in many hospital studies but not in the community, even though this is where most antibiotics are used. At the beginning of 1990s, erythromycin resistance in group A streptococci increased rapidly in Finland. The geographical variations found led to a nationwide study of the possible relation between local erythromycin consumption and variations in erythromycin resistance in the community. Erythromycin resistance was found to be significantly ($P = 0.006$) linked to local consumption of erythromycin. In further experiments, we found that a new erythromycin resistance phenotype belonging to the T4 serotype was spread over the whole country; 83% of the erythromycin-resistant isolates were of this new phenotype in 1994. In 1991, recommendations were given to reduce use of erythromycin in Finland. Following these recommendations, macrolide consumption decreased by 40% from 1991-1994. Studies are now in progress to evaluate the effect of this reduction on erythromycin resistance of group A streptococci.

Hurst M. et al. *Meropenem: a review of its use in patients in intensive care.* Drugs. 2000; 59(3) : 653-80.p Abstract: Meropenem is a carbapenem antibacterial agent that has antimicrobial activity against gram-negative, gram-positive and anaerobic micro-organisms. In vitro studies involving isolates from patients in intensive care units (ICUs) indicate that meropenem is more active against most gram-negative pathogens than other comparators (including imipenem), although, compared with imipenem, meropenem is less active against most gram-positive organisms. Resistance to meropenem is uncommon in most bacteria. Treatment with meropenem as initial empirical monotherapy was effective in a range of serious infections in adult and paediatric ICU patients. Meropenem monotherapy was as effective as imipenem/cilastatin in 4 comparative trials in terms of satisfactory clinical and bacteriological responses. Meropenem monotherapy was significantly more effective than ceftazidime-based combination treatments in 2 trials in patients with nosocomial lower respiratory tract infections (LRTIs) in terms of both clinical and bacteriological responses. Meropenem was also more active than ceftazidime-based treatments against both gram-positive and gram-negative organisms. However, 2 studies in patients with a range of serious infections found no significant differences between meropenem and cephalosporin-based treatments in terms of clinical or bacteriological response. Meropenem was also as effective as cephalosporin-based treatments in comparative trials in children with serious infections. Meropenem is well tolerated as either a bolus or an infusion, and clinical trials have shown similar incidences of adverse events to those observed with cephalosporin-based treatments. It is well tolerated by the CNS, with seizures reported infrequently, and can therefore be used at high doses and in patients with meningitis. The incidence of drug-related nausea and vomiting is low and, in contrast to imipenem/cilastatin, does not increase with dose or speed of administration. Conclusions: Meropenem is a well tolerated broad spectrum antibacterial agent that, when used as initial empirical monotherapy, is as effective as imipenem/cilastatin in the treatment of a range of serious infections (including nosocomial) in adults and children in ICUs. Compared with cephalosporin-based combination treatments, meropenem monotherapy may be more effective in the treatment of nosocomial LRTIs and can be used as monotherapy. Meropenem has an important role in the empirical treatment of serious infections in adults and children in ICUs.

Hutchinson P.J. et al. *Head injury monitoring using cerebral microdialysis and Paratrend multiparameter sensors.* Zentralbl Neurochir. 2000; 61(2) : 88-94.p Abstract: INTRODUCTION: Following head injury complex pathophysiological changes occur in brain metabolism. The objective of the study was to monitor brain metabolism using the Paratrend multiparameter sensor and microdialysis catheters. PATIENTS, MATERIAL AND METHODS: Following approval by the Local Ethics Committee and consent from the relatives, patients with severe head injury were studied using a triple bolt inserted into the frontal region, transmitting an intracranial pressure monitor, microdialysis (10 mm or 30 mm membrane; glucose, lactate, pyruvate, glutamate) catheter and Paratrend multiparameter (oxygen, carbon dioxide, pH and temperature) sensor. A Paratrend sensor was also inserted into the femoral artery for continuous blood gas analysis. RESULTS: 21 patients were studied with cerebral microdialysis for a total of 91 monitoring days (range 19 hours to 12 days). Of these, 14 patients were also studied with cerebral and arterial Paratrend sensors. The mean (+/- 95% confidence intervals) arterial and cerebral oxygen levels were 123 +/- 10.9 mmHg and 27.9 +/- 5.71 mmHg respectively. The arterial and cerebral carbon dioxide levels were 34.3 +/- 2.35 mmHg and 45.3 +/- 3.07 mmHg respectively. Episodes of systemic hypoxia and hypotension resulting in falls in cerebral oxygen and rises in cerebral carbon dioxide were rapidly detected by the arterial and cerebral Paratrend sensors. Systemic pyrexia was reflected in the brain with the cerebral Paratrend sensor reading 0.17 degree C (mean) higher than the arterial sensor. Elevations of cerebral glucose were detected, but the

overall cerebral glucose was low (mean 1.57 +/- 0.53 mM 10 mm membrane; mean 1.95 +/- 0.68 mM 30 mm membrane) with periods of undetectable glucose in 6 patients. Lactate concentrations (mean 5.08 +/- 0.73 mM 10 mm membrane; mean 8.27 +/- 1.31 mM 30 mm membrane) were higher than glucose concentrations in all patients. The lactate/pyruvate ratio was 32.1 +/- 5.16 for the 10 mm membrane and 30.6 +/- 2.17 for the 30 mm membrane. Glutamate concentrations varied between patients (mean 15.0 +/- 10.5 microM 10 mm membrane; mean 28.8 +/- 17.8 microM 30 mm membrane). CONCLUSION: The combination of microdialysis catheters and Paratrend sensors enabling the monitoring of substrate delivery and brain metabolism, and the detection of secondary metabolic insults has the potential to assist in the management of head-injured patients.

Huwe P. et al. *Influence of different uropathogenic microorganisms on human sperm motility parameters in an in vitro experiment*. Andrologia. 1998; 30 Suppl 1 : 55-9.p Abstract: The influence of different uropathogenic microorganisms (E. coli, enterococcus, Pseudomonas aeruginosa, Staphylococcus saprophyticus, Candida albicans) on human sperm motility was studied in vitro with a computer-assisted sperm analyser (CASA). Native ejaculates were prepared with the swim-up technique and adjusted to 22 x 10(6) spermatozoa ml-1. The sperm suspension was artificially infected with microorganisms in concentrations varying from 2 x 10(3) to 2 x 10(7). Sperm motility was examined directly after incubation, 2, 4 and 6 h later using the Mika motion analysis, a computer-based, automatic motility analysis. Former results with E. coli (serotype 06) could be confirmed that a significant inhibitory effect on sperm motility was associated with bacterial growth. Experiments with the enterococcus strain and Staphylococcus saprophyticus indicated no significant influence on sperm motility parameters. Tests with Pseudomonas aeruginosa showed a decrease of progressive motility according to time, but not to different bacterial concentrations. A significant inhibitory effect of Candida albicans was only detected in the samples with the initial bacterial concentration of 2 x 10(7) microorganisms ml-1.

Hwang S.S. et al. *The value of CT-guided percutaneous needle aspiration in immunocompromised patients with suspected pulmonary infection*. AJR Am J Roentgenol. 2000; 175(1) : 235-8.p Abstract: OBJECTIVE: We evaluated the diagnostic efficacy of CT-guided percutaneous needle aspiration in immunocompromised patients with suspected pulmonary infection. SUBJECTS AND METHODS: We reviewed the findings and yields of 24 CT-guided percutaneous needle aspirations in 21 immunocompromised patients. Cytologic evaluation and culture for aerobes, anaerobes, Mycobacterium species, and fungus were performed in all aspirates. RESULTS: We identified one or more etiologic microorganisms in 19 (79.2%) of 24 CT-guided percutaneous needle aspirations. Of 19 aspirates with positive findings, single causal microorganisms were identified in 18. Staphylococcus aureus was found in four aspirates, and Aspergillus fumigatus in seven; these microorganisms were the principal bacterial (4/11) and fungal (7/9) causative organisms. One of the 19 aspirates with positive findings yielded two microorganisms. In the remaining five aspirates, no microorganisms were identified and cytologic examination revealed nonspecific inflammatory cells. No major complications were observed during or after the procedure. CONCLUSION: CT-guided percutaneous needle aspiration is a safe and useful diagnostic method for the identification of specific microorganisms in immunocompromised patients with suspected pulmonary infection.

Hwu J.R. et al. *Syntheses of new isodethiaazacephems as potent antibacterial agents.* J Med Chem. 1998; 41(24) : 4681-5.p Abstract: New isodethiaazacephems (+/-)-3, (+/-)-4, and (+/-)-10 as well as the 4-sulfonylated isodethiaazacepham (+/-)-5 were synthesized by chemical methods and found to possess biological activity against five pathogenic microorganisms in vitro. The mesylate and the triflate functionalities in (+/-)-3 and (+/-)-4, acting as effective leaving groups, enhanced remarkably the biological activity in comparison with the parent 3-hydroxyisodethiaazacephem (+/-)-10. The mode of action related to (+/-)-3 and (+/-)-4 can be explained by a [1,4]-elimination process.

Hyatt J.M. et al. *Potential role of pharmacokinetics, pharmacodynamics, and computerized databases in controlling bacterial resistance.* Infect Control Hosp Epidemiol. 2000; 21(1 Suppl) : S18-21.p Abstract: Bacterial resistance to antibiotics continues to be a problem, in spite of increased knowledge of resistance mechanisms. Due to the multifactorial nature of bacterial resistance, studies that evaluate the association between antimicrobial exposure and emergence of resistance may fail to find a relationship unless other factors, in particular the association between patient-pathogen pharmacokinetics (PK) and pharmacodynamics (PD) and the emergence of bacterial resistance, are evaluated as well. It has been hypothesized that, in conjunction with good infection control practices, cycling of antimicrobial agents may prove to be effective in reducing resistance emergence. There is some indication that there may be a relationship between the level of antibiotic exposure and the probability of emergence of bacterial resistance. As shown in our companion article in this supplement, factors associated with ciprofloxacin resistance in Pseudomonas aeruginosa included increased length of stay prior to isolation, exposure to ciprofloxacin, and respiratory tract site of bacterial isolation. However, in patients who received ciprofloxacin therapy, when exposure was at an area under the 24-hour inhibitory concentration curve (AUIC24)>110 (microg x h/mL)/microg/mL, resistance was decreased to 11%, a rate similar to that seen in respiratory isolates not exposed to ciprofloxacin (7%). While the length of time the patient spends in the hospital and the site of infection cannot be controlled, by using PK and PD principles for dosing of ciprofloxacin, the emergence of ciprofloxacin resistance in P aeruginosa may be reduced. Prospective antibiotic-cycling studies may help to determine not only the impact of antibiotic cycling on the institution's antibiogram but also, through the use of PK and PD principles, may help to determine appropriate dosing schedules for antibiotics in order to reduce the probability of emergence of bacterial resistance.

Hyvarinen J. et al. *Multiresistance in Staphylococcus spp. blood isolates in Finland with special reference to the distribution of the mecA gene among the Staphylococcus epidermidis isolates. The Finnish Study Group for Antimicrobial Resistance.* APMIS. 1995; 103(12) : 885-91.p Abstract: A total of 570 Staphylococcus spp. blood isolates collected in Finland in 1991 were tested for susceptiblity to oxacillin and 19 additional antimicrobial agents. The Staphylococcus epidermidis isolates were also analyzed for the presence of the mecA gene by the polymerase chain reaction (PCR). Of the 238 S. epidermidis, 137 (58%) were in vitro identified as methicillin-resistant and 5 (2%) exhibited oxacillin MICs between 1 and 3 micrograms/ml. All these isolates were positive for the mecA gene in PCR as an indication of genetic resistance to methicillin, while none of the remaining 96 S. epidermidis isolates (oxacillin MICs < or = 0.25 microgram/ml) was positive. Multiresistance was observed in 123 (87%) of the 142 mecA-positive S. epidermidis. Of the 332 Staphylococcus aureus isolates, only one (0.3%) was phenotypically resistant to methicillin; the strain was also resistant to three other unrelated classes of antimicrobials. True methicillin resistance of this strain was manifested by the presence of the mecA gene in PCR. Based on these results, multiresistance was still extremely rate among the S. aureus in our country, whereas among the S. epidermidis as many as half of the blood isolates in central hospitals were multiresistant.

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Iakovlev S.V. et al. *[The clinical efficacy of ticarcillin/clavulanate in severe pneumonia]*. Antibiot Khimioter. 2000; 45(3) : 30-4.p Abstract: Efficacy of ticarcillin/clavulanate was studied in the treatment of 11 patients with severe community- and hospital-acquired pneumonia

in an open controlled trial. The drug was administered in a dose of 3.1 g every 4 or 6 hours depending on the infection severity. When pneumonia was due to Pseudomonas aeruginosa, amikacin was additionally used. The positive clinical effect of ticarcillin/clavulanate was stated in 73 per cent of the patients. The pathogen eradication was stated in all the patients. However, in 2 cases superinfection due to P.aeruginosa developed. Mild adverse effects were observed in 2 cases. It is concluded that ticarcillin/clavulanate is highly efficient in the treatment of patients with severe or complicated pneumonia. In cases with ventilator-associated pneumonia it is advisable to use ticarcillin/clavulanate in combination with an aminoglycoside.

Iakovlev V.P. et al. *[Antimicrobial chemotherapy in patients with pyo-septic diseases in intensive care units].* Khirurgiia (Mosk). 1999; (10) : 29-34.p Abstract: The analysis of the treatment of 900 patients with large festered wounds of various genesis and location for the period from 1973 to 1998 years in the intensive care department has shown, that infection of respiratory ways is encountered in 30% of cases (in patients with nonsporeforming anaerobic bacteria—in 11-12%), bacteriuria—in 70-80%, bacteriamia—in 75% of patients with sepsis. In acute pyogenous diseases of soft tissues microbes from the wounds in monoculture were isolated out in 83.3% of cases, associations of gram-positive and gram-negative bacteria—in 16.7%, in chronic pyogenous diseases of soft tissues—in 60 and 40% of cases, respectively. In sepsis associations of gram-positive and gram-negative microbes were isolated in 55.6% of cases. Most often (91%) pathogenic staphylococcus was found in hemocultures. Uring in 62% of cases contained association of gram-positive and gram-negative microorganisms, in sputum gram-positive microflora in monoculture (69%) prevailed. In the group of patients with peritonitis, phlegmon of the anterior abdominal wall, diabetic phlegmon and gangrene, crush syndrome the association of anaerobic and aerobic microflora (from 57.1 to 98.8%) prevailed in the wounds. Application of up-to-date antimicrobial means in the intensive care unit resulted in a decrease of mortality rate in sepsis and complicated course of wound infection up to 23%, and in anaerobic nonsporeforming infection—up to 15%.

Ibrahim E.H. et al. *The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting.* Chest. 2000; 118(1) : 146-55.p Abstract: STUDY OBJECTIVE: To evaluate the relationship between the adequacy of antimicrobial treatment for bloodstream infections and clinical outcomes among patients requiring ICU admission. DESIGN: Prospective cohort study. SETTING: A medical ICU (19 beds) and a surgical ICU (18 beds) from a university-affiliated urban teaching hospital. PATIENTS: Between July 1997 and July 1999, 492 patients were prospectively evaluated. INTERVENTION: Prospective patient surveillance and data collection. RESULTS: One hundred forty-seven patients (29.9%) received inadequate antimicrobial treatment for their bloodstream infections. The hospital mortality rate of patients with a bloodstream infection receiving inadequate antimicrobial treatment (61.9%) was statistically greater than the hospital mortality rate of patients with a bloodstream infection who received adequate antimicrobial treatment (28.4%; relative risk, 2. 18; 95% confidence interval [CI], 1.77 to 2.69; $p < 0.001$). Multiple logistic regression analysis identified the administration of inadequate antimicrobial treatment as an independent determinant of hospital mortality (adjusted odds ratio [AOR], 6.86; 95% CI, 5.09 to 9.24; $p < 0.001$). The most commonly identified bloodstream pathogens and their associated rates of inadequate antimicrobial treatment included vancomycin-resistant enterococci (n = 17; 100%), Candida species (n = 41; 95.1%), oxacillin-resistant Staphylococcus aureus (n = 46; 32.6%), coagulase-negative staphylococci (n = 96; 21.9%), and Pseudomonas aeruginosa (n = 22; 10.0%). A statistically significant relationship was found between the rates of inadequate antimicrobial treatment for individual microorganisms and their associated rates of hospital mortality (Spearman correlation coefficient = 0.8287; $p = 0.006$). Multiple logistic regression analysis also demonstrated that a bloodstream infection attributed to Candida species (AOR, 51.86; 95% CI, 24.57 to 109.49; $p < 0.001$), prior administration of antibiotics during the same hospitalization (AOR, 2.08; 95% CI, 1.58 to 2.74; $p = 0.008$), decreasing serum albumin concentrations (1-g/dL decrements) (AOR, 1.37; 95% CI, 1.21 to 1.56; $p = 0.014$), and increasing central catheter duration (1-day increments) (AOR, 1.03; 95% CI, 1.02 to 1.04; $p = 0.008$) were independently associated with the administration of inadequate antimicrobial treatment. CONCLUSIONS: The administration of inadequate antimicrobial treatment to critically ill patients with bloodstream infections is associated with a greater hospital mortality compared with adequate antimicrobial treatment of bloodstream infections. These data suggest that clinical efforts should be aimed at reducing the administration of inadequate antimicrobial treatment to hospitalized patients with bloodstream infections, especially individuals infected with antibiotic-resistant bacteria and Candida species.

Ibrahim E.H. et al. *A comparative analysis of patients with early-onset vs late-onset nosocomial pneumonia in the ICU setting.* Chest. 2000; 117(5) : 1434-42.p Abstract: STUDY OBJECTIVE: To compare the clinical outcomes of critically ill patients developing early-onset nosocomial pneumonia (NP; ie, within 96 h of ICU admission) and late-onset NP (ie, occurring after 96 h of ICU admission). DESIGN: Prospective cohort study. SETTING: A medical ICU and a surgical ICU from a university-affiliated urban teaching hospital. PATIENTS: Between July 1997 and November 1998, 3, 668 patients were prospectively evaluated. INTERVENTION: Prospective patient surveillance and data collection. RESULTS: Four hundred twenty patients (11.5%) developed NP. Early-onset NP was observed in 235 patients (56.0%), whereas 185 patients (44.0%) developed late-onset NP. Among patients with early onset NP, 114 patients (48. 5%) spent at least 24 h in the hospital prior to ICU admission, compared to 57 patients (30.8%) with late-onset NP ($p = 0.001$). One hundred eighty-three patients (77.9%) with early-onset NP received antibiotics prior to the development of NP, as compared to 162 patients (87.6%) with late-onset NP ($p = 0.010$). The most common pathogens associated with early-onset NP were Pseudomonas aeruginosa (25.1%), oxacillin-sensitive Staphylococcus aureus (OSSA; 17.9%), oxacillin-resistant S aureus (ORSA; 17.9%), and Enterobacter species (10.2%). P aeruginosa (38.4%), ORSA (21.1%), Stenotrophomonas maltophilia (11.4%), OSSA (10.8%), and Enterobacter species (10.3%) were the most common pathogens associated with late-onset NP. The ICU length of stay was significantly longer for patients with early-onset NP (10.3 +/- 8.3 days; $p < 0.001$) and late-onset NP (21. 0 +/- 13.7 days; $p < 0.001$), as compared to patients without NP (3.5 +/- 3.2 days). Hospital mortality was significantly greater for patients with early-onset NP (37.9%; $p = 0.001$) and late-onset NP (41.1%; $p = 0.001$) compared to patients without NP (13.1%). CONCLUSIONS: Both early-onset and late-onset NP are associated with increased hospital mortality rates and prolonged lengths of stay. The pathogens associated with NP were similar for both groups. This may be due, in part, to the prior hospitalization and use of antibiotics in many patients developing early-onset NP. These data suggest that P aeruginosa and ORSA can be important pathogens associated with early-onset NP in the ICU setting. Additionally, clinicians should be aware of the common microorganisms associated with both early-onset NP and late-onset NP in their hospitals in order to avoid the administration of inadequate antimicrobial treatment.

Ichiyama S. *[Recent advances in diagnostic microbiology for mycobacterial infections].* Rinsho Byori. 1996; 44(9) : 813-7.p Abstract: Definitive diagnosis of tuberculosis continues to depend on microscopy and culture. Since routine diagnostic methods are insensitive and time-consuming (3 to 8 weeks), the development of more sensitive and rapid tests is desirable. More sensitive liquid media, radiometric BACTEC system and nonradiometric Septi-Chek AFB system are currently used in clinical laboratories. Advances in DNA techniques have provided a new approach to rapid diagnosis of mycobacterial

diseases. Species-specific DNA probes for identifying Mycobacterium tuberculosis complex, M. avium, M. intracellulare, M. kansasii, and M. gordonae from cultures of acid-fast microorganisms are now commercially available. Amplification techniques such as polymerase chain reaction (PCR) provide rapid methods for detecting mycobacterial DNA or RNA directly from clinical samples. Two amplification kits, an rRNA amplification-based Gen-Probe Amplified Mycobacterium Tuberculosis Direct Test system and a PCR-based Roche AMPLICOR MYCOBACTERIUM system, are commercially available. These systems have the speed, reliability and requisite diagnostic capability for detecting mycobacteria directly from clinical specimens.

Ieven M. et al. *Relevance of nucleic acid amplification techniques for diagnosis of respiratory tract infections in the clinical laboratory.* Clin Microbiol Rev. 1997; 10(2) : 242-56.p Abstract: Clinical laboratories are increasingly receiving requests to perform nucleic acid amplification tests for the detection of a wide variety of infectious agents. In this paper, the efficiency of nucleic acid amplification techniques for the diagnosis of respiratory tract infections is reviewed. In general, these techniques should be applied only for the detection of microorganisms for which available diagnostic techniques are markedly insensitive or nonexistent or when turnaround times for existing tests (e.g., viral culture) are much longer than those expected with amplification. This is the case for rhinoviruses, coronaviruses, and hantaviruses causing a pulmonary syndrome, Bordetella pertussis, Chlamydia pneumoniae, Mycoplasma pneumoniae, and Coxiella burnetii. For Legionella spp. and fungi, contamination originating from the environment is a limiting factor in interpretation of results, as is the difficulty in differentiating colonization and infection. Detection of these agents in urine or blood by amplification techniques remains to be evaluated. In the clinical setting, there is no need for molecular diagnostic tests for the diagnosis of Pneumocystis carinii. At present, amplification methods for Mycobacterium tuberculosis cannot replace the classical diagnostic techniques, due to their lack of sensitivity and the absence of specific internal controls for the detection of inhibitors of the reaction. Also, the results of interlaboratory comparisons are unsatisfactory. Furthermore, isolates are needed for susceptibility studies. Additional work remains to be done on sample preparation methods, comparison between different amplification methods, and analysis of results. The techniques can be useful for the rapid identification of M. tuberculosis in particular circumstances, as well as the rapid detection of most rifampin-resistant isolates. The introduction of diagnostic amplification techniques into a clinical laboratory implies a level of proficiency for excluding false-positive and false-negative results.

Igari J. et al. *[Antimicrobial activities of roxithromycin against recently obtained clinical isolates].* Jpn J Antibiot. 1997; 50(7) : 640-9.p Abstract: The purpose of our investigation was to monitor current trends in the susceptibility patterns of clinical bacterial isolates to roxithromycin (RXM). We measured the MICs of macrolide antibiotics, such as RXM, erythromycin (EM), clarithromycin (CAM), rokitamycin (RKM) and midecamycin (MDM), and other classes of antibacterial compounds against various clinical isolates at seven institutions between October and December in 1994 and 1995. RXM had excellent antibacterial activities for S. pyogenes, S. agalactiae, M. (B.) catarrhalis and methicillin sensitive S. aureus. Against methicillin sensitive S. epidermidis, RXM activity was fairly good but about 20% of the strains had MIC > or = 128 micrograms/ml. The activity against S. pneumoniae was not so potent and similar to activities of EM, CAM, MDM, and clindamycin. The vast majority of methicillin resistant S. aureus and S. epidermidis were also resistant to macrolide antibiotics and other classes of compounds tested. In conclusion, RXM is an unique macrolide antibiotic by retaining potent activity against S. pyogenes, S. agalactiae, S. aureus except MRSA, M. (B.) catarrhalis and M. pneumoniae.

Ikeda N. *[Serotypes and antimicrobial susceptibility of Streptococcus pneumoniae from clinical specimens].* Kansenshogaku Zasshi. 1995; 69(10) : 1093-102.p Abstract: Studies were made on 66 strains of Streptococcus pneumoniae which were obtained from clinical specimens in 1991 through 1993 and showed 19 mm or less of disk inhibition zone diameter (DIZD) against 1 microgram oxacillin (MPIPC) disk. The studies included the determination of their serotypes, antimicrobial susceptibility, and comparison between microbroth dilution (MD) method and Kirby-Bauer (K-B) method. In the study of distribution of serotypes, additional 32 strains which showed 20 mm or more in DIZD were included for study. The results were as follows. 1) About 70% of 98 strains of S. pneumoniae were serotyped by 6 kinds of antisera. Among penicillin-susceptible S. pneumoniae (PSSP), type 3 were 20.6%, type 19, 15.9%, type 6, 14.3%, type 18, 9.5%, type 14, 7.9%, and type 4, 1.6%. Among penicillin-intermediate S. pneumoniae (PISP), and penicillin-resistant S. pneumoniae (PRSP), type 19 were 60%, and type 18, 8.6%. In PISP and PRSP, more than half were type 19, which indicates they are distinctly different from PSSP in serotypical distribution. 2) As to the difference between screening by MPIPC disk and minimum inhibitory concentration (MIC) by benzylpenicillin (PCG), among 66 MPIPC resistant strains, PSSP strains were 31 in number (47%). 3) MIC showed that PISP and PRSP strains were more resistant than PSSP against cefaclor (CCL), cefazolin (CEZ), cefotiam (CTM), cefotaxime (CTX), imipenem (IPM), minocycline (MINO), and erythromycin (EM), but no difference was found in the 2 groups of strains in MIC with clindamycin (CLDM) and ofloxacin (OFLX). 4) All type 3 strains formed mucoid colonies and were resistant to MINO and highly resistant to EM and CLDM. 5) By NCCLS, category of antimicrobial susceptibility is determined against CCL, EM, OFLX, in MD method and K-B method. Against these antibiotics, the complete agreement rates were 75.8%, 92.4% and 86.4% respectively.

Ikeda N. et al. *[In vitro susceptibility of Streptococcus agalactiae clinical isolates to beta-lactam antibiotics].* Kansenshogaku Zasshi. 1999; 73(2) : 163-71.p Abstract: The susceptibility of Streptococcus agalactiae (S. agalactiae) clinical isolates of Juntendo University Urayasu Hospital, and type strain ATCC 13813 to beta-lactam antimicrobial agents was evaluated by means of macro-broth dilution MIC determination, killing kinetics and population analysis. When 10(6) cells of S. agalactiae were inoculated and cultured in Todd-Hewitt broth containing two-fold serial dilutions of penicillin, the viable cell count showed that about 10(2) cells survived irrespective of the penicillin concentration which ranged from 0.063 to 128 micrograms/ml. The result indicated that S. agalactiae had tolerance to penicillin (MICs were around 0.063 microgram/ml). Furthermore, the S. agalactiae strains were found to have a paradoxical response to penicillin in an acidic condition (pH 5.5). When the cell counts were performed at pH 5.5, about 10(2) cells survived at penicillin concentrations from 0.016 to 0.125 microgram/ml, while about 10(4) cells survived at the concentrations of 1 to 8 micrograms/ml. The antibiotic tolerance and paradoxical effects of S. agalactiae were also observed in killing kinetics. The ATCC 13,813 and 10 out of 11 clinical strains showed slow response to penicillin-mediated killing at pH 7.8 and ATCC 13,813 and one of the clinical strains showed a reduced response with increase in penicillin concentration at pH 5.5. These results suggested that the tolerance and paradoxical effect of S. agalactiae cells to beta-lactam antibiotics may be one of the reasons for frequent re-colonization of S. agalactiae at the time of delivery after the chemophylaxis in the 2nd trimester.

Ikemoto H. et al. *[Susceptibilities of bacteria isolated from patients with respiratory infectious diseases to antibiotics (1992)].* Jpn J Antibiot. 1996; 49(1) : 34-70.p Abstract: Bacteria isolated from lower respiratory tract infections were collected in cooperation with institutions located throughout Japan since 1981, and Ikemoto et al. have been investigating susceptibilities of the isolates to various antibacterial agents and antibiotics, and the relationships between the isolates and characteristics of the patients and so forth each year. We discuss the results in detail. In 20 institutions around the entire Japan from October

1992 to September 1993, 690 strains of bacteria were isolated mainly from sputa of 549 patients with lower respiratory tract infections and presumed to be the etiological bacteria. MICs of various antibacterial agents and antibiotics were determined against 101 strains of Staphylococcus aureus, 121 strains of Streptococcus pneumoniae, 122 strains of Haemophilus influenzae, 92 strains of Pseudomonas aeruginosa (non-mucoid), 32 strains of Pseudomonas aeruginosa (mucoid), 52 strains of Moraxella subgenus Branhamella catarrhalis, 28 strains of Klebsiella pneumoniae etc., and the drug susceptibilities of these strains were measured except the strains which died during transportation. 1. S. aureus S. aureus strains for which MICs of methicillin were higher than 4 micrograms/ml (methicillin-resistant S. aureus) accounted for 61.4% and the frequency of the drug resistant bacteria was higher than the previous year's 58.3%. MICs values indicated that arbekacin was as active as vancomycin against all the strains on S. aureus. 2. S. pneumoniae Benzylpenicillin among the penicillins showed potent activities against S. pneumoniae. Cefuzonam, cefazolin, cefotaxime and cefmenoxime among the cephems showed excellent antimicrobial activities against S. pneumoniae. Imipenem; carbapenems, showed the most potent activity, and MIC80 was 0.015 microgram/ml. 3. H. influenzae All the drugs tested were potent against H. influenzae. Ampicillin among the penicillins showed MIC80 1 microgram/ml against H. influenzae. Cefotaxime, cefmenoxime, cefuzonam and cefixime showed the most potent activities, and MIC80s were 0.063 microgram/ml. The antimicrobial activity of ofloxacin was equivalent to those of cephems. 4. P. aeruginosa (mucoid) Ciprofloxacin showed the most potent activity against P. aeruginosa (mucoid), and MIC80 was 1 microgram/ml. Cefsulodin, aztreonam, carumonam and tobramycin showed the next most potent activities with an MIC80s of 2 micrograms/ml. 5. P. aeruginosa (non-mucoid) Tobramycin and ciprofloxacin showed the highest activities against P. aeruginosa (non-mucoid) with an MIC80s of 2 micrograms/ml. Norfloxacin also showed some activity, and MIC80 was 4 micrograms/ml. Comparing to activities against P. aeruginosa (mucoid), all the drugs tested showed lower activities against P. aeruginosa (non-mucoid). 6. K. pneumoniae The activities of all drugs except penicillins were high activities against K. pneumoniae. Carumonam showed the most potent activity with an MIC80 of 0.063 microgram/ml, followed by flomoxef, cefixime and cefozopran with their MIC80s of 0.125 microgram/ml. 7. M.(B.) catarrhalis Imipenem; carbapenems, showed the most potent activity against M.(B.) catarrhalis with an MIC80 0.063 microgram/ml. Minocycline and ofloxacin showed MIC80s 0.125 microgram/ml, respectively. We also investigated year to year changes in the background of patients, as well as types of respiratory infectious diseases, and the etiological bacteria. As for patients backgrounds, there were many infectious diseases found among patients in a high age bracket, and the patients over age 60 accounted for 60.8% of the diseases. The distribution by lower respiratory tract infections was as follows: bacterial pneumonia and chronic bronchitis accounted for the greatest numbers of cases with 30.4%, 29.5%, respectively, followed by bronchiectasis with 12.2%. As for frequencies of etiologic bacteria for respiratory tract infections, H. influenzae: 22.2%, and S. pneumoniae: 15.1% in chronic bronchitis; S. pneumoniae: 2.

Ikezawa K. et al. *Pretreatment antimicrobial susceptibilities of paired gastric Helicobacter pylori isolates: antrum versus corpus.* Helicobacter. 1999; 4(4) : 218-21.p Abstract: BACKGROUND: Antimicrobial susceptibility testing of Helicobacter pylori isolates is the most useful tool for guiding specific therapy, especially when primary resistance is suspected. However, the most informative gastric biopsy site for detection of resistant H. pylori isolates is uncertain. We sought to determine whether susceptibilities to commonly used antimicrobials (amoxicillin, clarithromycin, minocycline, and metronidazole) were related to biopsy site. METHODS: H. pylori isolates were obtained from patients who had duodenal ulcer and had not received any therapy directed against H. pylori. Agar-dilution minimum inhibitory concentrations of each antimicrobial were compared between paired H. pylori isolates from the antrum and the proximal corpus. RESULTS: Differences in minimum inhibitory concentrations exceeding twofold were observed within the pairs of H. pylori isolates in 5 of the 40 patients tested. In three patients with clarithromycin-resistant isolates and two with metronidazole-resistant isolates, both antral and corporeal specimens revealed resistance. However, no patient had pairs of isolates categorized as resistant at one site and sensitive at the other. CONCLUSIONS: While we found that an individual may have a mixed H. pylori infection with respect to differing antimicrobial susceptibility in different parts of the stomach, a single biopsy specimen from either the antrum or the corpus should provide reliable detection of H. pylori isolates with primary resistance.

Inoue M. et al. *[Susceptibilities of Enterococcus faecium, PRSP and MRSA to RP59500 and their correlations with those to other drugs].* Jpn J Antibiot. 1999; 52(4) : 302-12.p Abstract: Investigations on emergence of vancomycin-resistant Enterococcus faecium (VREF) which has recently been attracting attention, especially in the Western countries, have been conducted in Japan. A total of 1,239 isolates of E. faecium were collected from 19 institutions during the period of April 1995 and June 1996, in the purpose of evaluating susceptibilities to variety of antimicrobial agents, including RP59500 and vancomycin (VCM), and detecting vancomycin-resistant genes (van genes). Susceptibilities of penicillin-resistant Streptococcus pneumoniae (PRSP) and methicillin-resistant Staphylococcus aureus (MRSA) were also studied. As a result, 2 isolates of E. faecium were found to be moderately resistant to VCM showing MIC of 8 micrograms/ml though the final identification in species level and the detection of van genes by PCR method have not been completed. On the other hand there detected no MRSA nor PRSP showing moderately resistant or resistant to VCM. It was concluded that RP59500 and VCM possessed favorable activity against clinically isolated E. faecium, PRSP and MRSA. Among other species of enterococci, moderately resistant strains to VCM showing MIC of 8 micrograms/ml were detected; 10 isolates of E. gallinarum, 4 of E. casseliflavus and 2 of E. flavescens. In those isolates, vanC1 and vanC2 were detected by PCR, and vanB was also detected in a isolates of E. gallinarum simultaneously.

Inoue Y. et al. *Clinical evaluation of catheter-related fungemia and bacteremia.* Intern Med. 1995; 34(6) : 485-90.p Abstract: Forty-four patients with catheter-related infection admitted to Hokusho Central Hospital between 1985 and 1991 were studied retrospectively. The rate of catheter-related fungemia or bacteremia to all corresponding cases of fungemia and bacteremia increased from 7.7% in 1985 to 28.8% in 1991. The isolated pathogens were Candida parapsilosis (8 strains), Candida tropicalis (6 strains), methicillin-resistant Staphylococcus aureus (MRSA) (6 strains), methicillin-sensitive S. aureus (MSSA) (5 strains) and Streptococcus epidermidis (3 strains). Bacteremia occurred after catheterization of the femoral vein for a mean duration of 37 days. The period was significantly shorter than that after catheterization of the subclavian vein (56 days). The major isolates from the subclavian vein were Candida spp. (14/17, 82.4%), followed by MRSA (1/17, 5.9%) and MSSA (1/17, 5.9%), while isolates from the femoral vein were Candida spp. (6/16, 37.5%), MRSA (5/16, 31.3%) and MSSA (3/16, 20.8%). Catheter removal alone did not improve the clinical condition, particularly in MRSA bacteremia; the combination of antimicrobial therapy and removal of the catheter was necessary for a better prognosis.

Iovene M.R. et al. *Prevalence of antimicrobial resistance in eighty clinical isolates of Helicobacter pylori.* Chemotherapy. 1999; 45(1) : 8-14.p Abstract: We studied the in vitro susceptibility of 80 Helicobacter pylori clinical isolates to several antimicrobials commonly used to treat the infection, using the Epsilometer test (E-test). We also compared E-test and disk diffusion test in determining H. pylori susceptibility to the same antibiotics. We found a high prevalence of H. pylori strains resistant to metronidazole (23.7%), whereas the preva-

lence of H. pylori strains resistant to clarithromycin was 10%. Also, a significant correlation was found between MICs obtained with the disk diffusion test and E-test for metronidazole and clarithromycin. In conclusion, our study confirms a high prevalence of metronidazole- or clarithromycin-resistant H. pylori strains. Also, our data suggest that the E-test is a single, reliable, and cost-effective method to assess in vitro susceptibility of H. pylori to antimicrobial agents commonly used to eradicate the infection.

Iroha E.O. et al. *Bacterial eye infection in neonates, a prospective study in a neonatal unit*. West Afr J Med. 1998; 17(3) : 168-72.p Abstract: One hundred and fifty five neonates with conjunctivitis admitted into the neonatal unit at the Lagos University Teaching Hospital were microbiologically investigated. This was to determine the bacterial aetiologic agent(s) in neonatal eye infection and highlight some risk factors. Antimicrobial susceptibility testing was done on the pathogens isolated using the diskagar diffusion method. The incidence of conjuctivitis in the newborn was 18 per 1000 live births. Predisposing factor noted were vaginal delivery, asphyxia neonatorum and prolonged rupture of membrane. Pathogens predominantly isolated were Staphylococcus aureus (37.4%), Coagilase negative Staphylococci (12.3%), Klebsiella pneumoniae (12.9%) and Pseudomonas aeruginosa (8.2%). Antimicrobial suscepibility results revealed varied degrees of susceptibility to ofloxacin (75%), Cloxacillin, erythromycin, Gentamicin and augumentin (30%) by the gram positive bacteria while most of the gram negative were susceptible to colistin and ofloxacin (above 90%). The high incidence of bacterial eye infection should be minimized by the elimination of the risk factors and adoption of stringent aseptic measures in the care of the neonate.

Ishida M. et al. *[Microbiological and clinical studies with Streptococcus pneumoniae isolated in 5 Kitakyushu municipal hospitals]*. Kansenshogaku Zasshi. 1999; 73(11) : 1116-22.p Abstract: Epidemiological and microbiological studies were carried out using 200 strains of pneumococci isolated from clinical specimens in 5 Kitakyushu municipal hospitals, between October 1994 and July 1995. Eighty nine percent of pneumococci were detected in the specimens from the respiratory tract. Pneumococci were isolated mainly from infants under 3-years of age and adults over 50-years of age, and the rates of isolation were 40.5% and 39.5%, respectively. MICs of 8 antimicrobial agents, such as PCG, NFLX, CPFX, LFLX, FLRX, TFLX, SPFX, LVFX, were determined using broth microdilution methods. According to NCCLS standard (1997), recovery rates of PSSP, PISP and PRSP were 48.0%, 39.5% and 12.5%, respectively. Among 7 quinolones, TFLX, SPFX and LVFX were effective so far examined, except for a few resistant strains. Four cases in which quinolones resistant pneumococci were isolated were reviewed retrospectively. Among them 3 cases had been given quinolones before the strains were detected.

Ishida T. et al. *Etiology of community-acquired pneumonia in hospitalized patients: a 3-year prospective study in Japan*. Chest. 1998; 114(6) : 1588-93.p Abstract: STUDY OBJECTIVE: To compare the etiology of community-acquired pneumonia in Japan and Western countries, the causative pathogens were prospectively investigated in patients requiring hospitalization. DESIGN: Prospective study over a 3-year period. SETTING: A community general hospital in Japan. PATIENTS: Three hundred twenty-six episodes of community-acquired pneumonia in 318 patients admitted to the hospital between July 1994 and June 1997. METHODS: The microbiological diagnosis was based on the results of quantitative sputum culture, blood culture, and other invasive procedures, including transthoracic needle aspiration or bronchoscopic examination. Serologic tests for Mycoplasma pneumoniae, Chlamydia spp, Legionella spp, and viruses were also routinely performed. RESULTS: Causative pathogens were identified in 199 episodes (61%). Streptococcus pneumoniae was the most common pathogen (23%), followed by Haemophilus influenzae (7.4%), M pneumoniae (4.9%), and Klebsiella pneumoniae (4.3%). The Streptococcus milleri group and Chlamydia pneumoniae were detected in 3.7 and 3.4% of the episodes, respectively. Pneumonia due to Legionella spp was recognized in only two patients. CONCLUSIONS: The etiology of community-acquired pneumonia in Japan did not differ markedly when compared with that of Western countries except for the low incidence of Legionella pneumonia. C pneumoniae and the S milleri group, which are emerging or newly recognized pathogens, were also significant causative microorganisms.

Ishiguchi T. et al. *Endovascular stent-graft deployment: temporary vena caval occlusion with balloons to control aortic blood flow-experimental canine study and initial clinical experience*. Radiology. 2000; 215(2) : 594-9.p Abstract: Vena caval occlusion was evaluated in animal experiments. In five patients with thoracic aortic aneurysms, two balloon catheters were introduced via the femoral vein to the inferior vena cava and superior vena cava and inflated before stent-graft deployment. Aortic pressure and flow were immediately decreased, which minimized the downstream shift of the stent-grafts. Temporary vena caval occlusion is safe and effective for precise aortic stent-graft deployment.

Ishiguro M. et al. *5,6-Cis-penems: broad-spectrum anti-methicillin-resistant Staphylococcus aureus beta-lactam antibiotics*. J Med Chem. 1997; 40(14) : 2126-32.p Abstract: 5,6-cis-Penem derivatives have been synthesized and evaluated as anti-MRSA antibiotics. The cis-penems 5 and 6 showed potent activities against not only MRSA but also a wide variety of bacteria including beta-lactamase-producing microorganisms. These compounds were designed to have high affinity to the penicillin-binding protein 2a of MRSA and to form stable acyl intermediates with beta-lactamases by blocking the deacylating water molecule.

Ishihara R. et al. *[Antimicrobial activities of cefcapene against clinical isolates from respiratory tract infections of outpatients]*. Jpn J Antibiot. 1998; 51(1) : 1-10.p Abstract: In order to evaluate antimicrobial activity of cefcapene (CFPN), minimum inhibitory concentrations (MICs) of CFPN and reference drugs were determined against clinical isolates from respiratory tract infection of out patients that were obtained in our laboratory from January to June of 1997. The results are summarized as follows; 1. The MIC90 of CFPN against penicillin (PC)-susceptible Streptococcus pneumoniae (PSSP) was equal to those of benzylpenicillin (PCG), ampicillin (ABPC) and cefditoren (CDTR), and was lower than those of cefaclor (CCL), cefdinir (CFDN) and erythromycin (EM). 2. The MIC90 of CFPN against PC-intermediate S. pneumoniae (PISP)/PC-resistant S. pneumoniae (PRSP) was equal to that of CDTR, and was lower than those of PCG, ABPC, CCL, CFDN and EM. CFPN showing strong antimicrobial activities against PISP. 3. CFPN showed strong antimicrobial activities against beta-lactamase producing and non-producing Haemophilus influenzae. The MIC90 of CFPN was stronger than those of ABPC, CCL, CFDN and EM, and was approximately equal to that of CDTR. CFPN also showed strong antimicrobial activities against strains which did not produce any beta-lactamase and were resistant to CCL with MIC of > or = 25 micrograms/ml. 4. Antimicrobial activities of CFPN against Moraxella subgenus Branhamella catarrhalis was stronger than that of ABPC and CCL, though the MIC90 of CFPN was rather high, 3.13 micrograms/ml. 5. CFPN showed strong antimicrobial activities against PISP and beta-lactamase producing H. influenzae, and also against the CCL-resistant H. influenzae indicative mutations of penicillin-binding proteins (PBPs). From those results, cefcapen-pivoxil was found to be clinically effective against community acquired respiratory tract infection.

Ishii Y. et al. *[Antimicrobial activities of cefetamet against clinical isolates from urinary tract infection]*. Jpn J Antibiot. 1996; 49(12) : 1073-84.p Abstract: In order to evaluate antimicrobial activity of cefetamet (CEMT), minimum inhibitory concentrations (MICs) of CEMT and control drugs were determined against Gram-negative rods mainly from complicated urinary tract infections examined in our

laboratory from April to September of 1994. The results are summarized as follows; 1. The obtained strains were Citrobacter diversus 20, Citrobacter freundii 30, Enterobacter aerogenes 20, Enterobacter cloacae 30, Serratia marcescens 30, Proteus mirabilis 30, Proteus vulgaris 20 and Morganella morganii 30 strains, a total of 210 strains. 2. Excluding some resistant strains, the MIC-distribution showed showed that CEMT had strong antimicrobial activities against those strains from the MIC-distribution of this investigation. Compared to reports on CEMT in 1989, the MIC80 of CEMT in this investigation against clinical isolates were similar. The MIC50's of CEMT against E. aerogenes, S. marcescens, P. mirabilis, P. vulgaris and M. morganii in the previous examination were equal to or similar to the current results, but the MIC50's against C. freundii and E. cloacae were lower than the value of this report. The detection frequency of highly resistant strains of C. freundii and E. cloacae to cefteram and cefixime were similar to that of CEMT-resistant strains. Multiple drug resistant strains, among these bacterial species seemed to be increasing. 3. Compared to oral antibacterial agents of oxime cephems that were used in the past, CEMT showed higher peak values of urinary excretion concentration and higher blood levels were sustained for a longer period of time. CEMT-PI will be effective against urinary tract infections.

Iskhakova K.h.I. et al. *[Modified method of inoculation of hemocultures from patients with suppurative-septic diseases and typhoid-paratyphoid fever].* Klin Lab Diagn. 1996; (5) : 41-3.p Abstract: A modified method of isolating hemocultures in pyoseptic processes is proposed. It consists in combined use of two known methods: inoculation of the blood by in-depth method and preliminary hemolysis of the blood, and use of commercial medium for assessing the sterility as the nutrient base. High efficacy of the proposed method has been demonstrated in experiments with 17 reference strains of microorganisms. The new approach helped improve the isolation rate of opportunistic enterobacteria, nonfermenting gram-negative bacteria, staphylococci, highly demanding streptococci, and other microorganisms similar in nutrient requirements, as well as the agents of typhoid and paratyphoid fever. This permits unifying the methods of investigation of hemocultures in pyoseptic diseases and typhoid-paratyphoid fevers'.

Ison C.A. *Antimicrobial agents and gonorrhoea: therapeutic choice, resistance and susceptibility testing.* Genitourin Med. 1996; 72(4) : 253-7.p Abstract: INTRODUCTION: Neisseria gonorrhoeae, the causative agent of gonorrhoea is a particularly well adapted pathogen that has continued to evolve mechanisms to evade treatment with antimicrobial agents. THERAPEUTIC CHOICE: The choice of antibiotic for use in the first-line treatment of gonorrhoea should be made with knowledge of the susceptibility of the isolates of N gonorrhoeae to be encountered. RESISTANCE: High-level resistance to penicillin and tetracycline in N gonorrhoeae is plasmid-mediated and a major therapeutic problem. Penicillinase-producing N gonorrhoeae, first described in 1976, have now spread worldwide and tetracycline-resistant N gonorrhoeae, described in 1985, are becoming increasingly prevalent. Chromosomal resistance to penicillin is low-level and affects a range of antibiotics. High-level resistance to spectinomycin has been sporadic and has not limited its use whereas the emergence of resistance to ciprofloxacin will have a significant impact on its use for gonorrhoea. SUSCEPTIBILITY TESTING: A variety of methods are available including disc diffusion, breakpoint agar dilution technique, E-test and determination of the minimum inhibitory concentration (MIC). The choice of methodology will depend on the number and type of isolates and the facilities available for testing. DISCUSSION: Surveillance programmes to monitor levels of antibiotic resistant isolates are essential to ensure therapeutic success.

Ista L.K. et al. *Surface-grafted, environmentally sensitive polymers for biofilm release.* Appl Environ Microbiol. 1999; 65(4) : 1603-9.p Abstract: Controlling bacterial biofouling is desirable for almost every human enterprise in which solid surfaces are introduced into nonsterile aqueous environments. One approach that is used to decrease contamination of manufactured devices by microorganisms is using materials that easily slough off accumulated material (i.e., fouling release surfaces). The compounds currently used for this purpose rely on low surface energy to inhibit strong attachment of organisms. In this study, we examined the possible use of environmentally responsive (or "smart") polymers as a new class of fouling release agents; a surface-grafted thermally responsive polymer, poly(N-isopropylacrylamide) (PNIPAAM), was used as a model compound. PNIPAAM is known to have a lower critical solubility temperature of approximately 32 degrees C (i.e., it is insoluble in water at temperatures above 32 degrees C and is soluble at temperatures below 32 degrees C). Under experimental conditions, >90% of cultured microorganisms (Staphylococcus epidermidis, Halomonas marina) and naturally occurring marine microorganisms that attached to grafted PNIPAAM surfaces during 2-, 18-, 36-, and 72-h incubations were removed when the hydration state of the polymer was changed from a wettability that was favorable for attachment to a wettability that was less favorable. Of particular significance is the observation that an organism known to attach in the greatest numbers to hydrophobic substrata (i.e., H. marina) was removed when transition of PNIPAAM to a more hydrated state occurred, whereas an organism that attaches in the greatest numbers to hydrophilic substrata (i.e., S. epidermidis) was removed when the opposite transition occurred. Neither solvated nor desolvated PNIPAAM exhibited intrinsic fouling release properties, indicating that the phase transition was the important factor in removal of organisms. Based on our observations of the behavior of this model system, we suggest that environmentally responsive polymers represent a new approach for controlling biofouling release.

Isu N.R. et al. *An evaluation of the microflora associated with fermented African oil bean (Pentaclethra macrophylla Bentham) seeds during ugba production.* Plant Foods Hum Nutr. 1997; 51(2) : 145-57.p Abstract: The microorganisms associated with fermented African oil bean (Pentaclethra macrophylla Bentham) seed during ugba production was studied. Only bacteria were isolated from the ugba samples used. Although the bacteria included Bacillus spp., Lactobacillus spp., Staphylococcus spp., Micrococcus spp. and members of the family Enterobacteriaceae, only the Bacillus spp. were found to ferment African oil bean seeds to ugba. Bacillus spp. were the predominant microorganisms present, constituting over 95% of the total microbial population density. An increase in the number of Bacillus cells of about 2 log units daily, which attained a maximum density of log10 9.00 - log10 11.90 cfu/g after 3 days was observed. Contrarily, the Lactobacillus spp. increased minimally and attained a maximum value of log10 4.20 - log10 6.35 cfu/g within the same period. The Staphylococcus spp., Micrococcus spp. and the members of the family Enterobacteriaceae remained fairly steady in number for 24h, increased slightly till the 3rd day followed by exponential increases which attained maximum values of between log10 9.20 - log10 11.00, about the 7th day. Bacillus spp. cells also had the highest protease activities which were significantly ($p < 0.05$) higher than the values for the other bacterial isolates. The Bacillus spp. responsible for the fermentation of African oil bean seeds to ugba were identified as Bacillus coagulans, B. macerans, B. megaterium, B. pumilis and B. subtilis.

Ito K. et al. *[Pharmacological study on the dry distillation tar of delipidated soybean (Glyteer) (5): Antimicrobial activity].* Nippon Yakurigaku Zasshi. 1995; 105(6) : 469-78.p Abstract: Glyteer (GL) possessed a broad antimicrobial spectra against bacteria and fungi. The antimicrobial activity of GL was bactericidal action, but not bacteriostatic action. GL was more effective against fungi than bacteria. GL ointment also showed antimicrobial activity equal to that of GL. Furthermore, GL had an effect on methicillin-resistant Staphylococcus aureus (MRSA). Resistance to GL was not induced in broth cultures of Escherichia coli, Staphylococcus aureus, Streptococcus pyogenes, Candida albicans, and Trichophyton mentagrophytes. These results

suggest that GL applied externally exerts a potent effect as an antimicrobial drug for dermopathy with various microbialpathogens.

Ito T. et al. *[Evaluation of antibiotics used for enterohemorrhagic Escherichia coli O157 enteritis—effect of various antibiotics on extracellular release of verotoxin].* Kansenshogaku Zasshi. 1997; 71(2) : 130-5.p Abstract: We tested antimicrobial activities of ten oral antibiotics; ampicillin (ABPC), cefdinir (CFDN), cefaclor (CCL), fosfomycin (FOM), norfloxacin (NFLX), nalidixic acid (NA), kanamycin (KM), minocycline (MINO), doxycycline (DOXY), and tetracycline (TC) against eleven enterohemorrhagic Esherichia coli (EHEC) O157 clinical strains. Two strains were resistant to ABPC and TC. Other strains were sensitive to all the ten antibiotics. To investigate the effect of antibiotics on extracellular release of verotoxin (VT), strain EHEC TT10 was grown in 10 ml of LB containing various concentrations of the antibiotics for 2 h. Number of viable cells were counted and the amounts of VT1 and VT2 released in the supernatants were measured with reverse passive latex agglutination (RPLA) using serially diluted sterilized culture supernatants. The amount of VT1 and VT2 was evidently increased with ABPC, CFDN, CCL, and FOM, the inhibitors of cell wall biosynthesis. In the case of quinolons, VT2 was markedly increased, but VT1 was not released to the supernatant. KM killed the bacteria efficiently, but no release of VT1 or VT2 was observed in the supernatant. Tetracyclines (MINO, DOXY, and TC) did not make the bacteria release either VT1 or VT2, but could not kill the bacteria appreciably. These results indicated that the inhibitors of protein synthesis (KM, MINO, DOXY, TC) are the safe antibiotics not causing the release of verotoxin from the cells and thus preventing development of hemolytic uremic syndrome (HUS) or thrombotic thrombocytopenic purpra (TTP), the important sequelae of the enteritis.

Itokazu G.S. et al. *Antimicrobial resistance rates among aerobic gram-negative bacilli recovered from patients in intensive care units: evaluation of a national postmarketing surveillance program.* Clin Infect Dis. 1996; 23(4) : 779-84.p Abstract: We assessed the rates of antimicrobial resistance between 1990 and 1993 in intensive care units in the United States. A standardized microtiter minimal inhibitory concentration panel was used to test approximately 100 consecutive gram-negative aerobic isolates that were recovered primarily from blood, wounds, urine, and pulmonary sites in patients treated in each of 396 intensive care units in 45 states. Amikacin and imipenem were the agents most active against the 33,869 nonduplicate isolates (those recovered only once) tested. Resistance of aerobic gram-negative bacilli to third-generation cephalosporins was found to be an emerging problem. Increases in rates of resistance to ceftazidime among isolates of Klebsiella pneumoniae (from 3.6% to 14.4%; P <<.01) and Enterobacter species (from 30.8% to 38.3%; P =.0004) were noted from 1990 to 1993; rates of resistance among Pseudomonas aeruginosa isolates remained stable. Ceftazidime-resistant bacteria were frequently resistant to aminoglycosides and ciprofloxacin. Risk factors for ceftazidime resistance included the number of beds in the hospital, the teaching status of the hospital, and specific body sites from which the isolates were recovered.

Ivanchenko O.B. et al. *[Antimutagenic activity of the enzyme preparation "binase" in microbial test systems].* Mikrobiologiia. 1995; 64(2) : 234-8.p Abstract: The occurrence of microorganisms and the rates of terminal biogenic reduction of sulfates and synthesis of methane in stratal waters in deposit 302 of Bashkir Carboniferous deposition at the Romashkinskoe oil field were studied. It was shown that deposit 302 is a dynamic, highly reduced ecosystem containing sulfates and hydrogen sulfide in considerable concentrations, in which active biogenic processes occur. Sulfate reduction is a dominating anaerobic process by which the organic constituents of oil are transformed. The sulfate-reducing microflora is quite varied and characterized by high metabolic potentials. Enriched cultures, which can oxidize many organic substances, such as benzoate, acetate, ethanol, or lactate, at the expense of reduction of sulfates and ferric ion, were isolated from the samples extracted from deposit 302. It was suggested that the sulfate-reducing microflora might be responsible not only for sulfate reduction in the stratum but also for mobilization of part of insoluble iron oxides in the oil trap rock. The findings indicate that the dissimilation sulfate- and iron-reducing bacteria can contribute to the geochemistry of organic and mineral compounds in underground ecosystems.

Ivanov A.I.u. et al. *[Toxic effect of hydroxylated ions of heavy metals on the cytoplasmic membrane of bacterial cells].* Mikrobiologiia. 1997; 66(5) : 588-94.p Abstract: The influence of nickel, copper, cadmium, and lead ions at concentrations of 50 to 100 microM on the barrier properties of the plasma membrane (PM) and the electrophoretic mobility (EPM) of Pseudomonas fluorescens 71, Escherichia coli K-12, and Mycobacterium phlei B-1291 VKM cells was studied at pH values from 5 to 9 by electro-orientational (EO) spectroscopy and microelectrophoresis of cells. According to the data of EO spectroscopy, the increase in the toxicity of heavy metal cations to cells corresponded to transition of cations to monovalent hydroxylated forms. Hydroxylated ions were found to more easily adsorb on, or penetrate across, the PM and to bind to competent proteins. During the treatment of all three investigated microorganisms with Cu and Pb ions, and gram-negative bacteria also with Ni ions, the EPM of cells changed in a pH range corresponding to the transition of bivalent metal ions to their monovalent hydroxylated forms. Changes in the EPM induced by increasing pH correlated well with the enhanced toxicity of these metals to the PM, as evidenced by the EO spectroscopy data. At the same time, this correlation was less pronounced for cadmium sulfate toxicity to all of the microorganisms studied and for nickel chloride toxicity to M. phlei cells.

Ivanovski S. et al. *Disinfection of dental stone casts: antimicrobial effects and physical property alterations.* Dent Mater. 1995; 11(1) : 19-23.p Abstract: OBJECTIVES. The purpose of this study was to evaluate the effectiveness of disinfecting solutions incorporated into dental stone casts against a standard and representative group of microorganisms and to note changes in the physical properties of the casts. METHODS. Irreversible hydrocolloid impressions were contaminated individually with Escherichia coli, Staphylococcus aureus, Enterobacter cloacae, Pseudomonas aeruginosa, Klebsiella pneumoniae, Actinobacter calcoaceticus, Bacillus subtilis, Mycobacterium phlei and Candida albicans. Four readily available disinfecting solutions (glutaraldehyde, povidone-iodine, chlorhexidine and sodium hypochlorite) were added to the die stone mix used to pour up the impressions. The set cast surfaces were swabbed at 1 h and 24 h, the samples plated on agar and incubated at 37 degrees C for 24 h and 3 d for M. phlei. Subsequently, colony forming units were counted. The physical properties assessed were setting time, setting expansion, compressive strength, detail reproduction and delayed expansion of the stone. RESULTS. Only glutaraldehyde and povidone-iodine killed all contaminating microorganisms within 1 h, while the 1:5 dilution of sodium hypochlorite solution was equally effective after 24 h. Two percent glutaraldehyde was the most effective disinfectant with the least adverse effects on the physical properties of the set cast. Although povidone-iodine caused a decrease in the compressive strength of the set cast, it can be considered to be a sound alternative. SIGNIFICANCE. This study supports the concept of incorporating disinfectants into model stone as a standard operating procedure for impressions of unknown history and, most sensibly, all dental impressions.

Iwen P.C. et al. *Revised approach for identification and detection of ampicillin and vancomycin resistance in Enterococcus species by using MicroScan panels.* J Clin Microbiol. 1996; 34(7) : 1779-83.p Abstract: The frequency of antimicrobial agent-resistant enterococci is increasing, making accurate identification and screening for susceptibility essential. We evaluated the ability of MicroScan Positive Breakpoint Combo Type 6 panels (Dade MicroScan Inc., West Sacramento, Calif.) to identify Enterococcus species and to detect ampicillin and vancomycin resistance. A total of 398 well-characterized Enterococcus isolates from two institutions were inoculated into MicroScan panels, into conventional biochemical assays, and into ampicillin and vancomycin agar dilution media. Resistance was verified by the broth macrodilution method. MicroScan panels accurately detected resistance to ampicillin in 132 of 132 enterococcal isolates, while three isolates for which the MICs were < 16 micrograms/ml were classified incorrectly by MicroScan panels as resistant. No beta-lactamase-producing enterococci were detected. All 64 isolates showing resistance to vancomycin (MICs > or = 32 micrograms/ml) were correctly classified by MicroScan panels. Seven isolates for which the vancomycin MICs were 8 and 16 micrograms/ml were incorrectly classified as susceptible by MicroScan panels, while eight isolates for which the MICs were 4 micrograms/ml were incorrectly labeled as intermediate. Fourteen of these 15 isolates were subsequently identified as motile enterococci. Overall, there were three major errors in susceptibility testing for ampicillin and 15 minor errors for vancomycin. Conventional testing confirmed the identity of 181 Enterococcus faecalis isolates, 157 E. faecium isolates, and 60 isolates of other species; however, 56 of these 60 isolates were misidentified by the MicroScan panels. After recognition of this problem, a revised approach which included tests for pigment, motility, and sucrose fermentation was devised. In combination with these additional assays, the conventional MicroScan panels accurately identified the 56 originally misidentified isolates. In summary, the ability of MicroScan panels to detect vancomycin and ampicillin resistance in enterococci was confirmed. Our study found that the inability of MicroScan panels to identify enterococci other than E. faecalis and E. faecium can be compensated for by the addition of standard assays.

Iyobe S. *[Appearance of extended-spectrum beta-lactamases].* Nippon Rinsho. 1997; 55(5) : 1219-24.p Abstract: Extended-spectrum beta-lactamases (ESBLs) are enzymes which hydrolyze broad-spectrum beta-lactam antibiotics by expanding the substrate spectra into the so-called anti-beta-lactamase beta-lactams such as oxyimino-cephalosporins, cephamycins, oxacephems, carbapenems and monobactams, conferring resistance to many kinds of beta-lactams on pathogenic bacteria. Recently, ESBLs have been demonstrated from various types of beta-lactamases phylogenetically belonging to the molecular class, A, B, C, or D. The genes coding for ESBLs are chromosome- or plasmid-mediated and some of them have developed by point or insertion mutations in the parental genes coding for the narrow-spectrum beta-lactamase. If the genes are plasmid-mediated, the dissemination among various species of pathogenic bacteria would cause hospital-acquired infections by ESBL-producing bacteria.

Izzillo R. et al. *[Leiomyosarcoma of the superior vena cava: diagnosis by endovascular biopsy].* J Radiol. 2000; 81(6) : 632-5.p Abstract: We report the case of a 69-year-old woman with leiomyosarcoma of the superior vena cava presenting with acute superior vena cava syndrome (SVCS). CT and MRI failed to fully characterize the endovascular process. Percutaneous endovascular biopsy, followed by metallic stent placement to treat the SVCS, confirmed the diagnosis. Symptoms resolved within 48 hours and surgical resection of the tumor was performed one month later. Unfortunately the patient died two weeks later because of intracranial hemorrhage.

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Jackson M.M. et al. *Pathogens, old and new: an update for cardiovascular nurses.* J Cardiovasc Nurs. 1999; 13(2) : 1-22.p Abstract: Infectious diseases remain the major cause of death throughout the world, and this is not likely to change in the foreseeable future. However, there are steps that can be taken to combat them, including both the recognition of and interventions against emerging infectious diseases. This article will provide general information about emerging infectious organisms, mechanisms of resistance to antimicrobial agents, and comments on a variety of prevention strategies. In addition, the reader is directed to a number of comprehensive references for additional information.

Jacobs M.R. *Respiratory tract infection: epidemiology and surveillance.* J Chemother. 1997; 9 Suppl 3 : 10-7.p Abstract: Streptococcus pneumoniae and Haemophilus influenzae are the key pathogens implicated in bacterial infections of the upper and lower respiratory tract. Choice of empiric oral antimicrobial chemotherapy is guided by the clinical presentation, severity of the infection and epidemiological knowledge. beta-Lactams and the macrolides are the two major groups of antibiotics used to treat respiratory tract infections. The prevalence of penicillin-resistant strains of S. pneumoniae is increasing world-wide (up to 30% in the USA), as is the prevalence of beta-lactamase-producing strains of H. influenzae. Macrolide resistance in S. pneumoniae is increasing and is absolute, and some of the macrolides have only limited activity against H. influenzae. Knowledge of local and global antibiotic resistance patterns should be used as the key to directing empiric choice of antibiotic treatment.

Jacobs M.R. et al. *Susceptibilities of Streptococcus pneumoniae and Haemophilus influenzae to 10 oral antimicrobial agents based on pharmacodynamic parameters: 1997 U.S. Surveillance study.* Antimicrob Agents Chemother. 1999; 43(8) : 1901-8.p Abstract: The susceptibilities of Streptococcus pneumoniae (1,476 strains) and untypeable Haemophilus influenzae (1,676 strains) to various oral beta-lactam, macrolide-azalide, and fluoroquinolone antimicrobial agents were determined by broth microdilution. Organisms were isolated from

specimens obtained from outpatients in six geographic regions of the United States. MIC data were interpreted according to pharmacodynamically derived breakpoints applicable to the oral agents tested. Among H. influenzae strains, 41.6% were beta-lactamase positive. Virtually all H. influenzae strains were susceptible to amoxicillin-clavulanate (98%), cefixime (100%), and ciprofloxacin (100%), while 78% were susceptible to cefuroxime, 57% were susceptible to amoxicillin, 14% were susceptible to cefprozil, 9% were susceptible to loracarbef, 2% were susceptible to cefaclor, and 0% were susceptible to azithromycin and clarithromycin. Among S. pneumoniae isolates, 49.6% were penicillin susceptible, 17.9% were intermediate, and 32.5% were penicillin resistant, with penicillin MICs for 50 and 90% of the isolates tested of 0.12 and 4 microg/ml, respectively. Overall, 94% of S. pneumoniae isolates were susceptible to amoxicillin and amoxicillin-clavulanate, 69% were susceptible to azithromycin and clarithromycin, 63% were susceptible to cefprozil and cefuroxime, 52% were susceptible to cefixime, 22% were susceptible to cefaclor, and 11% were susceptible to loracarbef. Although ciprofloxacin has marginal activity against S. pneumoniae, no high-level fluoroquinolone-resistant strains were found. Significant cross-resistance was found between penicillin and macrolides-azalides among S. pneumoniae isolates, with 5% of the penicillin-susceptible strains being macrolide-azalide resistant, compared with 37% of the intermediate isolates and 66% of the resistant isolates. Resistance was highest in S. pneumoniae isolates from patients younger than 10 years of age, middle ear and paranasal sinus specimens, and the southern half of the United States. With the continuing rise in resistance, judicious use of oral antimicrobial agents is necessary in all age groups.

Jacobs M.R. et al. *Prevalence of antimicrobial-resistant pathogens in middle ear fluid: multinational study of 917 children with acute otitis media.* Antimicrob Agents Chemother. 1998; 42(3) : 589-95.p Abstract: The management of acute otitis media is complicated by the emergence of resistance to beta-lactam and other antibiotics among common pathogens. We conducted a large, international study of infants and children with acute otitis media to identify pathogens and susceptibility patterns. During the winter of 1994 to 1995, middle ear fluid samples were collected from 917 patients with acute otitis media in Bulgaria, the Czech Republic, Hungary, Romania, Slovakia, Israel, and the United States. A single reference laboratory performed in vitro susceptibility testing. Pathogens were isolated from 62% of the patients. For Streptococcus pneumoniae (30% of the patients), untypeable Haemophilus influenzae (17%), and Moraxella catarrhalis (4%), there was significant variation among geographic regions ($P < 0.001$). The composite susceptibilities of these three organisms to amoxicillin ranged from 62% in the United States to 89% in Eastern and Central Europe; the corresponding susceptibilities to amoxicillin-clavulanate ranged from 90% in Israel to 95% in Eastern and Central Europe. beta-Lactamase was produced by 31 and 100% of the isolates of H. influenzae and M. catarrhalis, respectively. More isolates of S. pneumoniae were susceptible to amoxicillin (90%) or amoxicillin-clavulanate (90%) than to penicillin (70%; $P = 0.002$). The prevalence of resistant S. pneumoniae was highest in patients less than 12 months of age. S. pneumoniae, H. influenzae, and M. catarrhalis remain the most important bacterial pathogens in patients with acute otitis media; however, their prevalence is variable and resistance patterns are changing.

Jacobsen C.N. et al. *Screening of probiotic activities of forty-seven strains of Lactobacillus spp. by in vitro techniques and evaluation of the colonization ability of five selected strains in humans.* Appl Environ Microbiol. 1999; 65(11) : 4949-56.p Abstract: The probiotic potential of 47 selected strains of Lactobacillus spp. was investigated. The strains were examined for resistance to pH 2.5 and 0.3% oxgall, adhesion to Caco-2 cells, and antimicrobial activities against enteric pathogenic bacteria in model systems. From the results obtained in vitro, five strains, Lactobacillus rhamnosus 19070-2, L. reuteri DSM 12246, L. rhamnosus LGG, L. delbrueckii subsp. lactis CHCC 2329, and L. casei subsp. alactus CHCC 3137, were selected for in vivo studies. The daily consumption by 12 healthy volunteers of two doses of 10(10) freeze-dried bacteria of the selected strains for 18 days was followed by a washout period of 17 days. Fecal samples were taken at days 0 and 18 and during the washout period at days 5 and 11. Lactobacillus isolates were initially identified by API 50CHL and internal transcribed spacer PCR, and their identities were confirmed by restriction enzyme analysis in combination with pulsed-field gel electrophoresis. Among the tested strains, L. rhamnosus 19070-2, L. reuteri DSM 12246, and L. rhamnosus LGG were identified most frequently in fecal samples; they were found in 10, 8, and 7 of the 12 samples tested during the intervention period, respectively, whereas reisolations were less frequent in the washout period. The bacteria were reisolated in concentrations from 10(5) to 10(8) cells/g of feces. Survival and reisolation of the bacteria in vivo appeared to be linked to pH tolerance, adhesion, and antimicrobial properties in vitro.

Jadavji T. et al. *A practical guide for the diagnosis and treatment of pediatric pneumonia.* CMAJ. 1997; 156(5) : S703-11.p Abstract: OBJECTIVE: To develop guidelines for the diagnosis and management of community-acquired pediatric pneumonia. OPTIONS: Clinical assessment, radiography, laboratory testing, and empirical antimicrobial therapy. OUTCOMES: Increased awareness of age-related causes, improved accuracy of clinical diagnosis, better utilization of diagnostic testing and the rational use of empirical antimicrobial therapy resulting in more rapid diagnosis, initiation of appropriate therapy and decreased morbidity and mortality. EVIDENCE: A MEDLINE search for relevant articles published from 1996 to September 1996 using the MeSH terms "pediatric," "pneumonia," "respiratory tract infection," "pneumonitis," "etiology," "diagnosis," "therapy," "antibiotics," "resistance," "radiology," "microbiology" and "biochemistry." VALUES: A hierarchical evaluation of the strength of evidence modified from the methods of the Canadian Task Force on the Periodic Health Examination was used. When application of the hierarchy was not feasible or appropriate, different evaluation criteria were used. BENEFITS, HARMS AND COSTS: Increased awareness of the causes of pneumonia, accurate diagnosis and prompt treatment should reduce costs associated with unnecessary investigations and complications due to inappropriate treatment. RECOMMENDATIONS: Age is the best predictor of the cause of pediatric pneumonia, viral pneumonia being most common during the first 2 years of life. The absence of a symptom cluster of respiratory distress, tachypnea, crackles and decreased breath sounds accurately excludes the presence of pneumonia (level II evidence). Bacterial cultures of samples from the nasopharynx and throat have no predictive value; however, Gram staining and culture of sputum from older children and adolescents are useful (level III evidence). Oral antimicrobial therapy will provide adequate coverage for most mild to moderate forms of pneumonia in children (level III evidence). Parenteral therapy is typically reserved for neonates and patients with severe pneumonia admitted to hospital (level III evidence). VALIDATION: These recommendations are based on consensus of Canadian experts in infectious diseases and microbiology. They are the only guidelines to address antimicrobial treatment from an age-related, etiologic perspective. SPONSOR: The development of these guidelines and the technical support and assistance of Core Health Inc. in preparing this manuscript were funded through an unrestricted educational grant from Abbott Laboratories Canada. The sponsoring company was not involved in determining the membership of the consensus group or the content of the guidelines.

Jagarlamudi R. et al. *Infections in acute leukemia: an analysis of 240 febrile episodes.* Med Oncol. 2000; 17(2) : 111-6.p Abstract: Infections are the major cause of morbidity and mortality in acute leukemia patients. Case records of 91 consecutive patients (AML-48, ALL-40, RAEB-t/AML-3) treated between January 1997 and July 1999 were studied to determine the type, frequency and severity of infections. Patients' median age was 36 y (range 6-66) and male to female ratio was 2.5:1. A total of 240 febrile episodes were recorded; of them, 162

were associated with neutropenia (absolute neutrophil count, ANC<500/mm3) and 78 were without neutropenia. Among the neutropenic episodes, an infectious etiology could be documented in 52%; the remainder (48%) were defined as isolated febrile episodes. Chest was the most common site of infection (35. 7%) followed by skin, soft tissue (13%), GIT (7%) and genitourinary tract (6%) infections in order of decreasing frequency. Microbiologically, gram positive organisms (staphylococcus aureus, coagulase negative staphylococcus, streptococcus, enterococcus) were the most common isolates (52.8%) followed by gram negative organisms (E. coli, klebsiella, pseudomonas) in 42.8% of isolates. Two patients had pulmonary tuberculosis and three patients had fungal infections (candida-2, aspergillus-1). Among non-neutropenic patients, infection could be documented in 36%; the remaining 64% were isolated febrile episodes. Gram negative infections were documented in 50%, gram positive in 30% and fungal infections (candida-4, aspergillus-1, mucormycosis-1) in 20% of them. A combination of third generation cephalosporin and an aminoglycoside were used in 79% of episodes initially; a combination of a newer penicillin and aminoglycoside (4.6%), double betalactums (4.1%), oral antibiotics (9.8%) and others were used in the remaining episodes. Fever resolved in 38% of episodes using the above combinations; in the remainder second line antibiotics (mainly vancomycin) and antifungals (amphotericin-B) were added empirically or depending on culture and sensitivity. In 52.5% of episodes fever resolved after addition of second line antibiotics and antifungals. 11 of 91 patients died of infectious complications in this study. There is a need for improvised diagnostic tests to detect infections early as well as for new therapies to overcome antimicrobial resistance.

Jahan Y. et al. *Multiple drug-resistant Shigella dysenteriae type 1 in Rajbari district, Bangladesh*. J Diarrhoeal Dis Res. 1997; 15(1) : 17-20.p Abstract: Twenty-one Shigellae isolates were obtained from bloody faecal specimens of diarrhoeal patients at Rajbari District Hospital from January 1994 to June 1995, and serogrouped. Fourteen (67%) isolates belonged to the Shigella dysenteriae serogroup and 7 (33%) to Shigella flexneri serogroup. Shigella dysenteriae strains were further serotyped; all were Shigella dysenteriae 1. Each strain was tested for resistance to 6 common antimicrobial agents. The two strains had different antibiotic susceptibility patterns. The 7 S. flexneri showed 6 different resistant patterns and the 14 S. dysenteriae 1 isolates had 4 resistance patterns. One of the S. dysenteriae 1 isolates was resistant to all 6 antimicrobial agents; 10 to 5, and twice to a different combination of 4 antimicrobials. The 14 (100%) S. dysenteriae 1 strains were resistant to 3 major antimicrobial agents: ampicillin, tetracycline, and chloramphenicol; 13 (93%) were resistant to 5 agents: ampicillin, tetracycline, chloramphenicol, trimethoprim-sulphamethoxazole, and nalidixic acid. Ciprofloxacin was the only drug active against all 7 S. flexneri and 13 of the 14 (93%) S. dysenteriae 1 strains.

Jamal W.Y. et al. *An analysis of hospital-acquired bacteraemia in intensive care unit patients in a university hospital in Kuwait*. J Hosp Infect. 1999; 43(1) : 49-56.p Abstract: An analysis of hospital-acquired bacteraemia among ICU patients was carried out over a two-year period in order to determine the incidence, associated mortality rate and susceptibility pattern of causative pathogens. There was a high incidence of bacteraemia, occurring in 127 (18.4%) of 692 patients. Mortality attributable to nosocomial bacteraemia was 52% of the total 79 deaths from all causes. The highest mortality rate (58.5%) occurred in patients with fungal infections, whilst death from Gram-negative bacteraemia was only 17%. Over 98% of patients had underlying disease. Nearly half (46.8%) of 267 organisms isolated were Gram-positive. In comparison, Gram-negative bacteria accounted for 36.6% and the rest (17.6%) were fungi (mainly Candida albicans). The majority of the bactereamic episodes were monomicrobial (90.2%). Coagulase-negative staphylococci (CNS) were the commonest pathogens isolated, representing 32.6% of all organisms. Inducible beta-lactamase producing organism (Enterobacter spp. 9.7%, Serratia marcescens 6.7%, Klebsiella pneumoniae 6% and Pseudomonas aeruginosa 6%) formed the bulk of Gram-negative bacteria. In contrast, Escherichia coli (7.5%) and K. pneumoniae (4%) were the commonest Gram-negative bacteria from hospital-acquired bacteraemia in the general hospital population. The majority (80%) of CNS were resistant to methicillin (MRSE) but susceptible to vancomycin; they were relatively resistant to erythromycin, clindamycin and beta-lactams antibiotics. Whilst Gram-negative organisms were relatively susceptible to imipenem (85%), ciprofloxacin (88%) and amikacin (87%), they had unacceptably low levels of susceptibility to cefuroxime (59.3%), cefotaxime (71%), ceftazidime (60.9%), and piperacillin (51.1%). This study shows that hospital-acquired bacteraemia in ICU patients carries a poor prognosis. Information regarding the infective agents and their susceptibility in the ICU setting is valuable for the selection of empirical therapy before culture and susceptibility results are known. Copyright 1999 The Hospital Infection Society.

Jamal W.Y. et al. *Serogroups and antimicrobial susceptibility of clinical isolates of Salmonella species from a teaching hospital in Kuwait*. J Diarrhoeal Dis Res. 1998; 16(3) : 180-6.p Abstract: Salmonella strains isolated in a teaching-cum-general hospital in Kuwait during 1990-1993 and 1996 were analysed to determine the trend in the prevalence of the serogroups and their changing pattern of susceptibility. The records were reviewed for all the 661 isolates encountered during these periods. The most prevalent serogroup in both children and adults was serogroup B, followed by serogroup C and D. A sizeable proportion of the strains were resistant to first-line drugs. About 39% of the isolates were resistant to ampicillin, 17% to co-trimoxazole, 13% to chloramphenicol, and 15% to cephalothin. The majority were, however, susceptible to the other drugs with low to very low resistance rates: 7% to amoxicillin/clavulanic acid, and 0.3% to cefotaxime. All the strains were susceptible to ciprofloxacin. In all, resistant strains were more prevalent among children than adults.

Jamjian C. et al. *In vitro evaluation of a novel ketolide antimicrobial agent, RU-64004*. Antimicrob Agents Chemother. 1997; 41(2) : 454-9.p Abstract: Ketolides, a novel macrolide subclass, possess a mode of action that is similar to that of structurally related macrolide-lincosamide-streptogramin (MLS) compounds. By using reference in vitro tests, the in vitro activity of RU-64004 was compared to those of six other MLS compounds against more than 800 clinical pathogens, including 356 gram-positive organisms. The spectrum of activity of the ketolide was most similar to that of clindamycin versus staphylococci and streptococci and superior to those of all macrolides tested against oxacillin-resistant staphylococci and vancomycin-resistant (vanA, vanB, and vanC) enterococcal isolates. The activity of the ketolide was greater than those of the macrolides, azalides, or clindamycin tested against vancomycin-susceptible enterococci (MICs at which 90% of isolates are inhibited [MIC90S], 0.25 to 4 micrograms/ml), penicillin-resistant pneumococci (MIC90, 0.25 micrograms/ml), and most beta-hemolytic streptococci. All Streptococcus pneumoniae and beta-hemolytic streptococcus strain were inhibited by ketolide concentrations of < or = 0.25 micrograms/ml. Against 165 erythromycin-resistant strains, RU-64004 inhibited (MICs, < or = 0.5 micrograms/ml) approximately one-third of staphylococci, all streptococci, and slightly more than one-half of the enterococci. Quinupristin-dalfopristin (a streptogramin combination) was active against all tested isolates with the exception of non-Enterococcus faecium enterococci, against which the ketolide exhibited greater potency (MIC50S, 0.03 to 2 micrograms/ml). The ketolide was also active against Haemophilus influenzae (MIC90, 2 micrograms/ml), Moraxella catarrhalis (MIC90, 0.12 micrograms/ml), pathogenic Neisseria spp. (MIC90, 0.5 micrograms/ml), and many gram-positive anaerobes (MIC90, 0.5 micrograms/ml). RU-64004 may enhance the role of macrolide drugs in the treatment of some serious infections caused by MLS-resistant gram-positive organisms.

Janata J. et al. *Translation initiation factors of a tetracycline-producing strain of Streptomyces aureofaciens.* Biochem Biophys Res Commun. 1995; 208(2) : 569-75.p Abstract: Protein synthesis initiation factors from a tetracycline-producing strain of Streptomyces aureofaciens were purified and characterized. Two forms of IF3 (M(r) = 24,000 and 22,500) were found. By Western blot analysis, only one form of protein IF2 cross-reactive with anti-IF2 of Escherichia coli was revealed. The molecular mass of purified IF2 was 69,000 as determined by SDS-polyacrylamide gel electrophoresis. In spite of differences in molecular mass between the IF2 forms of E. coli and the factor from S. aureofaciens, the latter could substitute IF2 of E. coli in the stimulation of codon-specific binding of initiator tRNA. In contrast to the reported absence of IF1 in some Gram-positive microorganisms, we found "protein IF1" (M(r) = 9,000) in S. aureofaciens that increased the IF2-dependent binding of initiator tRNA to ribosomes.

Janatova J. *Activation and control of complement, inflammation, and infection associated with the use of biomedical polymers.* ASAIO J. 2000; 46(6) : S53-62.p Abstract: It is generally acknowledged that artificial biomaterials are much less immunologically active than transplants or tissue derived biomaterials. However, activation of both the coagulation cascade and the complement system is a common occurrence when human blood is exposed to biomaterial surfaces during extracorporeal procedures, such as renal hemodialysis or cardiopulmonary bypass. Both individual and collective activation of these cascades often produce local and systemic effects. A number of complement activation products function as the mediators of inflammation. They serve as ligands for specific receptors on polymorphonuclear leukocytes, monocytes, macrophages, mast cells, and other cells. Such an interaction leads to induction of cellular responses in adhered cells, including release of oxidative products, lysosomal enzymes, or both, which often contribute to a number of pathologic conditions. Most pathogens invading the human body are attacked by the immune system directly following entry, especially when they are in contact with blood. However, bacteria and parasites have developed a large number of specific strategies to overcome immune defense among others by avoiding either recognition or eradication by complement. In this aspect, of concern are several microorganisms responsible for formation of antibiotic resistant biofilms on biomaterial surfaces, namely Staphylococcus epidermidis, Staphylococcus aureus, and Pseudomonas aeruginosa.

Janicka G. et al. *[Resistance to antibiotics of Streptococcus pneumoniae strains].* Pol Merkuriusz Lek. 1997; 3(17) : 231-3.p Abstract: Streptococcus pneumoniae strains are exhibiting increasing rates of antibiotics resistance. A rapid increase of resistance was seen not only to penicillin but also other antimicrobial agents and therefore this paper describes the study of resistance and multiresistance of pneumococci to 7 antibiotics: penicillin (P), erythromycin (E), clindamycin (CC), tetracycline (T), co-trimoxazole (SXT), cefotaxime (CTX) and vancomycin (Va), using the disk-diffusion technique according to NCCLS procedure. We tested a total of 218 S. pneumoniae strains isolated from various materials: from sputum (54), noses (117), throats (28) and different swabs specimens (19). The overall percentage of resistant isolates to penicillin was 3.7%, to erythromycin—4.1%, to clindamycin—10.6%, to tetracycline—17.4%, to co-trimoxazole—15.6%, to cefotaxime—2.3%. In the sputum was most the monoresistant strains (66.7%). The multiresistance was highest in the penicillin resistant pneumococci. With the exception of vancomycin, the number of resistant strains to non-beta-lactam antibiotics (erythromycin, clindamycin, tetracycline, co-trimoxazole) was higher in penicillin-resistant strains compared with penicillin susceptible isolates. All isolates were susceptible to vancomycin.

Janier M. et al. *Male urethritis with and without discharge: a clinical and microbiological study.* Sex Transm Dis. 1995; 22(4) : 244-52.p Abstract: BACKGROUND: The definition of male urethritis in the absence of urethral discharge has not been well established. The sensitivity of urethral swabs and first-catch urine is controversial. GOAL OF THIS STUDY: To correlate clinical data (discharge or not), urethral swabs, and first-catch urine examinations with the microorganisms found within the urethra in a cohort of men attending the sexually transmitted disease clinic of Hopital Saint Louis (Paris) for treatment of urethral symptoms with or without discharge. STUDY DESIGN: Two-hundred-seventy-three consecutive male patients entered this prospective study between October 1, 1992 and November 30, 1992. Fifty-two patients were excluded because they had been treated with antibiotics in the previous 3 months. All patients were screened for Chlamydia trachomatis, Neisseria gonorrhoeae, Mycoplasma genitalium, Trichomonas vaginalis, Ureaplasma urealyticum, Mycoplasma hominis, and Candida albicans. RESULTS: Two-hundred-nineteen patients were eligible for the study (122 with discharge and 97 with no discharge). The prevalence of microorganisms was as follows: Chlamydia trachomatis in 13%, Neisseria gonorrhoeae in 11%, Ureaplasma urealyticum in 7%, Mycoplasma genitalium in 17%, Trichomonas vaginalis in 1%, and indeterminate pathogens alone in 20%. All major pathogens and Mycoplasma genitalium were more common in patients with discharge. Stratification of results according to the presence of polymorphonuclear leukocytes on the urethral swab and first-catch urine showed a low sensitivity of both tests for Chlamydia trachomatis (29%), Mycoplasma genitalium (50% and 62%), and Ureaplasma urealyticum (33%) in patients with no discharge. CONCLUSION: A specific and sensitive search for Chlamydia trachomatis should be done in every patient with urethral symptoms whether or not the classic symptoms of urethritis are present (discharge, presence of polymorphonuclear leukocytes in the urethra or first-catch urine).

Janssen A.G. et al. *Abscess of the lacrimal sac due to chronic or subacute dacryocystitis: treatment with temporary stent placement in the nasolacrimal duct.* Radiology. 2000; 215(1) : 300-4.p Abstract: Stents were placed temporarily in 10 obstructed lacrimal systems in patients with a chronic or subacute lacrimal abscess that did not respond to conventional antibiotic therapy. In all 10 cases, the abscess was treated successfully. Long-term patency of the lacrimal system was restored in five cases. Temporary stent placement appears to be a promising method to treat a chronic or subacute lacrimal abscess.

Janssens J.P. et al. *[Non-nosocomial pneumonias in the elderly: clinical findings, etiology, therapeutic approach].* Schweiz Med Wochenschr. 1996; 126(36) : 1515-23.p Abstract: Elderly subjects are at high risk for pneumonia, with an incidence 4 times that of younger adults and a higher mortality. Factors that contribute to this over-mortality and morbidity are age-related modifications of the immune system and of the respiratory system, co-morbidity, colonization of upper airways by gram-negative bacilli, and immunosuppression (iatrogenic or acquired). Clinical symptoms and signs are sometimes scarce or nonspecific; bacteremia and sepsis are more frequent. Responsible microorganisms are frequently undetermined. S. pneumoniae, H. influenzae, S. aureus and respiratory viruses are the most frequently incriminated organisms; the incidence of infection with gram-negative bacilli rises in institutionalized patients or frail elderly subjects. Atypical pneumonias are rare in elderly patients. In this age group prevention is of major importance and consists mainly in vaccination against influenza and S. pneumoniae.

Jaresko G.S. *Etiology of neutropenia in HIV-infected patients.* Am J Health Syst Pharm. 1999; 56 Suppl 5 : S5-8.p Abstract: The causes of neutropenia in HIV-infected patients are described, as is the association of absolute neutrophil count (ANC) and the risk of bacterial infections. In patients with HIV infection, neutropenia can result from the disease or related malignancies, drug therapies, or opportunistic infections. HIV can cause neutropenia by directly or indirectly impairing hematopoiesis. Similarly, microorganisms that cause opportunistic infections, such as cytomegalovirus and Mycobacterium avium complex, can infiltrate the bone marrow and cause myelosuppression. Hematologic toxicities of drug therapy tar-

geted against HIV and opportunistic infections, such as zidovudine, cidofovir, foscarnet, ganciclovir, and trimethoprim/sulfamethoxazole, can further reduce blood cell formation. Several retrospective studies are reviewed that examined the relationship between ANC and the development of bacterial infections in patients infected with HIV. Since neutropenia appears to be associated with increased risk of bacterial infections in HIV-infected patients, approaches to shorten or prevent neutropenia in these patients will likely provide substantial clinical benefit.

Jarvinen H. et al. *Susceptibility of Streptococcus mutans and Streptococcus sobrinus to antimicrobial agents after short-term oral chlorhexidine treatments.* Eur J Oral Sci. 1995; 103(1) : 32-5.p Abstract: Effects of three different types of short-term applications (1-3 times during 1 week) of chlorhexidine (1 or 40%) on the susceptibility of 863 clinical isolates of Streptococcus mutans and 53 isolates of Streptococcus sobrinus from 58 subjects were studied. Chlorhexidine-resistant isolates were not found either before or after the treatment. The minimum inhibitory concentrations (MICs) to chlorhexidine of all isolates of S. mutans were < or = 1 microgram/ml, and of S. sobrinus < or = 2 micrograms/ml. S. mutans and S. sobrinus were also susceptible to ampicillin, penicillin, cefuroxime, and tetracycline. In conclusion, different short-term chlorhexidine regimens do not induce resistance in S. mutans or S. sobrinus and, furthermore, these species have so far retained their susceptibility to common antibiotics.

Jarvis W.R. *The epidemiology of colonization.* Infect Control Hosp Epidemiol. 1996; 17(1) : 47-52.p Abstract: Colonization is the presence of a microorganism in or on a host, with growth and multiplication but without any overt clinical expression or detected immune response in the host at the time it is isolated. Normal colonization in humans begins during the birth process and through subsequent contacts with the inanimate or animate environments until a delicately balanced "normal" flora is established; subsequently, the precise components of this flora evolve. This normal flora, such as coagulase-negative Staphylococcus or Staphylococcus aureus on the skin or Candida albicans in the gastrointestinal tract, vagina, or perineal area, can result in infection when normal body defenses are impaired through underlying disease, immunomodulating therapy, or the use of invasive devices, or when the delicate balance of the normal flora is altered through antimicrobial therapy. Many, if not most, hospital-acquired infections result directly or indirectly from patient colonization; studies have shown that hospitalized patients are colonized rapidly with hospital flora. Recognizing this reservoir of patients colonized with epidemiologically important pathogens in our hospitals and improving barrier precaution measures or altering host susceptibility will be necessary if we are to reduce the incidence of infections with these organisms.

Jassem E. et al. *[Occurrence of non-spore forming anaerobic bacteria in the upper airways of patients with chronic obstructive pulmonary disease].* Med Dosw Mikrobiol. 1996; 48(1-2) : 49-54.p Abstract: The aim of this study was to assess the occurrence of anaerobic non-sporeforming bacteria upper airways flora in the exacerbation of COPD. Sputum from 35 COPD patients was sent to the laboratory in sterile, filled with CO2 containers and cultured under anaerobic conditions. In all patients bacteriological tests were positive. The most common anaerobic bacteria were as follows: Peptostreptococcus - in 28 pts, Fusobacterium - in 27 pts, Bacteroides - in 26 pts and Prevotella in 24. Less common were: Propionibacterium, Actinomyces, Eubacterium, Porphyromonas and Peptococcus. The susceptibility to most common antimicrobial agents was evaluated. All anaerobic bacteria show a significant sensitivity to amoxicillin either with clavulanic acid or ampicillin with sulbactam. Gram-positive rods were resistant to metronidazole and tinidazole.

Jassem E. et al. *[Non-sporeforming anaerobic bacteria in bronchoalveolar lavage fluid of patients with pneumonia during the course of lung cancer].* Pneumonol Alergol Pol. 1997; 65(9-10) : 643-8.p Abstract: The aim of this study was to assess the occurrence of non-sporeforming anaerobes in bronchoalveolar lavage in patients with pneumonia coexisting with lung cancer. Material consisted of 40 patients with lung cancer. Bronchoalveolar lavage was performed before administration of antimicrobial treatment and obtained material was cultivated in anaerobic and aerobic conditions. Quantitative assessment of anaerobic bacteria and their susceptibility to common antimicrobial agents were also performed. Peptostreptococcus, Prevotella, Fusobacterium and Bacteroides were the most common anaerobes. Among aerobic bacteria, the most frequent were G-negative bacilli. G-negative anaerobes were susceptible to most tested agents, whereas G-positive rods were resistant to metronidazole and tinidazole. This study demonstrates presence of non-sporeforming anaerobic bacteria in lower respiratory tract infections accompanying lung cancer.

Jaup B.H. et al. *[Antibiotic resistance among strains of Helicobacter pylori in Gothenburg. Bacteria resistant to metronidazole].* Lakartidningen. 1998; 95(4) : 279-81.p Abstract: AIM: Primary resistance of H pylori strains to antimicrobials has direct therapeutical implications. For this reason we studied the prevalence of primary resistance of H pylori of Sweden, in a regional setting. MATERIAL AND METHODS: A total of 244 patients referred to our endoscopy unit have been evaluated prospectively for the occurrence of H pylori. Helicobacter pylori infection was established by a positive rapid urease test on an antral biopsy. If positive the biopsy specimen was transferred to a transportmedium for culture on a Skirrow medium. Antimicrobial resistance was evaluated by the E-test. RESULTS: In 109 patients H pylori infection was seen and in all of them the culture was positive. No resistance was seen for amoxycillin and tetracycline. The resistance against metronidazole was 40.3% and and against clarithromycin it was 2.8%. For metronidazole there was a significantly higher resistance seen in women compared to men (53.3% vs 31.2%; $p < 0.001$). CONCLUSIONS: Primary resistance to metronidazole was higher than expected and over average in Europe. The resistance for clarithromycin is still rare. Further monitoring is mandatory to detect changes in the community.

Jaup B.H. et al. *Helicobacter pylori culture from a positive, liquid-based urease test for routine clinical use: a cost-effective approach.* Helicobacter. 2000; 5(1) : 22-3.p Abstract: BACKGROUND: The aim of our study was to test the feasibility of culturing Helicobacter pylori directly from biopsies aimed for rapid urease test in routine clinical practice. MATERIALS AND METHODS: In 260 consecutive patients referred for gastroscopy because of dyspepsia one antral biopsy was routinely used for our "in house" rapid urease test (RUT). Positive biopsies were placed in a transport medium and sent to the laboratory. The biopsies were cultured and incubated at 37 degrees C for 5-7 days. H. pylori was identified and routinely tested for antimicrobial resistance by using the E-test. RESULTS: In 118 out of 260 patients (45%) the urease test turned positive and the growth of H. pylori was sufficient to allow testing of antimicrobial resistance. CONCLUSION: H. pylori could be cultured from almost all positive RUT specimens. A liquid RUT is thus more suitable for culture, saving additional biopsies.

Jebaraj R. et al. *Nasopharyngeal colonization of infants in southern India with Streptococcus pneumoniae.* Epidemiol Infect. 1999; 123(3) : 383-8.p Abstract: To investigate the dynamics of nasopharyngeal colonization with Streptococcus pneumoniae, and to determine the prevalent serogroups/types (SGT) and their antimicrobial susceptibility, we studied 100 infants attending our well-baby clinic. Nasopharyngeal swab specimens were obtained at 6, 10, 14, 18 and 22 weeks and at 9 and 18 months of age and submitted for culture, serotyping and antimicrobial susceptibility testing of S. pneumoniae. Colonization with pneumococcus was seen on at least one occasion in 81 infants. The median age of acquisition was 11 weeks and the median duration of carriage was 1 3 months. The common SGTs identified were 6, 19, 14 and 15. SGT 1, which was a common inva-

1995; 155(8) : 854-9.p Abstract: OBJECTIVE: Investigate reports of tuberculosis in health care workers employed at a hospital with an outbreak of multidrug-resistant Mycobacterium tuberculosis. DESIGN: Case series of tuberculosis in health care workers, January 1, 1989, through May 31, 1992. Antimicrobial susceptibility testing and restriction fragment length polymorphism analysis of M tuberculosis isolates. Longitudinal analysis of cumulative tuberculin skin test surveillance data. Assessment of infection control. The patients consisted of 361 health care workers who had either serial tuberculin skin tests or tuberculosis. RESULTS: Six health care workers, the largest number linked to one multidrug-resistant tuberculosis outbreak, had disease due to M tuberculosis that matched the outbreak strain from hospitalized patients. The two who were seropositive for human immunodeficiency virus died, one of tuberculous meningitis and the other of multiple causes including tuberculosis. The estimated risk of a skin test conversion was positively associated with time and increased by a factor of 8.3 (1979 to 1992). In 1992 the annual risk for workers in the lowest exposure occupational group was 2.4%. In comparison, nurses and housekeepers had relative risks of 8.0 (95% confidence interval, 3.2 to 20.3) and 9.4 (95% confidence interval, 2.7 to 32.3), respectively. Laboratory workers had a relative risk of 4.2 (95% confidence interval, 1.1 to 15.5). Tuberculosis admissions increased, but the hospital had inadequate ventilation to isolate tuberculosis patients effectively. There were lapses in infection control practices. CONCLUSIONS: Health care workers who were exposed during a hospital outbreak of multidrug-resistant tuberculosis had occupationally acquired active disease. The human immunodeficiency virus-infected health care workers with tuberculosis had severe disease and died. The risk of skin test conversion increased during the study period, and higher exposure occupations had elevated risk. Effective infection control is essential to prevent the transmission of tuberculosis to health care workers.

Jernigan D.B. et al. *Minimizing the impact of drug-resistant Streptococcus pneumoniae (DRSP). A strategy from the DRSP Working Group.* JAMA. 1996; 275(3) : 206-9.p Abstract: Emergence of drug-resistant Streptococcus pneumoniae (DRSP) presents a challenge to the medical and public health communities since the magnitude of the problem is not known, the clinical impact of DRSP infections is not well described, national vaccination rates are low, and antimicrobial drugs are often used excessively and inappropriately. To address the problem of DRSP, a working group by Centers for Disease Control and Prevention was formed in June 1994 consisting of public health practitioners, health care providers, and clinical laboratorians representing state and federal agencies and various professional organizations. Through periodic open meetings, the working group has developed a strategy for surveillance, investigation, prevention, and control of infections due to DRSP. The strategy focuses on (1) implementing an electronic laboratory-based surveillance (ELBS) system for reporting invasive DRSP infections and providing clinically relevant feedback to clinicians, (2) identifying risk factors and outcomes of DRSP infection, (3) increasing pneumococcal vaccination, and (4) promoting judicious antimicrobial drug use. Data received through ELBS will be used to make timely estimates of the community-specific prevalence of drug-resistant pneumococci. National, regional, and local trends will be made available to health care providers and clinicians to promote optimal antimicrobial drug use and increased vaccination in targeted areas. Once in operation, the ELBS network will be adaptable to other diseases, improving the comprehensiveness and timeliness of public health surveillance. The intended outcome of the strategy is to reduce complications of DRSP infection, such as long-term sequelae of infection, health care expenditures, morbidity, and mortality.

Jesenska A. et al. *Dehalogenation of haloalkanes by Mycobacterium tuberculosis H37Rv and other mycobacteria*. Appl Environ Microbiol. 2000; 66(1) : 219-22.p Abstract: Haloalkane dehalogenases convert haloalkanes to their corresponding alcohols by a hydrolytic mechanism. To date, various haloalkane dehalogenases have been isolated from bacteria colonizing environments that are contaminated with halogenated compounds. A search of current databases with the sequences of these known haloalkane dehalogenases revealed the presence of three different genes encoding putative haloalkane dehalogenases in the genome of the human parasite Mycobacterium tuberculosis H37Rv. The ability of M. tuberculosis and several other mycobacterial strains to dehalogenate haloaliphatic compounds was therefore studied. Intact cells of M. tuberculosis H37Rv were found to dehalogenate 1-chlorobutane, 1-chlorodecane, 1-bromobutane, and 1,2-dibromoethane. Nine isolates of mycobacteria from clinical material and four strains from a collection of microorganisms were found to be capable of dehalogenating 1,2-dibromoethane. Crude extracts prepared from two of these strains, Mycobacterium avium MU1 and Mycobacterium smegmatis CCM 4622, showed broad substrate specificity toward a number of halogenated substrates. Dehalogenase activity in the absence of oxygen and the identification of primary alcohols as the products of the reaction suggest a hydrolytic dehalogenation mechanism. The presence of dehalogenases in bacterial isolates from clinical material, including the species colonizing both animal tissues and free environment, indicates a possible role of parasitic microorganisms in the distribution of degradation genes in the environment.

Jett B.D. et al. *In vitro activities of various beta-lactam antimicrobial agents against clinical isolates of Escherichia coli and Klebsiella spp. resistant to oxyimino cephalosporins.* Antimicrob Agents Chemother. 1995; 39(5) : 1187-90.p Abstract: Broth microdilution testing was used to study the activity of several beta-lactam antimicrobial agents, including piperacillin-tazobactam and cefepime, against 108 clinically derived Escherichia coli and Klebsiella sp. strains resistant to oxyimino cephalosporins (i.e., putative extended-spectrum beta-lactamase producers). On the basis of the percentage of susceptible strains, imipenem (100%), cefotetan (> or = 92%), and piperacillin-tazobactam (> or = 86%) were the most active agents. Cefepime activity (52 to 64% susceptible) was comparable to that of cefotaxime (40 to 63% susceptible) and aztreonam (20 to 63% susceptible). Among all beta-lactams tested, imipenem and cefotetan demonstrated the highest and most consistent level of activity and were the least affected by challenges with increased sizes of inocula of these resistant organisms.

Jette L.P. et al. *Evaluation of three glutaraldehyde-based disinfectants used in endoscopy.* J Hosp Infect. 1995; 30(4) : 295-303.p Abstract: The European suspension test was applied to compare the in vitro activity of three glutaraldehyde-based disinfectants: a 1:10 dilution of a 10% glutaraldehyde solution containing 0.5% phenylphenol-0.1% amylphenol, a 2% acid glutaraldehyde solution, and a 2% alkaline glutaraldehyde solution. The microbicidal effect of the disinfectants was evaluated by counting surviving cells of three indicator microorganisms (Pseudomonas aeruginosa, Mycobacterium chelonae and phage f2) after exposure times of 5, 10, 20 and 40 min to the agents at 20 degrees C. An inactivation factor (IF) of > or = 5 log10 was used as the criterion for effective disinfection. This IF was achieved with every microorganism/disinfectant combination after 5 min exposure except in experiments with phage f2 and the 1% glutaraldehyde-based disinfectant. The diminished inactivation noticed with the 1% glutaraldehyde-based disinfectant supports the recommendation to use a disinfectant containing a minimum of 2% glutaraldehyde for high level disinfection.

Jette L.P. et al. *Use of an oxacillin disk screening test for detection of penicillin- and ceftriaxone-resistant pneumococci*. J Clin Microbiol. 1999; 37(4) : 1178-81.p Abstract: In a context of worldwide emergence of resistance among Streptococcus pneumoniae strains, early detection of strains with decreased susceptibility to beta-lactam antibiotics is important for clinicians. If the 1-microgram oxacillin disk diffusion test is used as described by the National Committee for Clinical Laboratory Standards, no interpretation is available for strains showing zone sizes of </=19 mm, and there is presently no disk diffusion

sive isolate in children in our hospital during this period, was not isolated from these children. Sequential colonization by 2, 3 or 4 SGTs was observed in 18, 5 and 2 children, respectively. Resistance to penicillin, chloramphenicol, cotrimoxazole and erythromycin was observed in 0, 13 (6%) 11 (5 %) and 5 (3 %) isolates, respectively. There was a significant difference in susceptibility to cotrimoxazole between colonizing and invasive isolates (5 % vs. 40 %, P<0.0001).

Jelesic Z. et al. *[Shigellae isolated in 1997—plasmid profiles and antibiotic resistance].* Med Pregl. 1998; 51(7-8) : 305-9.p Abstract: INTRODUCTION: Shigella spp is one of the most frequently isolated bacteria causing acute diarrhea with us. Genetics of pathogenicity of Shigella spp. includes chromosomal and plasmid genes. Most virulence factors are coded by invasion plasmid antigen genes residing on a 180-230 MDa plasmid. There is a big problem with multiple resistance of Shigella spp. strains, which is mostly plasmid-borne. Genetic analysis of bacterial cells, that is plasmid profile analysis, is important for investigation of sources and ways of spreading of the infection. All isolates originating from the same clone have identical plasmid profiles, i.e. number and size of plasmids. The aim of the investigation was: comparing the type of resistance to antimicrobical agents found in epidemic and nonepidemic. Shigella strains isolated in 1997, analyzing plasmid profiles of these isolates and confirming their epidemic connection. MATERIAL AND METHODS: Susceptibility to antibiotics was examined by a standard disc-diffusion method. Plasmid profiles of 40 strains (20 from the outbreak and 20 from sporadic cases) were tested using a method of alkaline lysis by Birnboim and Doly followed by electrophoresis in agarose gel. RESULTS: Shigella strains were resistant to antimicrobial agents which are most commonly used. Epidemic isolates shared the same resistance type, they were resistant to cephalexin, streptomycin and co-trimoxazole. The dominant type of resistance of nonepidemic strains was to ampicillin, streptomycin and co-trimoxazole. Strains isolated during the outbreak had identical plasmid profiles (2 plasmid bands of 55 and 1.5 MDa). Non-epidemic isolates had different plasmid profiles as well as type of resistance. CONCLUSION: Strains of Shigella spp. isolated during an outbreak had the same type of resistance and the same plasmid profiles, which indicated their origin from the same clone. The plasmid profile analysis is a reliable and precise method for determination of epidemic connection of Shigella isolates.

Jenkins S.G. et al. *Synergistic interaction between ofloxacin and cefotaxime against common clinical pathogens.* Infection. 1995; 23(3): 154-61.p Abstract: Antimicrobial synergy resulting from combined antibiotic therapy is often important in the treatment of serious bacterial infections. To investigate the interactions between cefotaxime (CTX), desacetylcefotaxime (DES), and ofloxacin (OFL), 247 recent clinical isolates were tested for in vitro susceptibility to each antibiotic alone by an agar dilution technique and retested with the various antibiotic combinations using a checkerboard protocol. Fractional inhibitory concentrations were calculated for all organisms with all drug combinations. Time kill kinetic studies were performed on selected isolates to examine the bactericidal activity of the various antimicrobial combinations. Of the 110 gram-negative organisms tested, synergy or partial synergy between CTX, DES and OFL was demonstrable for 89 (81%). Included in the study were 70 members of the Enterobacteriaceae family, 20 isolates of Pseudomonas aeruginosa, 10 strains of Acinetobacter baumannii, and 10 isolates of Xanthomonas maltophilia. Additive activity was observed against an additional 13 (11%) isolates. Findings were similar for the 89 gram-positive isolates examined. Organisms tested included methicillin-resistant Staphylococcus aureus (20), methicillin-susceptible Staphylococcus aureus (20), methicillin-resistant Staphylococcus epidermidis (9), methicillin-susceptible S. epidermidis (10), Enterococcus faecalis (10), and Streptococcus pneumoniae (20). Synergy or partial synergy was observed against 81 (91%). Less synergistic activity was detected, however, with members of the Bacteroides fragilis group. Of the 48 organisms tested, synergy or partial synergy was noted for only 27 (57%). Isolates representative of each major group of organisms included in the study were tested to determine whether synergistic bactericidal activity was also demonstrable with the three drugs. Time kill studies supported the checkerboard results.(ABSTRACT TRUNCATED AT 250 WORDS).

Jenkinson H.F. *Ins and outs of antimicrobial resistance: era of the drug pumps.* J Dent Res. 1996; 75(2) : 736-42.p Abstract: Over the past five years, concerns have heightened over the escalating numbers of pathogenic micro-organisms isolated that are resistant to many antibiotics and drugs. This phenomenon poses major problems in the treatment of patients with hospital- or community-acquired infections caused by bacteria, fungi, or parasitic organisms. Microbial cells have acquired resistances to specific antibiotics and drugs by mechanisms that include antibiotic inactivation, target alteration, or drug exclusion. More recently, the importance of another mechanism, that of drug expulsion, has been recognized as contributing significantly to antibiotic and drug resistance in microbes. Drug expulsion, mediated by membrane-associated drug efflux pumps, can protect cells from a range of toxic compounds and therefore may confer single-step multidrug resistance. It is imperative that new drugs be designed or discovered that will poison the pumps or bypass the efflux mechanisms.

Jensen A.G. et al. *Risk factors for hospital-acquired Staphylococcus aureus bacteremia.* Arch Intern Med. 1999; 159(13) : 1437-44.p Abstract: BACKGROUND: Staphylococcus aureus bacteremia (SAB) acquired in hospitals continues to be a frequent and serious complication to hospitalization, and no previous case-control studies dealing with risk factors of this severe disease are available. METHODS: Based on a 1-year prospective analysis, the data from all patients with hospital-acquired SAB admitted to 4 hospitals in Copenhagen County, Denmark, from May 1, 1994, through April 30, 1995, were evaluated. Eighty-five patients with hospital-acquired SAB were matched to 85 control patients with a similar primary diagnosis at admission (matched controls). Of these, 62 patients with hospital-acquired SAB were compared with 118 other patients with a similar time of admission, who were randomly selected with no clinical evidence of SAB (unmatched controls). RESULTS: The incidence of hospital-acquired SAB was 0.71 per 1000 hospital admissions. The presence of a central venous catheter (odds ratio, 6.9; 95% confidence interval [CI], 2.8-17.0), anemia (odds ratio, 3.3; 95% CI, 1.4-7.6), and hyponatremia (odds ratio, 3.3; 95% CI, 1.5-7.0) was significantly associated with hospital-acquired SAB in a conditional and a usual logistic regression analysis. Nasal carriage was not an independent risk factor, but nasal carriers among patients in surgery (odds ratio, 4.0; 95% CI, 1.3-13.0) had a significantly higher risk for hospital-acquired SAB compared with matched and unmatched controls. The presence of hospital-acquired SAB increased the mortality rate 2.4-fold (95% CI, 1.1-5.2). CONCLUSIONS: The presence of a central venous catheter is an important risk factor, and hyponatremia and anemia are associated with the development of hospital-acquired SAB. Furthermore, hospital-acquired SAB in itself increases mortality.

Jensen G.H. et al. *[Pseudomonas aeruginosa as the cause of meningitis in a patient with epidural catheter].* Ugeskr Laeger. 2000; 162(20) : 2893-4.p Abstract: A case of epidural infection following epidural catheterization is presented. The clinical signs initially were backpain and a small swelling at the site of insertion. Treatment with dicloxacillin was begun, presuming a Staphylococcus-infection. The symptoms persisted. Weeks later the patient developed meningitis and Pseudomonas aeruginosa was cultivated. Antibiotic treatment was changed to ceftazidime, netilmycin and ciprofloxacin. Complete recovery followed.

Jereb J.A. et al. *Tuberculosis in health care workers at a hospital with an outbreak of multidrug-resistant Mycobacterium tuberculosis.* Arch Intern Med.

test available for screening cephalosporin resistance. The zones obtained by the diffusion method by using the 1-microgram oxacillin disk were compared with penicillin MICs for 1,116 clinical strains and with ceftriaxone MICs for 695 of these strains. Among the 342 strains with growth up to the 1-microgram oxacillin disk margin, none were susceptible (MIC, </=0.06 microgram/ml), 62 had intermediate resistance (MIC, 0.12 to 1.0 microgram/ml), and 280 were resistant (MIC, >/=2.0 microgram/ml) to penicillin. For ceftriaxone, among 98 strains with no zone of inhibition in response to oxacillin, 68 had intermediate resistance (MIC, 1.0 microgram/ml), and 22 were resistant (MIC, >/=2.0 microgram/ml). To optimize the use of the disk diffusion method, we propose that the absence of a zone of inhibition around the 1-microgram oxacillin disk be regarded as an indicator of nonsusceptibility to penicillin and ceftriaxone and recommend that such strains be reported as nonsusceptible to these antimicrobial agents, pending the results of a MIC quantitation method.

Jiang Y. et al. *Monocyte chemoattractant protein 1 and interleukin-8 production in mononuclear cells stimulated by oral microorganisms.* Infect Immun. 1996; 64(11) : 4450-5.p Abstract: Chemokines are a family of low-molecular-weight proinflammatory cytokines that stimulate recruitment of leukocytes. The chemokines interleukin-8 (IL-8) and monocyte chemoattractant protein 1 (MCP-1) are relatively specific chemoattractants for neutrophils and monocytes, respectively. Chemokine expression contributes to the presence of different leukocyte populations observed in normal and pathologic states. In the present studies, peripheral blood mononuclear cells (PBMC) were stimulated by microbes (Candida albicans, Streptococcus mutans, Porphyromonas gingivalis, and Actinobacillus actinomycetemcomitans) selected based upon their importance as oral pathogens. IL-8 and MCP-1 gene expression and protein release were determined by Northern blot (RNA blot) analysis and enzyme-linked immunosorbent assay. C. albicans, P. gingivalis, and A. actinomycetemcomitans induced high levels of production of both MCP-1 and IL-8. S. mutans was a strong inducer of MCP-1, but it did not stimulate significant production of IL-8. C. albicans, S. mutans, and A. actinomycetemcomitans were 500 to 5,000 times more potent than P. gingivalis in terms of MCP-1 production. In general, the microbe-to-PBMC ratios required for maximum gene expression of MCP-1 were lower than those for IL-8. However, for actual protein release of MCP-1 versus IL-8, differences in the effects of various microbe concentrations were observed only for A. actinomycetemcomitans. These results demonstrate that different oral pathogens induce specific dose-dependent patterns of chemokine gene expression and release. Such patterns may help explain the immunopathology of oral infections, particularly with regard to inflammatory leukocyte recruitment.

Jiang Z.D. et al. *Characterization of enterotoxigenic Escherichia coli strains in patients with travelers' diarrhea acquired in Guadalajara, Mexico, 1992-1997.* J Infect Dis. 2000; 181(2) : 779-82.p Abstract: The relationship between enterotoxigenic Escherichia coli (ETEC) and travelers' diarrhea was examined in a high-risk area in 1992-1997. Toxin patterns, colonization-factor antigens (CFAs), and in vitro antimicrobial susceptibility were determined. In total, 928 US students with diarrhea acquired in Guadalajara, Mexico, were screened for enteric pathogens. Diagnosis of ETEC infection was done with oligonucleotide probes. ETEC was isolated in 19.9% of the travelers with diarrhea. CFAs were identified in 51% of the ETEC strains. The highest CFA frequency was observed among heat-stable isolates. Ampicillin, furazolidone, and sulfisoxazole resistance of ETEC increased during the study period. ETEC isolation rates and CFA patterns varied little during the 6 years of the study, which has implications for immunoprophylactic strategies. The finding that differences in the results of ribotyping and plasmid analysis change over time suggests that multiple strains of ETEC were responsible for the illness in the region studied.

Jimenez L. et al. *Use of PCR analysis for detecting low levels of bacteria and mold contamination in pharmaceutical samples.* J Microbiol Methods. 2000; 41(3) : 259-65.p Abstract: PCR assays were developed and compared to standard methods for quality evaluation of pharmaceutical raw materials and finished products with low levels of microbial contamination. Samples were artificially contaminated with less than 10 CFU of Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Aspergillus niger. Bacterial DNA was extracted from each enrichment broth by mild lysis in Tris-EDTA-Tween 20 buffer containing proteinase K while mold DNA was extracted by boiling samples in Tris-EDTA-SDS buffer for 1 h. A 10-microl aliquot of extracted DNA was added to Ready-To-Go PCR beads and specific primers for E. coli, S. aureus, and P. aeruginosa. However, 50-microl aliquots of extracted mold DNA were used for amplification of specific A. niger DNA sequences. Standard methods required 6-8 days while PCR detection of all microorganisms was completed within 27 h. Low levels of microbial contamination were detected in all raw materials and products using PCR assays. Rapid quality evaluation of pharmaceutical samples resulted in optimization of product manufacturing, quality control, and release of finished products.

John J.F. Jr et al. *The microbial genetics of antibiotic cycling.* Infect Control Hosp Epidemiol. 2000; 21(1 Suppl) : S22-31.p Abstract: Cycling of currently available antibiotics to reduce resistance is an attractive concept. For cycling strategies to be successful, their implementation must have a demonstrable impact on the prevalence of resistance determinants already dispersed throughout the hospital and associated healthcare facilities. While antibiotic use in hospitals clearly constitutes a stimulus for the emergence of resistance, it is by no means the only important factor. The incorporation of resistance determinants into potentially stable genetic structures, including bacteriophages, plasmids, transposons, and the more newly discovered movable elements termed integrons and gene cassettes, forces some degree of skepticism about the potential for such strategies in institutions where resistance determinants are already prevalent. In particular, the expanding role of integrons may pose an ultimate threat to formulary manipulations such as cycling. Despite these concerns, the crisis posed by antimicrobial resistance warrants investigation of any strategy with the potential for reducing the prevalence of resistance. Over the next decade, new studies with carefully designed outcomes should determine the utility of antibiotic cycling as one control measure for nosocomial resistance.

Johnson A.P. et al. *Urinary isolates of apramycin-resistant Escherichia coli and Klebsiella pneumoniae from Dublin.* Epidemiol Infect. 1995; 114(1) : 105-12.p Abstract: Twenty-two gentamicin-resistant urinary isolates of Escherichia coli and five gentamicin-resistant urinary isolates of Klebsiella pneumoniae from a Dublin hospital were examined for resistance to the veterinary aminoglycoside antibiotic apramycin. Five isolates of E. coli and one isolate of K. pneumoniae were found to be resistant. The apramycin-resistant isolates, which were also resistant to the veterinary anthelmintic agent hygromycin B, hybridized with a DNA probe for the gene encoding the enzyme 3-N-aminoglycoside acetyltransferase type IV (AAC(3)IV). Resistance to apramycin and hygromycin B was co-transferable in four of the five isolates of E. coli and the isolate of K. pneumoniae. In one isolate of E. coli apramycin resistance was not transferable. On the basis of their restriction enzyme digestion profiles and the antimicrobial resistance traits encoded, the transferable plasmids encoding resistance to apramycin and hygromycin B comprised three distinct types. Genetic linkage between the gene encoding AAC(3)IV and genes encoding resistance to ampicillin and either tetracycline or trimethoprim, means that the relatively widespread use of these antimicrobial agents provides a selective pressure for the persistence of resistance to apramycin and gentamicin even in the absence of bacterial exposure to aminoglycosides.

Johnson B.J. et al. *Differential gene expression in response to adjunctive recombinant human interleukin-2 immunotherapy in multidrug-resistant tubercu-*

losis patients. Infect Immun. 1998; 66(6) : 2426-33.p Abstract: Administration of low-dose recombinant human interleukin 2 (rhuIL-2) in combination with multidrug chemotherapy to patients with multidrug-resistant tuberculosis (MDR TB) induces measurable changes in in vitro immune response parameters which are associated with changes in the clinical and bacteriologic status of the patients. To determine the molecular basis of these changes, we have used semiquantitative reverse transcriptase-initiated PCR (RT-PCR) and differential display technology. During rhuIL-2 treatment of MDR TB patients, decreased levels of gamma interferon (IFN-gamma) mRNA in peripheral blood mononuclear cells (PBMC) relative to baseline levels were observed. However, at the site of a delayed-type hypersensitivity (DTH) response to purified protein derivative of tuberculin (PPD), the expression of cellular IFN-gamma and IL-2 mRNAs was increased during rhuIL-2 therapy. Levels of other cytokine mRNAs were not significantly affected by rhuIL-2 administration. Using differential-display RT-PCR, we identified several genes expressed at the DTH skin test site which were up- or down-regulated during rhuIL-2 treatment. Cytochrome oxidase type I mRNA was increased in response to rhuIL-2 therapy relative to baseline levels, as was heterogeneous nuclear ribonuclear protein G mRNA. CD63, clathrin heavy chain, and beta-adaptin mRNAs, all of which encode proteins associated with the endocytic vacuolar pathway of cells, were also differentially regulated by rhuIL-2 administration. The differential effects of IL-2 were confirmed in vitro by using PBMC obtained from PPD-positive individuals stimulated with Mycobacterium tuberculosis and IL-2. The differential expression of genes may provide a surrogate marker for leukocyte activation at a mycobacterial antigen-specific response site and for the development of an enhanced antimicrobial response which may result in improved outcomes in MDR TB patients.

Johnson B.J. et al. *Clinical and immune responses of tuberculosis patients treated with low-dose IL-2 and multidrug therapy.* Cytokines Mol Ther. 1995; 1(3) : 185-96.p Abstract: The immune response to infection with M. tuberculosis depends on cytokine activation of effector cells. We therefore conducted a pilot study of recombinant human interleukin-2 (rhuIL-2) as an adjunct to multidrug therapy (MDT) to evaluate the safety of this approach and to determine whether IL-2 can enhance the cellular immune response in patients with pulmonary tuberculosis (TB). Patients included in this study presented with a wide range of extent and duration of infection, and were grouped into three categories for data analysis: (1) patients with newly diagnosed, acute-stage TB who were just beginning MDT; (2) patients who had received a minimum of 45 days MDT before the start of the study and who had responded to treatment; and (3) patients with multidrug-resistant (MDR) TB who had been on MDT for at least seven months without apparent beneficial clinical response. Twenty patients received 30 days of twice-daily intradermal injections of 12.5 micrograms of IL-2. Patients from all three groups showed improvement of clinical symptoms over the 30-day period of treatment with IL-2 and MDT. Results of direct smear for acid fast bacilli (AFB) demonstrated conversion to sputum-negative following IL-2 and MDT treatment in all newly diagnosed patients and in 5/7 MDR TB patients. (The size of the skin test response to purified protein derivative (PPD) of tuberculin increased during the 30-day IL-2 adjunctive therapy in newly diagnosed patients, but decreased or disappeared in the other two groups of treated patients.) Assays in vitro for phenotype distribution, natural killer (NK) cell activity, frequency of cells proliferating in response to exogenous IL-2, and antigen-induced blastogenesis demonstrated systemic responses to intradermally administered rhuIL-2. Levels of interferon-gamma (IFN-gamma) in plasma, peripheral blood mononuclear cell (PBMC) IFN-gamma mRNA and IFN-gamma mRNA in biopsy of site of skin test response to purified protein derivative (PPD) were highest in those patients with the most acute symptoms at the beginning of the study, and decreased during rhuIL-2 and MDT. IL-2 immunotherapy did not modify levels of mRNA expression for other cytokines. Patients receiving IL-2 did not experience clinical deterioration or significant side effects. These results suggest that IL-2 administration in combination with conventional MDT is safe and may potentiate the antimicrobial cellular immune response to TB.

Johnson J.R. et al. *Molecular epidemiological and phylogenetic associations of two novel putative virulence genes, iha and iroN(E. coli), among Escherichia coli isolates from patients with urosepsis.* Infect Immun. 2000; 68(5) : 3040-7.p Abstract: Two novel putative Escherichia coli virulence genes, iha and iroN from E. coli (iroN(E. coli)), were detected in 55 and 39%, respectively, of 67 E. coli isolates from patients with urosepsis. iha and iroN(E. coli) exhibited divergent associations with other putative virulence genes, phylogenetic markers, host characteristics, and antimicrobial resistance.

Johnson S. et al. *Epidemics of diarrhea caused by a clindamycin-resistant strain of Clostridium difficile in four hospitals.* N Engl J Med. 1999; 341(22) : 1645-51.p Abstract: BACKGROUND: Large outbreaks of diarrhea caused by a newly recognized strain of Clostridium difficile occurred in four hospitals located in different parts of the United States between 1989 and 1992. Since frequent use of clindamycin was associated with the outbreak in one of the hospitals, we examined the resistance genes of the epidemic-strain isolates and studied the role of clindamycin use in these outbreaks. METHODS: Case-control studies were performed at three of the four hospitals to assess the relation of the use of clindamycin to C. difficile-associated diarrhea. All isolates of the epidemic strain and representative isolates of other strains identified during each outbreak were tested for susceptibility to clindamycin. Chromosomal DNA from these representative isolates was also analyzed by dot blot hybridization and amplification with the polymerase chain reaction (PCR) with the use of probes and primers from a previously described determinant of erythromycin resistance - the erythromycin ribosomal methylase B (ermB) gene - found in C. perfringens and C. difficile. RESULTS: In a stratified analysis of the case-control studies with pooling of the results according to the Mantel-Haenszel method, we found that the use of clindamycin was significantly increased among patients with diarrhea due to the epidemic strain of C. difficile, as compared with patients whose diarrhea was due to nonepidemic strains (pooled odds ratio, 4.35; 95 percent confidence interval, 2.02 to 9.38; P<0.001). Exposure to other types of antibiotics or hospitalization in a surgical ward was not significantly associated with the risk of C. difficile-associated diarrhea due to the epidemic strain. All epidemic-strain isolates were highly resistant to clindamycin (minimal inhibitory concentration, >256 microg per milliliter). DNA hybridization and PCR analysis showed that all these isolates had an ermB gene, which encodes a 23S ribosomal RNA methylase that mediates resistance to macrolide, lincosamide, and streptogramin antibiotics. Only 15 percent of the nonepidemic strains were resistant to clindamycin. CONCLUSIONS: A strain of C. difficile that is highly resistant to clindamycin was responsible for large outbreaks of diarrhea in four hospitals in different states. The use of clindamycin is a specific risk factor for diarrhea due to this strain. Resistance to clindamycin further increases the risk of C. difficile-associated diarrhea, an established complication of antimicrobial use.

Johnsson E. et al. *Role of the hypervariable region in streptococcal M proteins: binding of a human complement inhibitor.* J Immunol. 1998; 161(9) : 4894-901.p Abstract: Antigenic variation allows pathogenic microorganisms to evade the immune system of the infected host. The variable structure must play an important role in pathogenesis, but its function is in most cases unknown. Here, we identify a function for the surface-exposed hypervariable region of streptococcal M5 protein, a virulence factor that inhibits phagocytosis. The hypervariable region of M5 was found to bind the human complement inhibitor FHL-1 (factor H-like protein 1), a 42-kDa plasma protein. Plasma absorption experiments with M5-expressing bacteria showed that the interaction with FHL-1 occurs also under physiologic conditions. Studies of another extensively characterized M protein, M6, indicated that this protein also has a binding site for FHL-1 in the

hypervariable region. The complement-inhibitory function of FHL-1 was retained after binding to streptococci, suggesting that bound FHL-1 protects bacteria against complement attack. All available data now indicate that FHL-1, or another human complement inhibitor, binds to the hypervariable region of M proteins. These findings provide insights into the forces that drive antigenic variation and may explain why the hypervariable region of M protein is essential for phagocytosis resistance. Moreover, these data add to a growing body of evidence that human complement inhibitors are major targets for pathogenic microorganisms.

Jonas J.B. et al. *Indwelling temporary retrobulbar catheter for long-lasting titratable local anesthesia.* Arch Ophthalmol. 2000; 118(7) : 996-1000.p Abstract: OBJECTIVE: To evaluate an indwelling temporary retrobulbar catheter for repeatable injections of local anesthetics for long-lasting and titratable retrobulbar anesthesia in intraocular surgery. PARTICIPANTS: The prospective clinic-based study included 153 patients who underwent vitreoretinal surgery (n=111) or buckling procedures with cryocoagulation (n=34). The mean duration of surgery was 84.7 +/- 49.5 minutes (range, 25-310 minutes). Using commercially available retrobulbar needles with a diameter of 0.60 or 0.80 mm and a length of 38 mm, 5 mL of 2% mepivacaine hydrochloride was injected. Through the same needle, a 28-gauge commercially available flexible catheter was introduced into the retrobulbar space. The needle was withdrawn and the catheter was fixed. When the patients started to feel pain during surgery, 2 mL of mepivacaine hydrochloride was reinjected through the catheter. RESULTS: Ten to 240 minutes after the start of the operation, 96 patients needed an intraoperative reinjection of mepivacaine after which they felt comfortable again. Forty-two patients needed a second reinjection of mepivacaine 30 to 270 minutes after the start of the operation, and 13 patients needed a third reinjection 45 to 145 minutes after the start of surgery. Removal of the catheter after surgery was unremarkable. No infections were observed. Microbiologic examination results of the catheter tip were negative for organisms. Diplopia or other motility problems were not detected. Introduction and fixation of the catheter took less than 5 minutes in all patients. CONCLUSIONS: An indwelling temporary retrobulbar catheter for repeatable intraoperative injections of local anesthetics is simple, effective, and useful, and in comparison with general anesthesia, it is a time-saver for long-lasting and titratable local anesthesia in intraocular surgery. Arch Ophthalmol. 2000;118:996-1000.

Jones B.L. et al. *Aeromonas infections and their treatment*. J Antimicrob Chemother. 1995; 35(4) : 453-61.p Abstract: With advances in the identification and molecular taxonomy of Aeromonas spp., these organisms, which are widely distributed in the environment, are increasingly being recognised as human pathogens. Clinical infections include gastroenteritis, skin and soft tissue infections and bacteraemia. Antibiotic resistance poses a potential problem in the antimicrobial therapy of infections cased by Aeromonas spp. While most strains are susceptible to chloramphenicol, ciprofloxacin, co-trimoxazole and the aminoglycosides, the activity of amoxycillin/clavulanate and the acylureidopenicillins is inconsistent. Addition of a beta-lactamase inhibitor does not significantly enhance the activity of the acylureidopenicillins. Aztreonam and the carbapenems, imipenem and meropenem remain highly active. Although resistance to the first and second generation cephalosporins is variable, more than 90% of Aeromonas spp. are susceptible to the third generation agents. Of potential significance is the identification of chromosomally-encoded inducible beta-lactamases, associated with resistance to extended spectrum penicillins, cephalosporins, monobactams and carbapenems, in clinical isolates of Aeromonas spp. Two distinct enzymes are produced: the A1 enzyme, a serine beta-lactamase behaving as a group 1 cephalosporinase, and the A2 enzyme, a metallo beta-lactamase which hydrolyses a wide range of beta-lactam agents including the carbapenems. The clinical relevance of these enzymes in Aeromonas spp. is unclear.

Jones E.M. et al. *Antimicrobial chemotherapy of human infection due to Listeria monocytogenes.* Eur J Clin Microbiol Infect Dis. 1995; 14(3) : 165-75.p Abstract: Listeriosis is an uncommon infection, but when it occurs it carries a high mortality rate. Early diagnosis is essential and thereafter appropriate antimicrobial chemotherapy. Ampicillin or penicillin plus gentamicin remains the treatment of choice for most manifestations of listeriosis, and adequate doses must be given, i.e. greater than 6g/day of ampicillin or penicillin. Co-trimoxazole appears to be an excellent alternative agent with good penetration into the cerebrospinal fluid. Vancomycin is an appropriate agent for the treatment of primary bacteraemia but does not cross the blood-brain barrier sufficiently well to be useful in meningitis, while erythromycin may be used to treat listeriosis in cases of pregnancy. Treatment of bacteraemia requires one to two weeks' therapy, while meningitis cases may need to be treated for longer; for example, it has been found that most patients with acute meningitis in the UK were treated for 20 days. Infective endocarditis needs treatment for six to eight weeks. Doses should be varied with patients' altered organ function and antimicrobial serum monitoring performed when appropriate.

Jones M.E. et al. *Frequency of occurrence and antimicrobial susceptibility of bacterial pathogens associated with skin and soft tissue infections during 1997 from an International Surveillance Programme. SENTRY Participants Group.* Eur J Clin Microbiol Infect Dis. 1999; 18(6) : 403-8.p Abstract: The SENTRY Antimicrobial Surveillance Programme was established to provide a coordinated, standardised, international surveillance on antimicrobial resistance. In one part of the programme, isolates from skin and soft tissue infections sent from 20 hospitals in 12 different European countries were investigated in the European coordinating centre. Of 1013 isolates, Staphylococcus aureus and Pseudomonas aeruginosa were the most significant species, constituting almost 50% of the referred isolates. Methicillin resistance in Staphylococcus aureus averaged 22% across Europe, only slightly less than that in isolates derived from blood. Less than 5% of the enterococcal isolates were resistant to vancomycin. Piperacillin/tazobactam was the most active penicillin-derived beta-lactam compound against Pseudomonas aeruginosa, inhibiting 91.3% of the isolates, while ceftazidime and cefepime were the most active cephalosporins, inhibiting 85.8% and 80.3% of the isolates, respectively. Putative extended-spectrum beta-lactamase production was not detected in Escherichia coli and was found in only 5.1% of the Klebsiella pneumoniae isolates. In general, strains of the family Enterobacteriaceae remained mostly susceptible to carbapenems, cefepime, and amikacin.

Jones M.R. et al. *Hospital-acquired blood stream infections in New Zealand.* N Z Med J. 1998; 111(1059) : 28-30.p Abstract: AIM: To determine the number and rates of hospital-acquired blood stream infections in New Zealand public hospitals. METHOD: From October 1994 to December 1996 each of the 23 Crown Health Enterprises (CHEs) provided the Crown Company Monitoring Advisory Unit with data on the number of episodes of hospital-acquired blood stream infection (HA-BSI) and the number of inpatient admissions. RESULTS: During the 27 month study period, 3049 episodes of HA-BSI occurred in an inpatient population of 1 300 892 giving a national average rate of 0.23%. HA-BSI rates were highest for the six tertiary level, metropolitan CHEs (range 0.19% - 0.56%) in which 79% of all HA-BSIs occurred. CONCLUSION: The HA-BSI rate for New Zealand is within the range that would be expected for a developed country with a comprehensive health service. The variability between CHEs in terms of the clinical services provided and case mix differences invalidates direct comparison of HA-BSI rates. Surveillance for HA-BSI should continue with the collection of data which would allow meaningful comparison of similar tertiary level services.

Jones R.D. et al. *Triclosan: a review of effectiveness and safety in health care settings.* Am J Infect Control. 2000; 28(2) : 184-96.p Abstract:

Triclosan is a widely accepted antimicrobial ingredient because of its safety and antimicrobial efficacy. Triclosan is a unique antimicrobial well suited for use in the health care industry in which mildness is a necessity to protect the health care worker during repeated use and antimicrobial activity is a necessity to protect public health. Triclosan has demonstrated immediate, persistent, broad-spectrum antimicrobial effectiveness and utility in clinical health care settings. This review highlights the utility and effectiveness of a 1% triclosan formulation for use in high-risk, high-frequency handwashing.

Jones R.N. *Can antimicrobial activity be sustained? An appraisal of orally administered drugs used for respiratory tract infections.* Diagn Microbiol Infect Dis. 1997; 27(1-2) : 21-8.p Abstract: Respiratory tract infections (RTIs) represent a major cause of illness worldwide. Therefore, it is of great concern that common RTI pathogens have become increasingly resistant to many of the antimicrobial agents used for therapy. For example, Haemophilus influenzae and Moraxella catarrhalis have become resistant to beta-lactam drugs by producing efficient beta-lactamases (> 35 and 90% of strains, respectively). More recently, pneumococci have become more resistant through the mechanism of altered penicillin-binding proteins (PBPs). The rate of penicillin nonsusceptible isolates has risen to > 25% in the United States (1994-1995). It is important to monitor the resistance characteristics of such pathogens and, if possible, to use regionally acquired data to guide empiric selection of therapeutic agents for RTIs. Currently, some antimicrobials remain effective against the majority of these three bacterial species, as exemplified by amoxicillin/clavulanic acid. Furthermore, amoxicillin alone seems to possess greater inhibition than other orally administered beta-lactams at clinically achievable concentrations against pneumococci with altered PBPs. It is critical that steps are taken to limit resistance problems, particularly through; 1) education of prescribers and the public; 2) initiation of the development of novel drugs with alternative modes of action or stability to existing resistance mechanisms; and 3) by continuing to generate quality susceptibility testing data to guide empiric chemotherapy against bacterial pathogens causing RTI.

Jones R.N. *Contemporary antimicrobial susceptibility patterns of bacterial pathogens commonly associated with febrile patients with neutropenia.* Clin Infect Dis. 1999; 29(3) : 495-502.p Abstract: One of the most challenging problems in antimicrobial chemotherapy is the effective empirical treatment of infection in patients with neutropenia. The rates of occurrence for pathogens have significantly changed (from predominance of gram-negative to gram-positive organisms) under selective pressure of broad-spectrum antimicrobial therapy or prophylaxis, and novel resistance mechanisms have emerged. To address the need for appropriate monotherapy or combination regimens for patients with neutropenia, physicians must prescribe agents with a spectrum of antimicrobial activity to inhibit the major, prevalent pathogens encountered in bloodstream infection and pneumonia; in addition, these selected agents must be active against recently described resistant organisms. Data from the SENTRY Antimicrobial Surveillance Program indicate that several broad-spectrum agents remain highly active and can be used alone or in combinations. In most cases, the newer compounds with increased activity and spectrum against gram-positive cocci (i.e., carbapenems, cefepime, levofloxacin, and trovafloxacin) offer a greater inhibitory potential for empirical therapy among patients with neutropenia and severe infections.

Jones R.N. *The impact of antimicrobial resistance: changing epidemiology of community-acquired respiratory-tract infections.* Am J Health Syst Pharm. 1999; 56(22 Suppl 3) : S4-11.p Abstract: Current surveillance data and mechanisms of resistance for the three most common bacteria infecting the respiratory tract are reviewed. Many pathogens, once susceptible to available antimicrobials, are now demonstrating high levels of resistance to commonly prescribed antimicrobial agents for the treatment of respiratory-tract infections. The three most common respiratory-tract pathogens, Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis, all exhibit high-level resistance to one or a number of agents, including penicillin, ampicillin, erythromycin, tetracycline, and first-generation cephalosporins. To determine the prevalence of resistance in these organisms, surveillance programs have begun tracking the emergence of antimicrobial resistance in the United States and worldwide. Data recovered from several national surveillance studies should help guide decisions about empirical therapeutic treatment.

Jones R.N. *Impact of changing pathogens and antimicrobial susceptibility patterns in the treatment of serious infections in hospitalized patients.* Am J Med. 1996; 100(6A) : 3S-12S.p Abstract: The selection of drug-resistant pathogens in hospitalized patients with serious infections such as pneumonia, urinary tract infections (UTI), skin and skin-structure infections, and primary or secondary bacteremia has generally been ascribed to the widespread use of antimicrobial agents. Issues of concern regarding gram-negative bacilli include the expression of extended spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumonias and constitutive resistance in some Enterobacteriaceae caused by Bush group 1 beta-lactamases. Current concerns with gram-positive pathogens are increasing multidrug resistance in methicillin-resistant Staphylococcus aureus, enterococci, and coagulase-negative staphylococci, and increasing incidence of penicillin-resistant Streptococcus pneumoniae. Contemporary treatment strategies for pneumonia in hospitalized patients mandate early empiric therapy for the most likely gram-positive and gram-negative pathogens. Newer beta-lactams, such as fourth-generation cephalosporins, may be useful in the treatment of pneumonia, including those cases associated with bacteremia. Combination beta-lactam/beta-lactamase inhibitor drugs, an aminoglycoside co-drug, or a carbapenem may also be indicated. The initial treatment of UTI in the hospital setting also may be empirically treated with the newer cephalosporins, combination broad-spectrum penicillins plus an aminoglycoside, a quinolone, or a carbapenem. Current problems in treating UTI include the emergence of extended spectrum beta-lactamase-producing Escherichia coli, the tendency of fluoroquinolones both to select for resistant strains of major UTI pathogens and to induce cross-resistance among different drug classes, and beta-lactam and vancomycin resistance of enterococci and coagulase-negative staphylococci. Treatment of skin and skin-structure infections is complicated by the coexistence of gram-positive and gram-negative infections, which may be drug resistant. Both fourth-generation beta-lactams and carbapenems may have in vitro activity against these pathogens; however, where these drugs—with their increased spectra and lower affinity for beta-lactamases and less susceptibility to beta-lactamase hydrolysis—fit into the therapeutic armamentarium remains to be determined. Initial clinical studies appear to be promising, nonetheless. The ability of both nosocomial and community-acquired pathogens to develop resistance to powerful broad-spectrum agents presents a great challenge for prescribing patterns and in the development of new drugs to be relatively resistant to inactivation.

Jones R.N. *Isepamicin (SCH 21420, 1-N-HAPA gentamicin B): microbiological characteristics including antimicrobial potency of spectrum of activity.* J Chemother. 1995; 7 Suppl 2 : 7-16.p Abstract: Isepamicin (formerly SCH 21420 or 1-N-HAPA-gentamicin B) is a novel broad-spectrum aminoglycoside which possesses a high level of stability to aminoglycoside inactivating enzymes and low levels of toxicity to the kidney and inner ear. The only modifying enzymes capable of inactivating isepamicin are ANT(4')-I (staphylococci), ANT(4')-II and APH(3')-VI, in addition to resistance mediated by permeability mutations. The spectrum of isepamicin is most similar to that of amikacin, another aminoglycoside with high enzyme stability. Reviews of isepamicin activity demonstrate MIC90s ranging from 1.1 to 8.5 mg/L for members of the Enterobacteriaceae, slightly more potent than amikacin. Pseudomonas aeruginosa, Acinetobacter spp. and other pseudomonads had isepamicin consensus MIC90s of

7.8, 7.2 and 6.8 mg/ml, respectively. Staphylococci were generally very susceptible to isepamicin (MIC90s 0.5-6.9 mg/L), but enterococci and Streptococcus spp. were resistant (MIC90s > or = 64 mg/L), as were anaerobes, Xanthomonas (Stenotrophomonas) maltophilia, pathogenic Neisseria spp., Flavobacterium spp., Pseudomonas (Burkholderia) cepacia, Alcaligenes spp. and Vibrio spp. Additional studies of isepamicin microbiology revealed: 1) MICs were adversely influenced by elevated divalent cation content of the medium; 2) minimum inoculum effects were observed by using elevated concentrations; 3) bactericidal action and concentration dependent killing was the rule; 4) excellent stability in the presence of high beta-lactam co-drug concentrations was documented in several studies; 5) predictable synergistic or additive interactions with broad spectrum antimicrobial agents such as cephalosporins, penicillins, carbapenems and fluoroquinolones was observed by numerous investigators; and 6) in vitro susceptibility testing criteria (National Committee for Clinical Laboratory Standards) and quality control guidelines are established for routine clinical use. Isepamicin's antimicrobial qualities position it as a potential alternative aminoglycoside in hospitals or in geographical areas where resistance to existing aminoglycosides has emerged. The wider stability of isepamicin to contemporary aminoglycoside inactivating enzymes, its predictable pharmacokinetics, lower toxicity risks and enhanced activity (synergy) with other broad spectrum antimicrobial agents, will make isepamicin a valuable addition to the antimicrobial armamentarium in areas where ACC(6') enzymes are prevalent (Europe, Latin America, Western Pacific) and amikacin has become less efficacious.

Jones R.N. *Perspectives on the development of new antimicrobial agents for resistant gram-positive pathogens.* Braz J Infect Dis. 2000; 4(1) : 1-8.p Abstract: There is great public and professional concern related to antimicrobial resistance, especially among Gram-positive pathogens associated with high morbidity and mortality. Penicillin-nonsusceptible Streptococcus pneumoniae, glycopeptide resistant enterococci, and oxacillin-resistant (MRSA) or vancomycin-intermediate (VISA) Staphylococcus aureus isolates continue to escalate in occurrence leading to the widespread use of empiric combination regimens. Newer, often novel, agents seem necessary to combat these pathogens. Among these, quinupristin/dalfopristin (Synercid), evernimicin or SCH 27899 (Ziracin), and linezolid (Zyvax) have the highest potency, widest spectrum, and most clinical experience. Among the quinolones (gatifloxacin, gemifloxacin, moxifloxacin), gatifloxacin is closest to clinical use and appears safe based on initial trial reports. Several broad-spectrum beta-lactams (''fourth-generation'' cephalosporins, carbapenems) are expected to be used with increasing frequency as a result of the emerging high rates of specific beta-lactamases that compromise the use of ceftriaxone, ceftazidime, and many beta-lactamase inhibition/ penicillin combinations. Among these agents, cefepime and meropenem are the most potent and broadest in clinical application in their respective classes. Physicians must stay informed about drug development and antimicrobial resistance by using results from local surveillance programs. When these data are unavailable, physicians should consider the use of national or global monitoring systems (SENTRY) to direct empiric antimicrobial selection.

Jones R.N. et al. *Antimicrobial activity of quinupristin-dalfopristin (RP 59500, Synercid) tested against over 28,000 recent clinical isolates from 200 medical centers in the United States and Canada.* Diagn Microbiol Infect Dis. 1998; 31(3) : 437-51.p Abstract: A total of 200 medical center laboratories in the USA and Canada contributed results of testing quinupristin-dalfopristin, a streptogramin combination (formerly RP 59500 or Synercid), against 28,029 Gram-positive cocci. Standardized tests [disk diffusion, broth microdilution, Etest (AB BIODISK, Solna, Sweden)] were utilized and validated by concurrent quality control tests. Remarkable agreement was obtained between test method results for characterizing the collection by the important emerging resistances: 1) oxacillin resistance among Staphylococcus aureus (41.0 to 43.7%); 2) vancomycin resistance among Enterococcus faecium (50.0 to 52.0%); and 3) the penicillin nonsusceptible rate for pneumococci (31.1% overall, with 10.6% at MICs of > or = 2 micrograms/mL). The quinupristin-dalfopristin MIC90 for oxacillin-susceptible and -resistant S. aureus was 0.5 microgram/mL and 1 microgram/mL, respectively. The quinupristin-dalfopristin MIC90 for vancomycin-resistant E. faecium was 1 microgram/mL, and only 0.2% of isolates were resistant. Other Enterococcus species were generally not susceptible to the streptogramin combination but were usually inhibited by ampicillin (86 to 97% susceptible; MIC50, 1.0 microgram/mL) or vancomycin (86 to 95%; MIC50, 1.0 microgram/mL). Among all tested enterococci, the rate of vancomycin resistance was 16.2%. The quinupristin-dalfopristin MIC90 (0.75 microgram/mL) for 4,626 tested Streptococcus pneumoniae strains was not influenced by the penicillin or macrolide susceptibility patterns. When five regions in the USA and Canada were analyzed for significant streptogramin and other antimicrobial spectrum differences, only the Farwest region had lower numbers of streptogramin-susceptible E. faecium. Canadian strains were generally more susceptible to all drugs except chloramphenicol and doxycycline when tested against E. faecalis (73% and 89% susceptible, respectively). The U.S. Southeast region had S. pneumoniae strains less susceptible to macrolides (73%) but had more susceptibility among E. faecium isolates tested against vancomycin and ampicillin. The Northeast region of the USA had the greatest rate of vancomycin resistance among enterococci. Strains retested by the monitor because of quinupristin-dalfopristin resistance (MICs, > or = 4 micrograms/mL) were generally not confirmed (2.2% validation), and only 0.2% of E. faecium isolates were identified as truly resistant. The most common errors were: 1) species misidentification (28.0%); 2) incorrect susceptibility results (65.6%); and 3) mixed cultures (4.3%) tested by participants. Overall, quinupristin-dalfopristin was consistently active (> or = 90% susceptible) against major Gram-positive pathogens in North America, regardless of resistance patterns to other drug classes and geographic location of their isolation.

Jones R.N. et al. *In vitro evaluation of sparfloxacin activity and spectrum against 24,940 pathogens isolated in the United States and Canada, the final analysis.* Diagn Microbiol Infect Dis. 1998; 31(1) : 313-25.p Abstract: Sparfloxacin, a recently marketed oral fluoroquinolone, was tested against 24,940 recent clinical strains isolated from blood stream and respiratory tract cultures at 187 hospitals in the USA and Canada. Sparfloxacin activity was compared with 5 to 13 antimicrobial agents using either Etest (AB BIODISK, Solna, Sweden) and a reference broth microdilution or a standardized disk diffusion method. When applying recommended MIC breakpoint criteria of sparfloxacin susceptibility (< or = 0.5 microgram/mL) for Streptococcus pneumoniae (4,410 strains) and other Streptococcus spp. (554 isolates), 93% and 88% were inhibited, respectively. Furthermore, at < or = 1 microgram/mL sparfloxacin susceptibility rates for streptococci increased to 98% overall and 99.3% for S. pneumoniae. In contrast, only 46% and 68% of pneumococci were susceptible to ciprofloxacin (MIC90, 3 micrograms/mL; susceptible at < or = 1 microgram/mL) and penicillin (MIC90, 1.5 microgram/mL; susceptible at < or = 0.06 microgram/mL), respectively. Differences between regions in the USA for rates of penicillin-resistant pneumococcal strains were observed (greatest resistances in southeast and midwest), but results indicate that the sparfloxacin potency was not adversely influenced (MIC90, 0.5 microgram/mL). Also pneumococcal isolates from the lower respiratory tract were more resistant to penicillin and other beta-lactams. Nearly all Haemophilus species and Moraxella catarrhalis strains, including those harboring beta-lactamases, were susceptible to tested fluoroquinolones (sparfloxacin, ciprofloxacin), amoxicillin/clavulanic acid, and newer oral cephalosporins. Sparfloxacin was very active against oxacillin-susceptible Staphylococcus aureus (MIC90, 0.12 microgram/mL; 96-97% susceptible), Klebsiella spp. (MIC90 0.12 microgram/mL), and other tested enteric bacilli (92-95% susceptible).

Comparisons between the broth microdilution MIC and disk diffusion interpretive results demonstrated excellent intermethod susceptibility category agreement (> 95%) using current sparfloxacin breakpoints, but some compounds (cefpodoxime disk diffusion tests for S. aureus) may require modifications. These results demonstrate that new Gram-positive focused fluoroquinolones (sparfloxacin) possess an excellent in vitro activity and spectrum against pathogens that cause respiratory tract infections. This spectrum of activity includes strains resistant to other antimicrobial classes, including the oral cephalosporins, macrolides, amoxicillin/clavulanic acid, and earlier fluoroquinolones (ciprofloxacin, ofloxacin). Overall, sparfloxacin inhibited 89% to nearly 100% of the isolates (species variable) tested against those species against which it has Food and Drug Administration indications for clinical use.

Jones R.N. et al. *Antimicrobial activity of trovafloxacin tested against ciprofloxacin-susceptible and -resistant Neisseria gonorrhoeae. Interpretive criteria and comparisons with Etest results.* Diagn Microbiol Infect Dis. 1997; 28(4) : 193-200.p Abstract: Trovafloxacin, a new fluorinated naphthyridine, has enhanced activity against Gram-positive cocci, while retaining an excellent spectrum against Gram-negative pathogens. It has been used successfully in clinical trials for therapy of gonorrhea, and this investigation proposes in vitro susceptibility testing criteria for trovafloxacin. A total of 150 Neisseria gonorrhoeae clinical isolates (50 resistant to ciprofloxacin; MICs > or = 0.12 microgram/mL) were tested by methods recommended by the National Committee for Clinical Laboratory Standards (NCCLS) and the Etest (AB BIODISK, Solna, Sweden). Trovafloxacin was very active against gonococci (MIC90, 0.008 to 0.015 microgram/mL), but was generally eightfold less potent versus ciprofloxacin-resistant strains. Etest results correlated well (r = 0.96; 98% of MICs +/- one log2 dilution) compared to the reference agar dilution test. Reference agar dilution and Etest MICs were compared to disk-diffusion test zones (10-micrograms trovafloxacin disk), and excellent categorical agreement (89.4 to 99.3%) was achieved without significant false-susceptible or -resistant error (< or = 1.3%). Tentative breakpoints were suggested initially to outline the ciprofloxacin-susceptible and trovafloxacin-susceptible as susceptible (MIC, < or = 0.015 microgram/mL; zones > or = 47 mm), and strains with various well-characterized mutations of the gyr A and par C genes as either intermediate or resistant to trovafloxacin. When the results of clinical studies treating ciprofloxacin-resistant N. gonorrhoeae with trovafloxacin become available, the alternative breakpoints could be utilized for resistant MIC breakpoints of > or = 0.06 microgram/mL or > or = 0.5 microgram/mL. Trovafloxacin was stable in supplemented GC agar for 21 days stored at refrigerated temperatures. These in vitro results indicate that trovafloxacin should be a very acceptable agent for therapy of gonorrhea and other common sexually transmitted pathogens.

Jones R.N. et al. *Antimicrobial activity of gatifloxacin tested against 1676 strains of ciprofloxacin-resistant gram-positive cocci isolated from patient infections in North and South America.* Diagn Microbiol Infect Dis. 1998; 32(3) : 247-52.p Abstract: Gatifloxacin (formerly AM-115) is a new 8-methoxy fluoroquinolone with an expanded spectrum against Gram-positive cocci and some anaerobes. To assess this new agent's activity, a collection of 1,676 Gram-positive cocci were selected for resistance to ciprofloxacin (> or = 4 micrograms/mL) and tested against gatifloxacin and 18 other compounds by reference broth microdilution methods. The strains (approximately 23,000 total isolates from the SENTRY Antimicrobial Surveillance Program) were from significant blood stream, respiratory tract, wound, and urinary tract infections in patients in North (38 hospitals) and South (10 hospitals) America. Against Enterococcus faecalis and E. faecium, gatifloxacin inhibited only 16% and 10% of strains compared with 12% and 5% for recently released trovafloxacin, respectively. Among Staphylococcus aureus (90% oxacillin-resistant) strains, gatifloxacin was more active (67% susceptible at < or = 4 micrograms/mL) than trovafloxacin (59%) or sparfloxacin (4%). Gatifloxacin had a wider spectrum than trovafloxacin against coagulase-negative staphylococci especially S. epidermidis, 2% versus 58% resistance. The glycopeptides, chloramphenicol and rifampin were most active. Against all genus/species groups with more than 100 sample strains (1,566), high-level resistance to gatifloxacin and trovafloxacin (> 4 micrograms/mL) was not significantly different (41.7% versus 39.1%; p > 0.05). Emerging resistance to the fluoroquinolones remains a clinical problem among Gram-positive species, and gatifloxacin seems to be active in vitro against many of these contemporary strains isolated in the Americas.

Jones R.N. et al. *Clindamycin resistance among erythromycin-resistant Streptococcus pneumoniae.* Diagn Microbiol Infect Dis. 1996; 25(4) : 201-4.p Abstract: The increasing proportion of Streptococcus pneumoniae isolates with reduced susceptibility to penicillin has created an urgent need for therapeutic alternatives to some beta-lactam agents. Clindamycin is an antimicrobial agent with excellent bioavailability after oral administration which has been considered for the therapy of community-acquired pneumococcal otitis media. Using the Etest methodology, we have studied the in vitro susceptibility of 59 erythromycin-resistant strains of S. pneumoniae to clindamycin, penicillin, trimethoprim-sulfamethoxazole, and rifampin. The study also addressed the impact of the susceptibility test medium [Mueller-Hinton (MH) vs IsoSensitest (Iso), both 5% blood supplement] on the results. A total of 20 isolates (37%) displayed constitutive clindamycin resistance on Iso blood agar, compared with only 11 (22%) on MH blood agar. The remaining nine strains found to be clindamycin susceptible on MH manifested resistance only with erythromycin induction. Resistance to penicillin, rifampin, and trimethoprim-sulfamethoxazole in erythromycin-resistant isolates was 83%, 2%, and 85%-89% (medium dependent), respectively. These results indicate that the choice of susceptibility test medium affects the expression (constitutive or inducible) of macrolide-lincosamide-streptogramin (MLS) resistance in S. pneumoniae. In addition, the common assumption that erythromycin resistance in S. pneumoniae implies clindamycin resistance may need to be reconsidered and routine susceptibility tests (including induction if MH medium is used) should be considered for MLS-class drugs.

Jones R.N. et al. *In vitro activity of selected cephalosporins and erythromycin against staphylococci and pneumococci isolated at 38 North American medical centers participating in the SENTRY Antimicrobial Surveillance Program, 1997-1998.* Diagn Microbiol Infect Dis. 2000; 37(2) : 93-8.p Abstract: The SENTRY Antimicrobial Surveillance Program employs a worldwide network of hospitals to monitor the predominant bacterial and fungal pathogens and antimicrobial susceptibility patterns associated with nosocomial and community-acquired bloodstream, respiratory tract, wound, and urinary tract infections. The purpose of this analysis of SENTRY data is to extract information on the current North American susceptibility patterns of pneumococci and oxacillin-susceptible staphylococci from the comprehensive SENTRY program database. Clinical isolates were provided by 30 centers in the United States (grouped into five regions) and eight centers in Canada. Susceptibility testing was performed at a central reference laboratory using broth microdilution methods and interpretive criteria specified by the National Committee for Clinical Laboratory Standards. Of 34 530 North American bacterial isolates tested during 1997 and 1998, 565 (1.6%) were oxacillin-susceptible, coagulase-negative staphylococci (CoNS). Cefazolin, cefepime, and ceftriaxone all had excellent activity against these CoNS (97.3%-99. 3% susceptible), and 90.4% were susceptible to ceftazidime. A total of 4404 isolates (12.8%) were oxacillin-susceptible Staphylococcus aureus. Overall, 98.9% to 99.2% were susceptible to cefazolin, cefepime, and ceftriaxone; ceftazidime did not have acceptable activity against these S. aureus. Streptococcus pneumoniae accounted for 1665 (4.8%) of North American SENTRY isolates. A total of 1212 isolates (72.8%) were fully susceptible to penicillin (MIC </= 0.06 microg/ml), 250 (15%) were penicillin intermediate (MIC 0.12-1 microg/ml), and 203 (12.2%) were penicillin resist-

ant (MIC >/= 2 microg/ml). The rate of penicillin susceptibility was highest in Canada, and lowest in the South Central and South East regions of the United States. Cefepime, cefuroxime, ceftazidime, and erythromycin all demonstrated excellent efficacy (94%-99.8% susceptibility) against fully penicillin-susceptible isolates of S. pneumoniae. Among pneumococci with intermediate penicillin resistance, 88% were susceptible to cefepime, 92% to cefotaxime, and only 14% to ceftazidime. None of the antimicrobial agents in this analysis demonstrated adequate activity against fully penicillin-resistant pneumococci. In summary, the fourth-generation cephalosporin, cefepime, demonstrated consistently excellent efficacy against oxacillin-susceptible staphylococci and most pneumococci, and remains an appropriate choice for empiric therapy of serious infections.

Jones R.N. et al. *In vitro efficacy of six cephalosporins tested against Enterobacteriaceae isolated at 38 North American medical centres participating in the SENTRY Antimicrobial Surveillance Program, 1997-1998.* Int J Antimicrob Agents. 2000; 15(2) : 111-8.p Abstract: The SENTRY Antimicrobial Surveillance Program is an ongoing international collaboration that monitors the predominant bacterial and fungal pathogens and antimicrobial susceptibility patterns associated with community-acquired and nosocomial infections. SENTRY data on the current cephalosporin susceptibility patterns (1997-98) of North American isolates of clinically important Enterobacteriaceae were analyzed. Susceptibility to a selection of cephalosporins was assessed at a central laboratory using reference broth microdilution methods and interpretive criteria specified by the National Committee for Clinical Laboratory Standards. The third- and fourth-generation cephalosporins tested demonstrated excellent activity against Escherichia coli and Klebsiella pneumoniae, whereas some of the older agents maintained good efficacy. Extended spectrum beta-lactamases were detected in all regions of the United States and Canada (1.8-10.7%). Cefepime was the most active agent tested against pathogens with the potential for enzyme-mediated resistance due to Amp C. The third-generation agents maintained acceptable efficacy against Serratia marcescens, but were less effective against Citrobacter and Enterobacter species. The older cephalosporins were generally inadequate against these pathogens, in contrast to cefepime, which was the widest spectrum cephalosporin overall. Some significant regional variations in spectrum were detected.

Jones R.N. et al. *Characteristics of pathogens causing urinary tract infections in hospitals in North America: results from the SENTRY Antimicrobial Surveillance Program, 1997.* Diagn Microbiol Infect Dis. 1999; 35(1) : 55-63.p Abstract: Urinary tract infection (UTI) is common and involves pathogens with changing susceptibility patterns. The SENTRY Antimicrobial Surveillance Program evaluates international pathogen incidence patterns to detect and manage the emergence of resistant strains. We describe the antimicrobial resistance patterns among 1617 pathogens recovered from UTIs during the third-quarter of 1997 in North America (United States and Canada), as part of this worldwide program. The isolates were tested against more than 50 antimicrobial agents (20 reported) by reference broth microdilution methods, and selected isolates were characterized by pulsed-field gel electrophoresis (PFGE) and automated ribotyping. The five most frequently isolated species were Escherichia coli (48.6%), Enterococcus spp. (13.7%), Klebsiella spp. (12.0%), Pseudomonas aeruginosa (6.2%), and Enterobacter spp. or Proteus mirabilis (3.8% each). For each nation, imipenem and cefepime produced the widest spectrum of coverage among the beta-lactams and amikacin was best among the aminoglycosides. For Gram-negative species, high resistance among beta-lactam antimicrobial agents was noted especially for various penicillins against E. coli (37.9% to 42.8%) and for the cephalosporins tested against enterococci (99.4% and 100%). Approximately 7.0% of enterococci in the USA were vancomycin-resistant (88% with Van A). P. aeruginosa provided the most consistent levels of resistance, but the following agents were most active against these organisms: amikacin (96.6 to 97.4% susceptible), tobramycin (89.5 to 100.0%), piperacillin/tazobactam (89.5 to 100.0%), piperacillin (89.5 to 96.6%), imipenem (89.7 to 92.1%), cefepime (77.6 to 89.7%), and ceftazidime (82.9 to 86.2%). E. coli (2.2 to 2.7%), K. pneumoniae (6.2 to 6.4%), and a single Enterobacter cloacae strain produced extended-spectrum beta-lactamases; and five other Enterobacter spp. were likely to have expressed chromosomally mediated (Amp C) Stably derepressed cephalosporinases with associated resistance to ceftazidime (16.7 to 21.2% resistance). These data demonstrated that several UTI isolates in SENTRY hospitals have high levels of resistance to various classes of antimicrobial agents with little evidence of clonal dissemination.

Jones R.N. et al. *Epidemiologic trends in nosocomial and community-acquired infections due to antibiotic-resistant gram-positive bacteria: the role of streptogramins and other newer compounds.* Diagn Microbiol Infect Dis. 1999; 33(2) : 101-12.p Abstract: The Gram-positive cocci have clearly re-emerged as important pathogens world-wide in the past two decades. Staphylococci, including the coagulase-negative staphylococci and Staphylococcus aureus, and the enterococci account for approximately one-third of all blood stream infections and as much as 50% of nosocomial blood stream infections. Although Streptococcus pneumoniae is often considered a community-acquired pathogen, it is also an important cause of nosocomial infection. The hallmark of these Gram-positive pathogens is increasing resistance to available antimicrobial agents. Of particular note is resistance to glycopeptides (vancomycin and teicoplanin), aminoglycosides (high-level), and penicillins among the enterococci (especially E. faecium), resistance to penicillinase-resistant penicillins (oxacillin and methicillin) and fluoroquinolones (ciprofloxacin and ofloxacin) among staphylococci, and resistance to penicillin, other beta-lactams and macrolides among the pneumococci. The recent detection of decreased susceptibility to vancomycin among S. aureus is also quite ominous. In many instances the ability of the clinical laboratory to accurately characterize these resistant isolates is suboptimal, further compounding the problem. Increased understanding of resistance mechanisms and correlations of resistance genes with the phenotypic expression of resistance has allowed for modifications and improvements of reference susceptibility tests and interpretive breakpoints. New compounds for effective therapy of infection with multi-resistant Gram-positive species are clearly needed. To this end, the streptogramin combination, quinupristin/dalfopristin, has demonstrated significant activity against oxacillin-resistant staphylococci, penicillin-resistant streptococci, and vancomycin-resistant E. faecium. Other candidate drugs including Gram-positive active fluoroquinolones (clinafloxacin, grepafloxacin, moxifloxacin, gatifloxacin, and trovafloxacin) and novel compounds such as the evernimicin derivatives (SCH27899), ketolides, and oxazolidinones (linezolid) have been shown to be active against these organisms and are under rapid clinical development.

Jones R.N. et al. *Antimicrobial interactions (synergy) of teicoplanin with two broad-spectrum drugs (cefotaxime, ofloxacin) tested against gram-positive isolates from Germany and the United States.* Diagn Microbiol Infect Dis. 1997; 29(2) : 87-94.p Abstract: Teicoplanin, a glycopeptide, has been widely used in some nations alone and in empiric therapy combinations to address infections caused by Gram-positive cocci. However, glycopeptide resistance and the increasing incidence of oxacillin-resistant staphylococci have compromised contemporary chemotherapy. In this study, teicoplanin was tested in combinations with ampicillin, cefotaxime with and without desacetylcefotaxime, and ofloxacin against 151 Gram-positive cocci to assess the potential for enhanced action. The strains included recent isolates from the United States and Germany having well-characterized resistance mechanisms (oxacillin-resistant staphylococci, vancomycin-resistant enterococci), each tested by NCCLS methods, checkerboard synergy tests, and kill-curves. Teicoplanin alone was active (MIC90s, 0.25-2 micrograms/mL) against all species except vanA enterococci. Drug interactions of teicoplanin with beta-lactams revealed synergy and partial synergy versus oxacillin-resistant Staphylococcus spp. (67-

100%) and vancomycin-resistant enterococci (70-100%), many at clinically achievable drug concentrations. However, confirming kill-curve experiments showed static action and no significant bactericidal effect. Combinations of ofloxacin with teicoplanin or cefotaxime plus desacetylcefotaxime showed a dominant additive and indifferent interaction. Teicoplanin continues to be a viable alternative to vancomycin, especially in combination therapy with selected broad-spectrum cephalosporins or fluoroquinolones. Many emerging pathogens that test resistant to individual drugs appear to be inhibited by tested combinations, extending their potential clinical utility.

Jones R.N. et al. *Nosocomial enterococcal blood stream infections in the SCOPE Program: antimicrobial resistance, species occurrence, molecular testing results, and laboratory testing accuracy. SCOPE Hospital Study Group.* Diagn Microbiol Infect Dis. 1997; 29(2) : 95-102.p Abstract: Characteristics of nosocomial enterococcal blood stream infection (NEBSI) isolates obtained from patients at 41 U.S. hospitals participating in the SCOPE Program were studied. Isolates from 480 episodes of NEBSI were characterized according to species and antimicrobial susceptibility profile. Selected isolates were also identified to species and vancomycin resistance genotype using polymerase chain reaction based methods. Polymerase chain reaction genotyping and ribotyping were used as genetic markers for molecular epidemiologic typing. Enterococci were the third most common cause of nosocomial blood stream infection in this study, accounting for 11.7% of all isolates reported. Enterococcus faecalis was the most common species (59.6%), followed by E. faecium (19.4%). Species identification errors involving E. faecium, E. durans, E. avium, and E. raffinosus were observed. Vancomycin resistance was observed in 36.4% of all participating medical centers and varied from 11.1% of medical centers in the Northwest to 60.9% of medical centers in the Southwest. Vancomycin-resistant enterococci accounted for 20.6% of NEBSI in the Northeast, 11.4% in the Southeast, 11.1% in the Southwest, and 9.5% in the Northwest regions. VanA genotypes predominated in the Northeast and Southwest, whereas vanA and vanB genotypes were equally prevalent in the Northwest and Southeast. Molecular typing studies identified strains that were unique to individual hospitals as well as strains that were prevalent in several different hospitals. NEBSI with vancomycin-resistant enterococci continues to escalate among hospitalized patients in all geographic areas of the USA.

Jones R.N. et al. *Activity of a broad-spectrum cephalosporin (Ro 48-8391) alone and in combination with two novel beta-lactamase inhibitors (Ro 48-5545 and Ro 48-8724).* Diagn Microbiol Infect Dis. 1998; 32(2) : 85-94.p Abstract: The susceptibility of a group of beta-lactamase-producing and drug-resistant Gram-positive and Gram-negative organisms was tested against a novel cephalosporin (Ro 48-8391) alone and in combination with two bridged carbacephem beta-lactamase inhibitors (Ro 48-5545 or Ro 48-8724) and compared with that of ceftriaxone, ceftazidime, and cefepime (representative "third- and fourth-generation" cephalosporins), imipenem, and a combination of piperacillin and tazobactam. Five hundred and one selected clinical isolates were tested using the reference broth microdilution method (National Committee for Clinical Laboratory Standards). Ro 48-8391 has a spectrum of activity and potency most similar to ceftriaxone but with improved activity against Gram-positive species. The two beta-lactamase inhibitors, Ro 48-5545 and Ro 48-8724, have modest antimicrobial activity. When combined with Ro 48-8391, the beta-lactamase inhibitor Ro 48-8724 was superior to the combination of Ro 48-8391 and Ro 48-5545 in spectrum and enzyme inhibition against extended spectrum beta-lactamase enzyme-producing Escherichia coli and Klebsiella pneumoniae, and against Enterobacteriaceae with "stably derepressed" Bush-Jacoby-Medeiros gr 1 enzymes (ceftazidime-resistant Enterobacter and Citrobacter). Ro 48-5545 and Ro 48-8724 appear to be promising beta-lactamase inhibitors with potential application against chromosomal- and plasmid-mediated enzymes. Ro 48-8391, although superior to some currently available "third-generation" cephems, was not a well-matched active codrug because of limited activity against several commonly isolated species of clinically important bacteria. Further efforts are necessary to find a penicillin or cephem with activity more complementary to that of the tested beta-lactamase inhibitors and the Ro 48-8391 compound could be focused for therapeutic use in serious streptococcal infections.

Jones R.N. et al. *Bacterial resistance: a worldwide problem.* Diagn Microbiol Infect Dis. 1998; 31(2) : 379-88.p Abstract: The therapeutic crisis produced by emerging antimicrobial resistances has compromised the chemotherapy of hospitalized patients with serious infections. For the most prevalent resistance problems, meropenem, a new carbapenem, appears to provide a potency and spectrum for: 1) extended-spectrum beta-lactamase-producing Enterobacteriaceae; 2) Bush-Jacoby-Merdeiros group 1 enzyme-producing ceftazidime-resistant Enterobacter spp., Citrobacter freundii, and some Serratia spp.; 3) ceftazidime- and imipenem-resistant Pseudomonas aeruginosa; and 4) some Streptococcus spp. with elevated penicillin MICs. Documented in vitro study results using 1997 gram-negative blood stream infection isolates indicate a wider spectrum and a two- to fourfold greater potency for meropenem compared with imipenem. This was especially true for P. aeruginosa where 93.4% of strains were susceptible to meropenem (84.1% for imipenem). Also among over 30,000 reported in vitro meropenem results from the United States and Europe, 90.6% of gram-positive cocci and 99.1% of anaerobes were inhibited at < or = 4 microg/ml. Over 90% of ceftazidime-resistant blood stream infection strains were meropenem susceptible, a rate greater than those of imipenem, ciprofloxacin, and gentamicin. As the clinical utility of many contemporary antimicrobial agents is challenged by emerging resistance, the carbapenems (meropenem, imipenem) appear positioned for a greater role in the treatment of infections in hospitalized patients.

Jones R.N. et al. *Comparative antimicrobial activity of trovafloxacin tested against 3049 Streptococcus pneumoniae isolates from the 1997-1998 respiratory infection season.* Diagn Microbiol Infect Dis. 1998; 32(2) : 119-26.p Abstract: Trovafloxacin is a new fluorinated naphthyridone having expanded activity against Gram-positive and anaerobic pathogens compared with ciprofloxacin or levofloxacin or ofloxacin. A multicenter in vitro trial (201 sites) was initiated in late 1997 to study the comparative activity of trovafloxacin against Streptococcus pneumoniae strains during the recently completed respiratory disease season. Each laboratory was asked to test 20 to 30 recent isolates (3049 strains) by the Etest (AB BIODISK, Solna, Sweden) method with observed phenotypes with elevated trovafloxacin results (MIC, > 1 microgram/mL) confirmed by the monitor laboratory (University of Iowa College of Medicine). Approximately one-third (34.0%) of isolates were penicillin nonsusceptible (12.8% high-level resistance at > or = 2 micrograms/mL). Also 20.4% and 4.5% of strains were resistant to macrolides (erythromycin) and ceftriaxone, respectively. The macrolide resistance rate was lowered to 16.8% when the adverse effect of CO2 incubation was considered. Only 0.3% of S. pneumoniae were vancomycin-nonsusceptible using the current National Committee for Clinical Laboratory Standards breakpoint (< or = 1 microgram/mL) with nearly all results were at 1.5 micrograms/mL. Trovafloxacin (MIC50 and MIC90, 0.094 and 0.19 microgram/mL, respectively) was eight fold more potent than levofloxacin (MIC90, 0.75 and 1.5 micrograms/mL), and fewer strains (0.10%) were discovered with high-level resistance (MIC, > or = 8 micrograms/mL). The four resistant isolates from different states had alterations in both par C and gyr A. Trovafloxacin had the best potency observed against contemporary pneumococcal isolates, and has a spectrum (> 99.8% susceptible) for an orally administered agent that was comparable to the tested parenteral glycopeptide, vancomycin (> 99.7%). Blood and spinal-fluid culture isolates were generally more susceptible to penicillin (74.4 to 75.6%), other beta-lactams, and erythromycin (84.4%); throat and sputum isolates were significantly more resistant ($p < 0.01$). Increases in resistance among S. pneumoniae strains to beta-lactams and erythromycin were docu-

mented in all geographic regions monitored, other resistances also continue to evolve, and high-level fluoroquinolone resistance remains very rare.

Jones R.N. et al. *Antimicrobial activity of 12 broad-spectrum agents tested against 270 nosocomial blood stream infection isolates caused by non-enteric gram-negative bacilli: occurrence of resistance, molecular epidemiology, and screening for metallo-enzymes.* Diagn Microbiol Infect Dis. 1997; 29(3) : 187-92.p Abstract: A total of 270 recent nosocomial blood stream isolates of non-Enterobacteriaceae Gram-negative bacilli representing nearly 50 U.S. medical centers were characterized. The numbers of isolates of individual organisms were: Pseudomonas aeruginosa (n = 204), Acinetobacter spp. (n = 48), and Stenotrophomonas maltophilia (n = 18). MICs were determined using the broth microdilution susceptibility method with 12 antimicrobial agents: piperacillin, piperacillin/tazobactam, ceftriaxone, ceftazidime, cefepime, imipenem, ciprofloxacin, ofloxacin, amikacin, gentamicin, tobramycin, and trimethoprim/sulfamethoxazole. Based on current National Committee for Clinical Laboratory Standards breakpoints, rates of resistance to cefepime, ceftazidime, and imipenem were as follows: P. aeruginosa, 3, 9, and 5%; Acinetobacter spp., 2, 37, and 0%; and S. maltophilia, 88.7, 35.3, and 100%, respectively. Trimethoprim/sulfamethoxazole was the most active agent against S. maltophilia (100% susceptible). Twenty-eight isolates of P. aeruginosa that expressed high levels of resistance to ceftazidime (MIC, > 256 micrograms/mL) and imipenem (MIC, > 32 micrograms/mL) were examined for potential metallo-beta-lactamase production by polymerase chain reaction and were found to be negative. Molecular typing of P. aeruginosa isolates revealed many patient-unique strains, but also noted clustering of infections due to isolates of the same DNA type, suggesting possible nosocomial transmission in 9 of 14 medical centers. Given the resistance profile and pathogenic potential of these non-enteric Gram-negative bacilli, considerable effort should be exerted to develop and enforce infection control and antimicrobial utilization practices that will limit the spread of these organisms in the hospital environment.

Jones R.N. et al. *Emerging multiply resistant enterococci among clinical isolates. I. Prevalence data from 97 medical center surveillance study in the United States. Enterococcus Study Group.* Diagn Microbiol Infect Dis. 1995; 21(2) : 85-93.p Abstract: To assess the evolving problem of therapeutic drug resistances among enterococci, we organized a comprehensive national (United States) surveillance trial using 99 recruited microbiology laboratories in 48 of the 49 contiguous states or districts. All but two sites completed the protocol that generated information from nearly 2000 enterococci, usually isolated from blood cultures. All strains were speciated by the same method (API 20S) and were susceptibility tested by three methods (broth microdilution, disk diffusion, and Etest) against ampicillin, penicillin, vancomycin, teicoplanin, gentamicin, and streptomycin. Strains resistant to a glycopeptide or penicillin, or possessing high-level aminoglycoside resistance were referred to the monitor's laboratory for validation and additional susceptibility testing against other alternative antimicrobial agents. The most common species were Enterococcus faecalis and Enterococcus faecium. However, antimicrobial resistance occurred most often among the E. faecium isolates. Twenty-three percent of participant centers (22 sites) reported 87 vancomycin-resistant isolates, which accounts for 4.4% of the isolates evaluated. A recent audit (March 1994) of the laboratories not reporting vancomycin resistance during the study interval (October-December 1992) revealed that 61% of sites have now recognized these strains, a threefold increase in 12-15 months. Teicoplanin remained active against 28% (Van B phenotype) of vancomycin-resistant enterococci (10 E. faecalis, 13 E. faecium, and one Enterococcus spp.). Ampicillin-resistant beta-lactamase-positive strains were found only at one medical center (two strains, 0.2% of referred or validated strains); however, ampicillin-resistant strains represented 12% of all enterococcal, but nearly 60% of E. faecium strains. (ABSTRACT TRUNCATED AT 250 WORDS).

Jorgensen J.H. et al. *Rapid automated antimicrobial susceptibility testing of Streptococcus pneumoniae by use of the bioMerieux VITEK 2.* J Clin Microbiol. 2000; 38(8) : 2814-8.p Abstract: The VITEK 2 is a new automated instrument for rapid organism identification and susceptibility testing. It has the capability of performing rapid susceptibility testing of Streptococcus pneumoniae with specially configured cards that contain enriched growth medium and antimicrobial agents relevant for this organism. The present study compared the results of testing of a group of 53 challenge strains of pneumococci with known resistance properties and a collection of clinical isolates examined in two study phases with a total of 402 and 416 isolates, respectively, with a prototype of the VITEK 2. Testing was conducted in three geographically separate laboratories; the challenge collection was tested by all three laboratories, and the unique clinical isolates were tested separately by the individual laboratories. The VITEK 2 results of tests with 10 antimicrobial agents were compared to the results generated by the National Committee for Clinical Laboratory Standards reference broth microdilution MIC test method. Excellent interlaboratory agreement was observed with the challenge strains. The overall agreement within a single twofold dilution of MICs defined by the VITEK 2 and reference method with the clinical isolates was 96.3%, although there were a number of off-scale MICs that could not be compared. The best agreement with the clinical isolates was achieved with ofloxacin and chloramphenicol (100%), and the lowest level of agreement among those drugs with sufficient on-scale MICs occurred with trimethoprim-sulfamethoxazole (89.7%). Overall there were 1.3% very major, 6.6% minor, and no major interpretive category errors encountered with the clinical isolates, although >80% of the minor interpretive errors involved only a single log(2) dilution difference. The mean time for generation of susceptibility results with the clinical isolates was 8.1 h. The VITEK 2 provided rapid, reliable susceptibility category determinations with both the challenge and clinical isolates examined in this study.

Jorgensen J.H. et al. *Antimicrobial susceptibility testing: special needs for fastidious organisms and difficult-to-detect resistance mechanisms.* Clin Infect Dis. 2000; 30(5) : 799-808.p Abstract: Clinical microbiology laboratories are faced with the challenge of accurately detecting emerging antibiotic resistance among a number of bacterial pathogens. In recent years, vancomycin resistance among enterococci has become prevalent, as has penicillin resistance and multidrug resistance in pneumococci. More recently, strains of methicillin-resistant Staphylococcus aureus with reduced susceptibility to vancomycin have been encountered. In addition, molecular techniques have demonstrated that there are still problems detecting methicillin resistance in staphylococci, especially in coagulase-negative species. Among members of the family Enterobacteriaceae, mutated beta-lactamase enzymes may confer difficult-to-detect resistance to later-generation penicillins and cephalosporins. Anaerobic bacteria are no longer entirely predictable in their susceptibility to agents that might be selected for empiric therapy. Therefore, clinical microbiology laboratories may not be able to rely on a single susceptibility testing method or system to detect all those emerging resistant or fastidious organisms. For reliable detection, laboratories may need to employ conventional, quantitative susceptibility testing methods or use specially developed, single concentration agar screening tests for some resistant species. Certain of these screening tests are highly specific, while others may require additional confirmatory testing for definitive results. Therefore, laboratories must retain the versatility to apply several different approaches to detect resistance in both common and infrequently encountered bacterial pathogens.

Jorgensen J.H. et al. *Evaluation of the Dade MicroScan MICroSTREP antimicrobial susceptibility testing panel with selected Streptococcus pneumoniae challenge strains and recent clinical isolates.* J Clin Microbiol. 1998; 36(3) : 788-91.p Abstract: The MicroScan MICroSTREP panel is a recently marketed frozen broth microdilution panel for susceptibility testing of various streptococci, including Streptococcus pneu-

moniae. The panel contains 10 antimicrobial agents in cation-adjusted Mueller-Hinton broth supplemented with 3% lysed horse blood, similar in concept to the National Committee for Clinical Laboratory Standards (NCCLS) reference broth microdilution method for testing streptococci. A group of 210 isolates of S. pneumoniae were selected to include isolates with previously documented resistance to agents incorporated in the MICroSTREP panel, as well as recent invasive clinical isolates. All isolates were tested simultaneously with the MICroSTREP panel and an NCCLS reference panel whose drug concentrations were prepared to coincide with those of the MICroSTREP panel. Of the 210 isolates, 5 failed to grow in the MICroSTREP panel; 3 of those also did not grow in the reference panel. Essential agreement of MICs determined by the two methods (test MIC +/- one dilution of the reference MIC) was 99.6% overall and ranged from 98.0% with chloramphenicol to 100% with penicillin, ceftriaxone, erythromycin, tetracycline, and vancomycin. There were no very major or major interpretive category errors resulting from the MICroSTREP panel tests. Minor interpretive category errors ranged from 12.2% with cefotaxime and 9.8% with ceftriaxone (due mainly to clustering of MICs for the selected strains near the breakpoints) to 0% with chloramphenicol and vancomycin. These results indicate that the MicroScan MICroSTREP frozen panels provide susceptibility results with pneumococci that are essentially equivalent to results derived by the NCCLS reference broth microdilution procedure.

Jorgensen J.H. et al. *Development of interpretive criteria and quality control limits for macrolide and clindamycin susceptibility testing of Streptococcus pneumoniae.* J Clin Microbiol. 1996; 34(11) : 2679-84.p Abstract: A six-laboratory collaborative study was conducted to develop MIC and zone diameter quality control limits and interpretive criteria for antimicrobial susceptibility testing of Streptococcus pneumoniae with azithromycin, clarithromycin, dirithromycin, and clindamycin. The MICs of all of the agents plus erythromycin for 302 clinical isolates of pneumococci that had been selected with an emphasis on resistant strains were determined by use of the National Committee for Clinical Laboratory Standards (NCCLS)-recommended broth microdilution procedure. The zone diameters of the isolates were also determined for the same agents except erythromycin by the NCCLS disk diffusion test procedure. Repeated testing of S. pneumoniae ATCC 49619 with different sources and lots of media and disks allowed development of MIC and zone diameter quality control ranges for these agents. Interpretive criteria for the MIC of azithromycin were established and were as follows: susceptible, < or = 0.5 microgram/ml; intermediate, 1 microgram/ml; and resistant, > or = 2 micrograms/ml. The interpretive criteria advocated for the MICs of clarithromycin and clindamycin were as follows: susceptible, < or = 0.25 microgram/ml; intermediate, 0.5 microgram/ml; and resistant, > or = 1 microgram/ml. Comparison of MICs and disk diffusion zone diameters led to the development of interpretive criteria for the zone diameters for azithromycin, clarithromycin, and clindamycin that correlated well with these MIC breakpoints. Testing of this organism collection also led to the reestablishment of the erythromycin MIC breakpoints as being identical to those of clarithromycin, which resulted in equivalent cross-susceptibility and cross-resistance for the three macrolides that are currently marketed in the United States. Thus, the susceptibility of pneumococci to azithromycin and clarithromycin can be predicted accurately by testing only erythromycin in clinical laboratories. This recommendation, as well as the interpretive and quality control criteria that are described, have been accepted by NCCLS and are included in the latest NCCLS susceptibility testing guidelines.

Jousimies-Somer H. et al. *Susceptibilities of bovine summer mastitis bacteria to antimicrobial agents.* Antimicrob Agents Chemother. 1996; 40(1) : 157-60.p Abstract: The susceptibility to 9 antimicrobial agents of 32 aerobic bacterial isolates and to 10 antimicrobial agents of 37 anaerobic bacterial isolates from 23 cases of bovine summer mastitis (16 Actinomyces pyogenes isolates, 8 Streptococcus dysgalactiae isolates, 3 S. uberis isolates, 3 S. acidominimus isolates, 2 Streptococcus spp., 15 Peptostreptococcus indolicus isolates, 10 Fusobacterium necrophorum isolates, and 12 isolates of anaerobic gram-negative rods) was determined by the agar dilution method. All isolates except one Bacteroides fragilis isolate (beta-lactamase producer) were susceptible to penicillin G, amoxicillin, amoxicillin-clavulanate, cefoxitin, clindamycin, and chloramphenicol (the B. fragilis strain was susceptible to the last four), which had MICs at which 90% of isolates were inhibited (MIC90s) of < or = 0.06, < or = 0.06, < or = 0.06 0.25, < or = 0.06, and 4.0 micrograms/ml, respectively. Spiramycin was active against the gram-positive aerobes (MIC90, 1.0 microgram/ml) but not against the anaerobes (MIC90, 16.0 micrograms/ml). Similar trends were noted for susceptibilities of aerobic and anaerobic bacteria to ofloxacin (MIC90s, 2.0 and 8 micrograms/ml, respectively). Occasional strains of aerobic streptococci were resistant to oxytetracycline, but all anaerobes were susceptible. Tinidazole was active against all anaerobes (MIC90, 2.0 micrograms/ml). beta-Lactamase was produced only by the B. fragilis isolate.

Joyanes P. et al. *[Usefulness of the disk diffusion method for evaluating the sensitivity of Neisseria meningitidis to penicillin and cefotaxime (see comments)].* Enferm Infecc Microbiol Clin. 1997; 15(10) : 515-8.p Abstract: BACKGROUND: Routine susceptibility testing of Neisseria meningitidis to penicillin and other beta lactams is recommended after the isolation of N. meningitidis of moderately resistant to penicillin (MRP). We have evaluated the disk-diffusion method to determine susceptibility of N. meningitidis to penicillin (using disks of either penicillin or oxacillin) and to cefotaxime. METHODS: Fifty-four strains of N. meningitidis isolated from clinical samples were studied. MICs of penicillin and cefotaxime were determined by microdilution. Disks of 2 U of penicillin, 1 microgram of oxacillin and 30 micrograms of cefotaxime and two culture media, Mueller-Hinton agar (MHA) and MHA supplemented with 5% sheep blood (MHS) were used in the disk-diffusion assay. RESULTS: For disk of 2 U of penicillin assayed in MHA, 86.4% of the susceptible strains and 20% of MRP strains were considered susceptible when a breakpoint of 28 mm was considered. None of the MRP strains was considered susceptible when using MHS, but only 38.6% of susceptible strains appeared as such on this medium. When a 1 microgram oxacillin disk was used all MRP strains presented an inhibition zone < or = 10 mm on both MHA and MHS, but 54.4 and 4.5% of susceptible strains presented an inhibition zone > or = 11 mm on MHA and MHS, respectively. All strains were susceptible to cefotaxime, showing inhibition zones around a 30 micrograms disk on MHA and MHS of > or = 35 mm and > or = 25 mm, respectively. CONCLUSION: Disk diffusion with cefotaxime (30 micrograms) allows to determine susceptibility of N. meningitidis to this antimicrobial agent. Discs of penicillin (2 U) and oxacillin (1 microgram) are not useful for screening of MRP N. meningitidis.

Joynt G.M. et al. *Deep venous thrombosis caused by femoral venous catheters in critically ill adult patients.* Chest. 2000; 117(1) : 178-83.p Abstract: STUDY OBJECTIVES: To determine the frequency of and potential risk factors for catheter-related deep venous thrombosis (DVT) in critically ill adult patients. DESIGN: Prospective, controlled, observational cohort study. SETTING: A mixed medical and surgical ICU in a university hospital. PATIENTS: All adult patients undergoing femoral vein catheterization. INTERVENTIONS: None. MEASUREMENTS: ICU diagnosis, underlying disease, demographic data, type of catheter, complications during cannulation, use of anticoagulants, coagulation status, medications infused, and duration of catheterization were recorded. Compression and duplex Doppler ultrasound studies of both femoral veins were performed prior to insertion, at 12 h after insertion, and daily until catheter removal. Follow-up investigation was performed at 24 h and 1 week after removal. RESULTS: Of 140 cases entered into the study, 124 were evaluated. Fourteen patients developed iliofemoral vein DVTs. Two were clinically obvious. Twelve (9.6%) were line

related (uncannulated leg normal) and two (1.6%) occurred only in the uncannulated leg (p = 0.011; relative risk, 6.0; confidence interval, 1.5 to 23.5). Line-related DVT can occur any time from the day after insertion to 1 week after removal. The incidence of catheter-related DVT was unrelated to number of insertion attempts, arterial puncture or hematoma, duration of catheterization, coagulation status, or type of infused medications. No other predisposing or protective factors were identified. Three of the 12 patients with catheter-related DVT died. In no patient was clinical pulmonary embolus suspected. CONCLUSION: Although the femoral route is convenient and has potential advantages, the use of femoral lines increases the risk of iliofemoral DVT. Catheter-related DVT may occur as soon as 1 day after cannulation and is usually asymptomatic. This increased risk should be carefully considered when the femoral route of cannulation is chosen.

Juffermans N.P. et al. *Interleukin-1 signaling is essential for host defense during murine pulmonary tuberculosis.* J Infect Dis. 2000; 182(3) : 902-8.p Abstract: Interleukin (IL)-1 signaling is required for the containment of infections with intracellular microorganisms, such as Listeria monocytogenes and Leishmania major. To determine the role of IL-1 in the host response to tuberculosis, we infected IL-1 type I receptor-deficient (IL-1R(-/-)) mice, in which IL-1 does not exert effects, with Mycobacterium tuberculosis. IL-1R(-/-) mice were more susceptible to pulmonary tuberculosis, as reflected by an increased mortality and an enhanced mycobacterial outgrowth in lungs and distant organs, which was associated with defective granuloma formation, containing fewer macrophages and fewer lymphocytes, whereas granulocytes were abundant. Lymphocytes were predominantly confined to perivascular areas, suggesting a defective migration of cells into inflamed tissue in the absence of IL-1 signaling. Impaired host defense in IL-1R(-/-) mice was further characterized by a decrease in the ability of splenocytes to produce interferon-gamma. Analysis of these data suggests that IL-1 plays an important role in the immune response to M. tuberculosis.

Julve R. et al. *[Clinical manifestations of Stenotrophomas (Xanthomonas) maltophilia infection].* An Med Interna. 1998; 15(9) : 476-80.p Abstract: OBJECTIVE: Stenotrophomonas maltophilia (SM) is a gram-negative bacillus whose incidence like nosocomial pathogen has been incremented in the last years, especially in immunocompromised patients, subjected to invasive procedures and those receiving broad-spectrum antimicrobial therapy. METHOD: We report 15 isolations of SM between 1994-1996. RESULTS: The criteria for SM infection were fulfilled by 9 patients (60%), and 6 patients (40%) were colonized. The mean age of the patient was 60 +/- 12 years. Major predisposing factors in infections included venous catheterization (100%), prior surgery (86%), residence in ICU (80%), prior antibiotic therapy (80%) and intubation (66%). The most common underlying disease were heart disease (60%), treatment with immunosuppressors and/or steroids (46%) and chronic lung disease (46%). Ten cases (66%) had polymicrobial culture. The mortality rate was 40%. Risk factors associated with fatal outcome included the following: chronic lung disease (p = 0.043), nasogastric catheterization (p = 0.01), urinary tract catheterization (p = 0.02), intubation (p = 0.04) and the presence of pneumonia or sepsis by SM (p = 0.02). The most active agents were colistina (100%), cotrimoxazol (71%) and ceftazidima (53%). The isolates were highly resistant to first and second-generation cephalosporins (100%) tetracyclines (86%), aztreonam (91%) and imipenem (71%). CONCLUSION: SM cause a wide range of clinical syndromes and is more likely to cause infection or colonization in patients who have underlying disease. Due to its inherent multiple-antimicrobial resistance, it would appear its potential as a nosocomial pathogen will continue to increase. Therapy of patients should include cotrimoxazole.

Jung S.O. et al. *Screening of new bioactive materials from microbial extracts of soil microorganism (I). Antimicrobial activity from 200 samples using microdilution assay.* Arch Pharm Res. 1998; 21(3) : 278-85.p Abstract: The microdilution assay recommended by NCCLS (National Committee for Clinical Laboratory Standards) is one of the standardized methods of antibiotic susceptibility test. This method has been widely used clinically to obtain MIC values of antibiotics on pathogenic microorganisms. It is more convenient, rapid and simple to test many samples than other test methods such as agar diffusion assay and broth macrodilution assay. The screening of antimicrobial agents from microbial extracts is too laborious in its process. Therefore, a number of screening methods having more simple procedure have been developed. In our laboratory, we applied microdilution assay for screening the antimicrobial agents. This assay showed dose-response results and was more sensitive than disc diffusion assay in our system. We tested 200 samples of microbial extracts originated from 100 microbial strains and selected several samples as potential candidates. In this report, we show that the microdilution assay is more convenient method in screening of antibiotic susceptibility than those previously reported.

Junquera Gutierrez L.M. et al. *[Primary tuberculosis of the oral cavity].* Rev Stomatol Chir Maxillofac. 1996; 97(1) : 3-6.p Abstract: Primary tuberculosis in the oral cavity is a rare entity. Usually, the microorganisms need a disruption of the oral mucosa to become pathogenic. In this article the authors describe a clinical case of primary oral tuberculosis, on a female of 52 years-old who suffered an exodontia 20 days before. The bacteria identificated was Mycobacterium tuberculosis hominis. The microbiologic identification is essential to assure the efficacy of the treatment.

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Kaandorp C.J. et al. *Incidence and sources of native and prosthetic joint infection: a community based prospective survey.* Ann Rheum Dis. 1997; 56(8) : 470-5.p Abstract: OBJECTIVES: To determine the incidence and sources of bacterial arthritis in the Amsterdam health district and the maximum percentage of cases that theoretically would be preventable. METHODS: Patients with bacterial arthritis diagnosed between 1 October 1990 and 1 October 1993 were prospectively reported to the study centre by all 12 hospitals serving the district. Data were gathered on previous health status, source of infection, and microorganisms involved. RESULTS: 188 episodes of bacterial arthritis were found in 186 patients. Most of the 38 children were previously healthy. Fifty per cent of the adults were 65 years or older. Of the adults 84% had an underlying disease, in 59% a joint disorder. Joint surgery constituted the largest part of direct infections (33%) and skin defects were the most important source of haematogenous infections (67%). Infection of joints containing prosthetic or osteosynthetic material by a known haematogenous source occurred 15 times (8%). Staphylococcus aureus was the causative organism in 44% of all positive cultures. CONCLUSION: The incidence of bacterial arthritis was 5.7 per 100,000 inhabitants per year. Preventive measures directed to patients with prosthetic joints or osteosynthetic material, and a known haematogenous source would have prevented at most 8% of all cases.

Kagawa K. et al. *Reduction of peritonitis with the rectus abdominis muscle flap in a CAPD patient.* Pediatr Nephrol. 2000; 14(2) : 114-6.p Abstract: An adolescent maintained on continuous ambulatory peritoneal dialysis (CAPD) for 8 years had relapsing peritonitis involving peritoneal catheter tunnel infections. We attempted catheter removal and replacement simultaneously, with the catheter covered cylindrically by a rectus abdominis muscle flap to prevent recurrent tunnel infections. During 3 years of follow-up, there have been no episodes of peritonitis involving tunnel infection. Our modified insertion technique can eradicate tunnel infection, thus reducing peritonitis.

Kahn E. *Gastrointestinal manifestations in pediatric AIDS.* Pediatr Pathol Lab

Med. 1997; 17(2) : 171-208.p Abstract: The pathologic changes in the gastrointestinal tract of children with AIDS are variable, clinically significant, and reflect multisystemic disease processes. Inflammation, changes in the lymphoid tissue, miscellaneous lesions, and tumors are documented in 58 patients in addition to cases reported in the literature. Cytomegalovirus infection of the gastrointestinal tract, associated with ulcerations, hemorrhage, perforations, and intestinal obstruction, carries a high morbidity and mortality, whereas the remaining infections are not life threatening. Special stains and electron micrographic examination are important to identify correctly certain microorganisms such as mycobacterium avium intracellulare, cryptosporidia, and microsporidia. Lymphoproliferative changes of the gastrointestinal tract, a component of the generalized lymphoproliferative process, need to be characterized by tumor markers and cytogenetic studies. Within the miscellaneous lesions, AIDS associated arteriopathy can be complicated by intestinal ulceration and perforation. Both lymphomas and smooth muscle tumor in children with AIDS are related to Epstein-Barr virus infection. The smooth muscle tumors are frequently malignant and multiple.

Kaitwatcharachai C. et al. *An outbreak of Burkholderia cepacia bacteremia in hemodialysis patients: an epidemiologic and molecular study.* Am J Kidney Dis. 2000; 36(1) : 199-204.p Abstract: The risk of blood stream infections increases in patients undergoing chronic hemodialysis. Outbreaks of infection are usually caused by contamination of the water supply, water treatment, distribution system, or dialyzer reprocessing. We report an outbreak of subclavian catheter-related Burkholderia cepacia bacteremia in nine patients undergoing hemodialysis. Using randomly amplified polymorphic DNA (RAPD) analysis, the bacterial isolates were clonally identical to Burkholderia cepacia isolated from residue of the diluted chlorhexidine-cetrimide solution used to disinfect the transfer forceps. These forceps were used to pick up cotton balls and gauze for dressing the subclavian catheter. Antibiotic therapy failed to cure the infections, and all patients required catheter removal. Pathology showed numerous bacilli embedded in the biofilm on the inner surface of the removed catheters. In conclusion, our study showed that contaminated chlorhexidine-cetrimide solution was the source of a bacteremic outbreak in nine patients who developed catheter-related Burkholderia cepacia infection.

Kalchayanand N. et al. *Interaction of hydrostatic pressure, time and temperature of pressurization and pediocin AcH on inactivation of foodborne bacteria.* J Food Prot. 1998; 61(4) : 425-31.p Abstract: High hydrostatic pressure, because it can kill microorganisms, is being investigated for potential use as a nonthermal food preservation method. The objective of this study was to determine the hydrostatic pressurization parameters, pressure, time, and temperature, and a bacteriocin that in combination would destroy 7 to 8 log cycles of pathogenic and spoilage bacterial populations. We suspended cells of Staphylococcus aureus, Listeria monocytogenes, Salmonella typhimurium, Escherichia coli O157:H7, Lactobacillus sake, Leuconostoc mesenteroides, Serratia liquefaciens, and Pseudomonas fluorescens in peptone solution and exposed them to the combination of treatments. The combined parameters used were hydrostatic pressure (138 to 345 MPa), time (5 to 15 min), temperature (25 to 50 degrees C), and pediocin AcH (3,000 AU/ml, final concentration). In general, cell death increased as the pressure, time, or temperature increased; however, the cells developed proportionately greater sensitivity as the pressure increased to 276 MPa and higher and the temperature increased above 35 degrees C. Pressurization for longer than 5 min, especially at lower pressure and temperature ranges, had very little added benefit. Among the four gram-negative species, E. coli O157:H7 was the most resistant to pressurization while among the four gram-positive species, L. sake and L. mesenteroides had greater resistance. The death rate at high pressure (345 MPa) and high temperature (50 degrees C) in combination followed first-order kinetics; at lower pressure and temperature combination it showed a late tailing effect. Estimated D value data indicated that even at 345 MPa and 50 degrees C an 8-log-cycle viability loss could not be achieved within 5 min for all eight species. However, when pediocin AcH was included during pressurization this loss was achieved.

Kalenic S. et al. *Helicobacter pylori: in vitro induction of resistance to azithromycin.* Chemotherapy. 1998; 44(1) : 17-20.p Abstract: Helicobacter pylori resistance to macrolides is possibly an important factor for the failure of macrolide therapy for H. pylori infection. The aim of this study was to assess the propensity of H. pylori to develop in vitro resistance to azithromycin. In 73 clinical isolates taken from patients before starting antimicrobial therapy of H. pylori infection, MIC was determined using an agar dilution method (Muller-Hinton agar with 7.5% unlysed horse blood, pH = 7.2, at 35 degrees C, during 72 h in a humid microaerobic atmosphere). Each strain was first cultivated at half minimal inhibitory concentration (MIC) then in doubling concentrations until growth arrest. All experiments for induction of resistance were performed on the same media, incubation temperature, atmosphere and time of MIC determination. MIC interpretative standards for sensitivity, intermediate sensitivity and resistance of H. pylori to azithromycin were < or = 2, 4 and > or = 8 mg/l, respectively. Of 73 strains, 5 died during the experiments, and in the remaining 68 strains, serial passage with increasing azithromycin concentrations resulted in the development of resistance in 19 (26.9%) strains. Two strains had an MIC of 16 mg/l azithromycin. Thirty-three (48.5%) strains kept the same MIC or doubled their MIC, 16 (23.5%) strains had 4- to 16-fold MIC but still remained sensitive, 2 resistant strains had 128-fold MICs and 17 resistant strains had increased their MICs more than 128 times. Seventeen highly resistant strains (MIC > 128 mg/l) were kept frozen at -70 degrees C for 3 months in a brain-heart infusion broth with 15% glycerol. MIC was assessed again to determine the stability of resistance. Eleven strains kept MICs > 128 mg/l, 2 became sensitive and 1 intermediate, but reverted easily, after only 2 passages, to an MIC of > 128 mg/l azithromycin. Although macrolides are very active against H. pylori, the propensity to develop resistance in a high proportion of strains has a clear impact on the choice of the right combinations of macrolides with other agents as well as the dosage of the macrolide antibiotics.

Kaluzynska A. et al. *[An incidence and etiology of Tenckhoff catheter in patients treated with CAPD].* Pol Merkuriusz Lek. 2000; 8(46) : 274-5.p Abstract: Continuous ambulatory peritoneal dialysis (CAPD) is a renal replacement therapy of choice in small children, the elderly, diabetics, subjects with cardiovascular disease and with difficulties in vascular access. Frequent complication of this method is the infection of the Tenckhoff catheter exit site, definition of which has not been firmly established yet. The aim of this study was to assess the frequency of catheter exit infections, its bacterial etiology and the efficacy of antibiotic treatment. The study material consisted of 21 subjects (11 female, 10 male) treated with CAPD in 1992-99 at our department, mean age 19.8 +/- 11.8 yrs, with mean CAPD treatment time 33 +/- 27 months. They were divided into two groups: group I—patients aged > or = 5 yrs, and group II—patients aged 15 yrs. Mean catheter usage time was 15.8 +/- 14.9 months. 43 cases of catheter exit site infection was diagnosed (0.7 case of infection per patient per year). Infection frequency was found to be 1 case in 9.4 months and 1 in 26.5 months, in group I and II, respectively ($p < 0.001$). Catheter usage in two groups was 10.4 +/- 8.2 and 21.4 +/- 15.4 months, respectively ($p < 0.01$). The most frequent pathogen was S. aureus (31 cases), with 5 cases of MRSA strains found. Antibiotic treatment was applied according to Keane's recommendations and it lasted 13.2% of CAPD treatment duration. In conclusion, catheter exit site infection occurred more often in children under the age of 5 yrs, and the catheter usage time was significantly shorter in this group of patients.

Kambal A.M. et al. *Childhood pneumococcal bacteraemia in Riyadh, Saudi*

Arabia. Ann Trop Paediatr. 1997; 17(3) : 245-51.p Abstract: Forty-nine children with pneumococcal bacteraemia seen during a 5-year period (1 January 1991 to 31 December 1995) at King Khalid University Hospital were studied. The majority (61.2%) were under 2 years of age. The focus of infection was pneumonia, pharyngitis or undetermined in 28.6%, 18.4% and 20.4%, respectively. Diseases that had probably predisposed them to pneumococcal bacteraemia (mainly nephrotic syndrome) were encountered in 24.5% of cases. Forty-five per cent of the cases occurred during the summer season and in 29% the disease was nosocomially acquired. No death was recorded in this series and the reasons for this are discussed. Detection of pneumococcal antigens from blood taken for culture was successful in 96% of cases; this test is important in the diagnosis of pneumococcal bacteraemia in partially treated patients. Antimicrobial susceptibility testing showed 20.4% of the isolates to be relatively penicillin-resistant. Resistance to other antimicrobial agents was also recorded and multiple resistance was noted in 22% of isolates. There was a significant difference between the ceftriaxone MIC of the relatively penicillin-resistant strains compared with penicillin-sensitive strains. The emergence and the steady increase in the numbers of relatively penicillin-resistant pneumococcal strains in Saudi Arabia during the last 10 years are discussed.

Kamiya Y. *Experiences and studies on antimicrobial resistance in Japan: useful lessons for developing countries.* East Afr Med J. 1997; 74(3) : 174-6.p Abstract: The use of antimicrobial drugs in Japan is remarkably high. In 1994, the total production cost of antimicrobial drugs amounted to 3.38 billion US dollars. The intensive use of broad-spectrum drugs, especially for treatment of increasing number of immunocompromised and elderly patients, resulted in the emergence and spread of antimicrobial-resistant organisms in Japan. A bacteriological study in a chronic care centre shows a variety of bacterial pathogens with increased antimicrobial resistance such as methicillin-resistant Staphylococcus aureus. Control measures of nosocomial infections with resistant organisms have been established and strengthened. This includes surveillance researches such as re-evaluation of disinfectants.

Kamohara Y. et al. *[Treatment of liver cancer: current status and future prospectives].* Gan To Kagaku Ryoho. 2000; 27(7) : 987-92.p Abstract: The most common liver cancers are hepatocellular carcinoma (HCC), cholangiocellular carcinoma (CCC), and metastatic colorectal cancer. In HCC patients, the extent of the surgical resection is limited due to the functional status of the underlying cirrhotic liver. Limited resection, transarterial catheter embolization, ethanol injection, and microwave coagulation have been applied to treat the patients with liver hypofunction; however, the intrahepatic recurrence rate was relatively high in those patients. Therefore, liver transplantation is the only radical treatment to remove HCC and cirrhotic livers with viral infections. Recent advances in anti-viral agents promise to improve the outcome after liver transplantation in patients with HCC. On the other hand, CCC is outside the indications for liver transplantation because of the broad extension of lymph node and nerve plexus. In liver metastasis from colorectal cancer, overall survival is not greatly improved, although arterial chemotherapy reduces mortality related to liver metastasis. Surgical resection including repeated hepatectomy indicates better survival in patients with liver metastases. In the future, both CCC and metastatic liver cancer could be candidates for gene therapy. For the 21 century, a new therapeutic strategy incorporating clinical evidence, molecular biology, and organ replacement needs to be established for the treatment of liver cancer.

Kampf G. et al. *Prevalence and risk factors for nosocomial lower respiratory tract infections in German hospitals.* J Clin Epidemiol. 1998; 51(6) : 495-502.p Abstract: The prevalence and risk factors for nosocomial lower respiratory tract infections (LRTI) in Germany were determined as part of a national survey on nosocomial infections. The study included 14,966 patients in 72 representatively selected hospitals with departments of general medicine, surgery, obstetrics, gynecology, and intensive care units (ICU). Surveillance was carried out by four previously validated medical doctors who strictly applied the CDC-criteria for diagnosis of nosocomial infections. The overall prevalence of hospital-acquired LRTI was 0.72% with the highest rate in hospitals with more than 600 beds (1.08%) and among the patients on intensive care units (9.00%). Ventilator-associated pneumonia rates were highest in patients on ICUs (13.27). Polytrauma, impaired consciousness, chronic airway disease, prior surgery, and cardiovascular disease were significantly related to the occurrence of nosocomial LRTI. P. aeruginosa was the predominant organism causing nosocomial LRTI. Nosocomial LRTI remain a problem mainly on ICUs. Patients at risk should be monitored with extra care.

Kampfer P. et al. *In vitro susceptibilities of Aeromonas genomic species to 69 antimicrobial agents.* Syst Appl Microbiol. 1999; 22(4) : 662-9.p Abstract: A total of 217 strains representing all 14 currently described genomic species in the genus Aeromonas were tested for susceptibility to 69 antimicrobial agents by a microdilution method. All species were susceptible to tetracyclines, quinolones, chloramphenicol, and most of the aminoglycosides and the cephalosporins, but were resistant to lincosamides, vancomycin, teicoplanin and some penicillins. In general, no significant differences were found that correlated with the taxonomic designation or the origin of the isolates tested. The microdilution method proved to be easy to perform allowing susceptibility testing of extensive strain collections for a large number of antimicrobial agents.

Kang D.H. et al. *Application of thin agar layer method for recovery of injured Salmonella typhimurium.* Int J Food Microbiol. 2000; 54(1-2) : 127-32.p Abstract: Xylose lysine decarboxylase (XLD) medium, a selective plating medium, can inhibit heat-injured Salmonella typhimurium from growing, whereas tryptic soy agar (TSA), a non-selective medium, does not. To facilitate recovery of heat-injured S. typhimurium cells while providing selectivity of isolation of S. typhimurium from other bacteria in the sample, a thin agar layer (TAL) procedure was developed by overlaying 14 ml of nonselective medium (TSA) onto prepoured and solidified XLD medium in a 8.5 cm diameter Petri dish. During the first few hours of incubating the plate, the injured S. typhimurium repaired and started to grow in the TSA. During the resuscitation of injured cells, the selective agents from XLD were diffused to the TSA top layer part. Once the selective agents diffused to the top part of the TAL, the resuscitated S. typhimurium started to produce a typical reaction (black color) and other microorganisms were inhibited by the selective agents. The recovery rate for heat-injured (55 degrees C for 15 min) S. typhimurium with the TAL method was compared with TSA, XLD, and the traditional overlay method (OV; pouring selective agar on top of resuscitated cells on TSA agar 3-4 h after incubation). No significant difference occurred among TSA, OV, and TAL ($P > 0.05$) for enumeration of heat-injured S. typhimurium, but they recovered significantly higher numbers than from XLD agar ($P < 0.05$).

Kang S.S. et al. *Expanded indications for ultrasound-guided thrombin injection of pseudoaneurysms.* J Vasc Surg. 2000; 31(2) : 289-98.p Abstract: PURPOSE: We previously reported preliminary data on a new procedure that we developed for the treatment of femoral pseudoaneurysms after catheterization. This study presents our current results of percutaneous ultrasound-guided thrombin injection for treating pseudoaneurysms that arise from various locations and causes. METHODS: Between February 1996 and May 1999, we performed thrombin injection of 83 pseudoaneurysms in 82 patients. There were 74 femoral pseudoaneurysms: 60 from cardiac catheterization (36 interventional), seven from peripheral arteriography (four interventional), five from intra-aortic balloon pumps, and two from dialysis catheters. There were nine other pseudoaneurysms: five brachial (two cardiac catheterization, two gunshot wounds, one after removal of an infected arteriovenous graft), one subclavian (central venous

catheter insertion), one radial (arterial line), and one distal superficial femoral and one posterior tibial (both after blunt trauma). Twenty-nine pseudo-aneurysms were injected while on therapeutic anticoagulation. Patients underwent repeat ultrasound examination within 5 days and after 4 weeks. RESULTS: Eighty-two of 83 pseudoaneurysms had initial successful treatment by this technique, including 28 of 29 in patients who were undergoing anticoagulation therapy. The only complication was thrombosis of a distal brachial artery, which resolved spontaneously. There were early recurrences in seven patients: four patients underwent successful reinjection; reinjection failed in two patients, who underwent surgical repair; and one patient had spontaneous thrombosis on follow-up. After 4 weeks, ultrasound examinations were completely normal or showed some residual hematoma, and there were no recurrent pseudoaneurysms. CONCLUSION: Ultrasound-guided thrombin injection of pseudoaneurysms has excellent results, which support its widespread use as the primary treatment for this common problem.

Kantor I.N.d. et al. *La resistencia y multirresistencia a los medicamentos antituberculosos en la Argentina y en otros paise de America Latina.* Medicina (B.Aires). 1998; 58(2) : 202-8.p Abstract: La resistencia simultánea del Mycobacterium tuberculosis a los dos medicamentos antibacterianos más importantes: isoniacida (INH) y refampicina (RPM), acompañada o no de la resistencia a otras drogas, se denomina multirresistencia (MR) y constituye el principal obstáculo para el xito del tratamiento antituberculoso. Entre 1994 y 1997 varios países de América Latina han efectuado estudios para conocer la prevalencia de la resistencia y MR primaria y adquirida. Se han seguido en estos estudios los lineamientos dados por OMS y la Unión internacional contra la Tuberculosis (UICTER). Los porcentajes de MR primaria (en pacientes sin tratamiento previo) variaron entre inexistentes o muy bajas (Uruguay, Chile, Cuba) hasta 4 por ciento o mayores (R. Dominicana, Argentina). En los mismos grupos de países, los porcentajes de pacientes ya tratados que presentaron aislamientos de bacilos MR (MR adquirida) variaron entre 4 y 22 por ciento. En Argentina se halló una marcada relación entre MR, infección HIV y asistencia en hospitales para enfermedades infecciosas situados en grandes urbes (Buenos Aires y Rosario), donde en el período del estudio se produjeron "brotes" nosocomiales de tuberculosis MR. Pero también se evidenció un preocupante incremento de la MR entre pacientes sin evidencias de riesgo de infección por HIV, con historia de tratamiento previo. La aplicación del tratamiento supervisado (DOT) y ambulatorio, el suministro completo y continuado de medicamentos y la descentralización del diagnóstico y tratamiento a centros de salud periféricos para facilitar la asistencia de los pacientes, podrían contribuir a aumentar la curación de la tuberculosis y a cortar la cadena de transmisión. (AU).

Kaplan A.E. et al. *Antimicrobial effect of six endodontic sealers: an in vitro evaluation.* Endod Dent Traumatol. 1999; 15(1) : 42-5.p Abstract: The aim of this study was to determine the in vitro antimicrobial effect of six endodontic sealers after 2, 20 and 40 days. The sealers studied were Apexit, Endion, AH26, AH-Plus. Procosol and Ketac Endo. The microorganisms used were Candida albicans, Staphylococcus aureus, Streptococcus mutans and Actinomyces israelii. Petri dishes were filled with sterile agar and 0.1-ml wells were prepared and filled with the sealers. The agar plates were stored for 24 h at 37 degrees C. The samples were then removed, immersed in 4.5 ml of culture medium and divided into three groups. The samples in group 1 were stored for 2 days at 37 degrees C whereas the samples of groups 2 and 3 were stored at 4 degrees C for 20 and 40 days respectively. The samples were then removed and discarded, and 0.1 ml of the culture medium was seeded on the agar plates in order to perform colony forming unit counts. Apexit, Endion and AH-Plus produced slight inhibition on Streptococcus mutans at 20 days and on Actinomyces israelii at every time interval. No effect was found on Candida albicans and Staphylococcus aureus. Ketac Endo only produced an antimicrobial effect on Actinomyces israelii at 2 and 40 days. AH26 and Procosol showed antimicrobial effect at 40 days on Candida albicans, at 20 and 40 days on Streptococcus mutans and Staphylococcus aureus, and an effective inhibition on Actinomyces israelii at every time interval. Statistical analysis revealed both sealers and microorganisms to be significant factors affecting results in groups 2 and 3. In conclusion, the sealers evaluated in this study showed different inhibitory effects depending on time span. Overall, sealers containing cugenol and formaldehyde proved to be most effective against the microorganisms at the time intervals studied.

Kaplan S.S. et al. *Effect of nitric oxide on staphylococcal killing and interactive effect with superoxide.* Infect Immun. 1996; 64(1) : 69-76.p Abstract: The role of reactive nitrogen intermediates (RNI) such as nitric oxide (.NO) in host defense against pyogenic microorganisms is unclear, and the actual interactive effect of RNI and reactive oxidative intermediates (ROI) for microbial killing has not been determined. Since, in nature, ROI and RNI might be generated together within any local infection, we evaluated the separate and interactive effects of.NO and O2- on staphylococcal survival by using a simplified system devoid of eukaryotic cells. These studies showed that prolonged exposure of staphylococci to.NO does not result in early loss of viability but instead is associated with a dose-related delayed loss of viability. This effect is abrogated by the presence of hemoglobin, providing further evidence that the effect is RNI associated. Superoxide-mediated killing also is dose related, but in contrast to RNI-mediated killing, it is rapid and occurs within 2 h of exposure. We further show that the interaction of.NO and O(2)- results in decreased O(2)—mediated staphylococcal killing at early time points..NO, however, appears to enhance or stabilize microbial killing over prolonged periods of incubation. This study did not produce evidence of early synergism of ROI and RNI, but it does suggest that.NO may contribute to host defense, especially when ROI-mediated killing is compromised.

Kapoor H. et al. *Resistance to quinolones in pathogens causing urinary tract infections.* J Commun Dis. 1997; 29(3) : 263-7.p Abstract: 157 bacterial isolates from cases with urinary tract infections (UTI) were studied for their susceptibility to some of the available quinolones as compared to other commonly used antimicrobial agents in UTI. Resistance to nalidixic acid was observed in 62.4% of isolates whereas for pefloxacin, norfloxacin, ciprofloxacin and lomifloxacin it was 54.7%, 52.5%, 51.5% and 50.3% respectively. Aminoglycosides and third generation cephalosporins showed resistance in fewer isolates. Gentamicin resistance was observed in 21% and corresponding figure for amikacin, cefotaxime and ceftriaxone was 7%, 8.9% and 12.1% respectively. Nitrofurantoin showed resistance in 36.3% of isolates and 48% isolates were resistant to cephalexin. The minimum inhibitory concentration (MIC) of quinolones was more than 64 mcg/ml which is > 8 times in resistant strains as compared to sensitive isolates.

Kapperud G. et al. *Outbreak of Shigella sonnei infection traced to imported iceberg lettuce.* J Clin Microbiol. 1995; 33(3) : 609-14.p Abstract: In the period from May through June 1994, an increase in the number of domestic cases of Shigella sonnei infection was detected in several European countries, including Norway, Sweden, and the United Kingdom. In all three countries epidemiological evidence incriminated imported iceberg lettuce of Spanish origin as the vehicle of transmission. The outbreaks shared a number of common features: a predominance of adults among the case patients, the presence of double infections with other enteropathogens, and the finding of two dominant phage types among the bacterial isolates. In Norway 110 culture-confirmed cases of infection were recorded; more than two-thirds (73%) were adults aged 30 to 60 years. A nationwide case-control study comprising 47 case patients and 155 matched control individuals showed that the consumption of imported iceberg lettuce was independently associated with an increased risk of shigellosis. Epidemiological investigation of a local outbreak incriminated iceberg lettuce from Spain, consumed from a salad bar, as the source. The presence of shigellae in the suspected food source could not be

documented retrospectively. However, high numbers of fecal coliforms were detected in iceberg lettuce from patients' homes. Three lettuce specimens yielded salmonellae. The imported iceberg lettuce harbored Escherichia coli strains showing resistance to several antimicrobial agents, including ampicillin, ciprofloxacin, gentamicin, and trimethoprim-sulfamethoxazole. During the outbreak it is likely that thousands of Norwegians and an unknown number of consumers in other countries were exposed to coliforms containing antibiotic resistance genes.

Kapur D. et al. *Incidence and outcome of vancomycin-resistant enterococcal bacteremia following autologous peripheral blood stem cell transplantation.* Bone Marrow Transplant. 2000; 25(2) : 147-52.p Abstract: A retrospective evaluation of 321 consecutive recipients of high-dose chemotherapy (HDC) and autologous peripheral blood stem cell transplantation (PBSCT) was conducted to ascertain the incidence and outcome of vancomycin-resistant enterococcal (VRE) bacteremia. Ten patients developed VRE bacteremia at a median of 6 days following PBSCT. Nine isolates were Enterococcus faecium and one was E. faecalis. The median duration of bacteremia was 5 days. The central venous catheter was removed in seven individuals. Nine patients were treated with a variety of antimicrobial agents including quinupristin-dalfopristin, chloramphenicol, doxycycline, oral bacitracin, co-trimoxazole, and nitrofurantoin. Bacteremia resolved without adverse sequelae in seven patients. Two individuals who died of other causes had persistent or relapsed bacteremia at the time of death. An additional patient suffered multiple relapses of VRE bacteremia and died as a result of VRE endocarditis 605 days following PBSCT. Mortality as a direct result of VRE bacteremia was 10% in this series. The optimal type and duration of treatment of VRE bacteremia has not been clearly defined. Therefore, we perform weekly stool surveillance cultures for VRE in our hospitalized transplant population and apply strict barrier precautions in those individuals in whom stool colonization has been identified. Furthermore, the empiric use of vancomycin has been restricted. Bone Marrow Transplantation (2000) 25, 147-152.

Kapur V. et al. *Rapid Mycobacterium species assignment and unambiguous identification of mutations associated with antimicrobial resistance in Mycobacterium tuberculosis by automated DNA sequencing.* Arch Pathol Lab Med. 1995; 119(2) : 131-8.p Abstract: OBJECTIVE—To develop and demonstrate the utility of automated DNA sequencing strategies for rapid and unambiguous identification of Mycobacterium species and mutations associated with antimicrobial resistance in Mycobacterium tuberculosis. DESIGN AND SPECIMENS—A 360-base pair segment of the gene (hsp65) encoding a 65-kd heat shock protein was characterized from 91 isolates assigned to 24 Mycobacterium species by traditional biochemical techniques. Areas of seven genes recently shown to contain mutations associated with antimicrobial resistance in M tuberculosis strains were also sequenced in a sample of 128 resistant organisms. Early positive BACTEC 460 cultures and acid-fast, bacterium-positive sputum specimens from patients with tuberculosis were also studied. RESULTS—Automated DNA sequencing identified species-specific polymorphism in the target segment of hsp65, successfully identified organisms to the species level in smear-positive sputum samples, and unambiguously characterized seven genes associated with antimicrobial resistance in M tuberculosis. CONCLUSIONS—Rapid identification of M tuberculosis and other Mycobacterium species is possible by automated DNA sequencing of a portion of hsp65. The technique is also feasible for analysis of some smear-positive sputum specimens. Unambiguous characterization of target segments of genes harboring mutations associated with antimicrobial resistance in M tuberculosis is possible from primary patient specimens. Taken together, the data demonstrate the feasibility of mycobacterial species identification and potential to identify mutations associated with antimicrobial resistance in less than 48 hours.

Karakaya D. et al. *Brachial plexus injury during subclavian vein catheterization for hemodialysis.* J Clin Anesth. 2000; 12(3) : 220-3.p Abstract: Although the subclavian vein is often used for placement of double-lumen hemodialysis catheters, the risk factors for complications for the patients with chronic renal failure are underestimated. We report a case of a patient with chronic renal failure in whom brachial plexus injury was caused by both a compressive hematoma and direct insertion of a needle resulting from a subclavian vein catheterization attempt for hemodialysis. This case emphasizes the need for determining the coagulation status of the patient especially with chronic renal failure before performing invasive procedures.

Karas J.A. et al. *Laboratory surveillance of Shigella dysenteriae type 1 in KwaZulu-Natal.* S Afr Med J. 1999; 89(1) : 59-63.p Abstract: OBJECTIVE: To collect data on the antimicrobial susceptibility of Shigella dysenteriae type 1 in KwaZulu-Natal, including the testing of newer therapeutic agents, and to evaluate the ability of laboratories to participate in a provincial surveillance programme. DESIGN: Prospective descriptive study. SETTING: Hospital laboratories in KwaZulu-Natal, including peripheral laboratories and the medical microbiology laboratory of the University of Natal. MAIN OUTCOME MEASURES: Antimicrobial susceptibility pattern of surveillance strains and evaluation of the ability of provincial laboratories to isolate Shigella. RESULTS: All 354 strains tested were resistant to ampicillin, chloramphenicol and tetracycline. Co-trimoxazole resistance was found in 92.2% of strains, and 0.8% of strains were resistant to nalidixic acid. All strains were susceptible to ceftriaxone, ciprofloxacin, ofloxacin, pivmecillinam, azithromycin, loracarbef and fosfomycin. Of the 29 laboratories surveyed, 18 (62.1%) were able to isolate and identify S. dysenteriae correctly, and 9 (32%) were able to serotype it further to S. dysenteriae type 1. Twenty-seven (93.1%) had appropriate culture media and 26 (89.7%) had antisera for Shigella identification. CONCLUSIONS: There is little variation among strains of S. dysenteriae type 1 in KwaZulu-Natal with regard to their antimicrobial susceptibility pattern. Nalidixic acid should remain the antimicrobial of choice for treatment of dysentery in our region as resistance to it is low. The majority of KwaZulu-Natal laboratories have the expertise and equipment to perform the isolation and identification of Shigella species.

Kariuki S. et al. *Analysis of Salmonella enterica serotype Typhimurium by phage typing, antimicrobial susceptibility and pulsed-field gel electrophoresis.* J Med Microbiol. 1999; 48(11) : 1037-42.p Abstract: Three typing methods commonly used for bacteria—phage typing, antimicrobial susceptibility and pulsed-field gel electrophoresis (PFGE)- were used to characterise 64 Salmonella enterica serotype Typhimurium isolates from individual adult patients from Nairobi, Kenya. The isolates encompassed 11 definitive phage types (DTs), which fell into eight PFGE clusters; 31.3% of isolates were either untypable or reacted nonspecifically with the phages used for typing and 26.6% were of DT 56. Plasmids of c. 100 kb were responsible for self-transferable multiresistance among the isolates. Analysis by PFGE and phage type demonstrated that multiresistant Typhimurium strains causing diarrhoea and invasive disease were multiclonal.

Karmeli Y. et al. *Conventional dose of omeprazole alters gastric flora.* Dig Dis Sci. 1995; 40(9) : 2070-3.p Abstract: Quantitative cultures were carried out on samples from gastric juice obtained from 12 ambulatory patients with esophagitis before and one month after omeprazole therapy. An increase in the number of patients in whom gastric juice was culture-positive, as well as an increment in the bacterial counts were noted. The spectrum of microorganisms isolated from gastric juice was identical to the normal flora of the oral cavity, mainly alpha-hemolytic streptococci, corynebacteria, and Candida species. Thus, the counts of organisms within gastric contents are simply a reflection of swallowed oral microflora that were able to survive due to the less acidic environment.

Karstaedt A.S. et al. *Pneumococcal bacteremia during a decade in children in Soweto, South Africa.* Pediatr Infect Dis J. 2000; 19(5) : 454-7.p

Abstract: OBJECTIVES: To monitor for a decade the incidence and the clinical and microbiologic characteristics of pneumococcal bacteremia in children in Soweto and to assess the influence of HIV infection on any changes. METHODS: Case records of children with pneumococcal bacteremia at Chris Hani Baragwanath Hospital from July, 1986, to June, 1987 (1986/ 1987), and from July, 1996, to June, 1997 (1996/ 1997), were retrospectively reviewed. RESULTS: There were 194 episodes, 62 in 19861 1987 and 132 in 1996/1997. The minimum annual incidence for children younger than 5 years of age increased from 61 per 100000 (179 per 100000 for those <12 months old) in 1986/1987 to 130 per 100000 (349 per 100000 for those <12 months old) in 1996/1997. Sixty-seven (60%) of 111 patients tested in 1996/1997 were HIV-seropositive; none were tested in 1986/1987. The HIV-infected compared with HIV-noninfected were more likely to be malnourished (61% vs. 36%, P = 0.02), less likely to have other underlying disease (12% vs. 50%, P = 0.00001) and more frequently used antibiotics recently (69% vs. 43%, P = 0.008). Penicillin-nonsusceptible isolates were found in 22 (35%) patients in 1986/1987 and 52 (39%) in 1996/1997. There was no significant change in antimicrobial susceptibility during the decade or by HIV serostatus. CONCLUSIONS: Children in Soweto had a high incidence of pneumococcal bacteremia which doubled during the decade mainly as a result of the impact of the HIV epidemic. There has been no significant change in antimicrobial susceptibility for the decade.

Karthikeyan S. et al. *Identification of synergistic interactions among microorganisms in biofilms by digital image analysis.* Int Microbiol. 1999; 2(4) : 241-50.p Abstract: Digital image analysis showed that reductions in biofilm plating efficiency were due to the loss of protection provided by two benzoate-degrading strains of Pseudomonas fluorescens. This loss in protection was due to the spatial separation of the protective organisms from benzoate-sensitive organisms during the dilution process. Communities were cultivated in flow cells irrigated with trypticase soy broth. When the effluent from these flow cells was plated on 0.15% benzoic acid, satellite colonies formed only in the vicinity of primary colonies. A digital image analysis procedure was developed to measure the size and spatial distribution of these satellites as a function of distance from the primary colony. The size of satellites served as a measure of growth, and the number per unit area served as a measure of survival. At the three dilutions tested, the size and concentration of satellite colonies varied inversely with distance from the primary colonies. When these measurements were plotted, the slopes were used to quantify the effect of bacterial association on the growth and survivability of the satellites. In the absence of the primary colonies, satellites grew in axenic culture only at low benzoate concentrations. Thus benzoate-degrading organisms are capable of creating a protective microenvironment for other members of biofilm communities.

Kasperk R. et al. *[Perioperative antibiotic prophylaxis in visceral surgery—pro and contra].* Langenbecks Arch Chir Suppl Kongressbd. 1997; 114 : 1022-5.p Abstract : Perioperative antibiotic prophylaxis aims at reducing the enormous cost of hospital-acquired infections. Primary indications for antibiotic prophylaxis are wounds of the clean-contaminated and contaminated category. Use of antibiotic prophylaxis in clean surgery is still very controversial. To be effective, the antibiotic must be given in the period immediately before incision. A single-dose application is at least as effective as a multiple-dose regimen. Second-generation cephalosporins are still the main stay of antibiotic prophylaxis. In colorectal surgery they should be combined with, e.g., Metronidazol.

Kasten M.J. *Clindamycin, metronidazole, and chloramphenicol.* Mayo Clin Proc. 1999; 74(8) : 825-33.p Abstract: Clindamycin, metronidazole, and chloramphenicol are three antimicrobial agents useful in the treatment of anaerobic infections. Clindamycin is effective in the treatment of most infections involving anaerobes and gram-positive cocci, but emerging resistance has become a problem in some clinical settings. Metronidazole is effective in the treatment of infections involving gram-negative anaerobes, but it is unreliable in the treatment of gram-positive anaerobic infections and is ineffective in treating aerobic infections. Additionally, metronidazole is often the drug of choice in treating infections in which Bacteroides fragilis is a serious concern. Chloramphenicol is effective in the treatment of a wide variety of bacterial infections, including serious anaerobic infections, but is rarely used in Western countries because of concerns about toxicity, including aplastic anemia and gray baby syndrome.

Kasuga Y. et al. *Bactericidal effects of mouth rinses on oral bacteria.* Bull Tokyo Dent Coll. 1997; 38(4) : 297-302.p Abstract: The bactericidal efficacy of two types of Listerine; Listerine and Cool Mint Listerine, and povidone iodine on oral microorganisms, methicillin-resistant Staphylococcus aureus (MRSA), Streptococcus pyogenes, Helicobacter pylori and Candida albicans were examined. Most of the oral bacteria were killed completely by a 10-sec exposure to Listerine or Cool Mint Listerine. H. pylori, MRSA and C. albicans were also reduced by a 30-sec exposure to the Listerine mouth rinse. Bacteria in dental plaque were decreased by exposure to Listerine, Cool Mint Listerine, and povidone iodine for 30 seconds. Mouthwashing with Listerine for 30 seconds resulted in a decrease to approximately 1/100 of the viable bacterial counts in saliva. These bactericidal effects against bacteria in saliva and dental plaque indicated that Listerine and Cool Mint Listerine antiseptic are useful in oral cavity as antiseptic mouth rinses.

Kasuya H. et al. *[Two cases of methicillin-resistant Staphylococcus aureus (MRSA) sepsis following craniotomy].* No Shinkei Geka. 2000; 28(5) : 429-34.p Abstract: We report here two cases of MRSA sepsis following craniotomy. In case 1, a petroclival meningioma was subtotally removed and lumbar drainage was inserted postoperatively to prevent cerebrospinal fluid leakage. Ventriculo-peritoneal shunt was performed after meningitis was treated with vancomycin and panipenem/betamipron. Two weeks after the procedure, the patient revealed continuous spiking fevers related to MRSA sepsis, which did not improve with vancomycin and arbekacin administration. The focus of infection was found by scintigraphy and CT by 67Ga to be spondylo-diskitis at the level of L2-L3. The lesion was removed and bone from the iliac crest grafted. In case 2, seven days after surgery for multiple meningioma, the patient exhibited spiking fevers and swelling in the left leg. The central venous catheter was removed from the left femoral vein and MRSA was found from blood culture. The patient was treated with arbekacin (200 mg/day). Venous thrombosis diagnosed by CT was treated with heparin. Symptoms related to the infection and laboratory data did not improve because the concentration of arbekacin in the blood did not reach an effective level. The symptoms markedly improved when the dose of arbekacin was doubled (400 mg/day).

Kataja J. et al. *Clonal spread of group A streptococcus with the new type of erythromycin resistance. Finnish Study Group for Antimicrobial Resistance.* J Infect Dis. 1998; 177(3) : 786-9.p Abstract: In 1990, a new type of erythromycin resistance phenotype, designated NR, was found in group A streptococcus (GAS) in Finland. In the present study, the distribution of GAS isolates with this and other erythromycin-resistance phenotypes was surveyed in Finland, and the clonality of the isolates was explored. Of 4179 GAS isolates collected from all over Finland, 695 (17%) were resistant to erythromycin, and 82% of these had the NR phenotype. Of a group of 96 isolates with the NR phenotype from different areas, 91% was T4 serotype, opacity factor-positive. The majority of these isolates were studied further: All were M4 serotype and 88% were of one clonal origin in genetic analyses. Thus, one single clone predominates among erythromycin-resistant GAS in Finland. This clone is of T4M4 serotype and mediates the new type of erythromycin resistance, characterized by the NR phenotype.

Kataja J. et al. *Erythromycin resistance genes in group A streptococci in Finland. The Finnish Study Group for Antimicrobial Resistance.* Antimicrob Agents Chemother. 1999; 43(1) : 48-52.p Abstract: Streptococcus pyogenes isolates (group A streptococcus) of different erythromycin resistance phenotypes were collected from all over Finland in 1994 and 1995 and studied; they were evaluated for their susceptibilities to 14 antimicrobial agents (396 isolates) and the presence of different erythromycin resistance genes (45 isolates). The erythromycin-resistant isolates with the macrolide-resistant but lincosamide- and streptogramin B-susceptible phenotype (M phenotype) were further studied for their plasmid contents and the transferability of resistance genes. Resistance to antimicrobial agents other than macrolides, clindamycin, tetracycline, and chloramphenicol was not found. When compared to our previous study performed in 1990, the rate of resistance to tetracycline increased from 10 to 93% among isolates with the inducible resistance (IR) phenotype of macrolide, lincosamide, and streptogramin B (MLSB) resistance. Tetracycline resistance was also found among 75% of the MLSB-resistant isolates with the constitutive resistance (CR) phenotype. Resistance to chloramphenicol was found for the first time in S. pyogenes in Finland; 3% of the isolates with the IR phenotype were resistant. All the chloramphenicol-resistant isolates were also resistant to tetracycline. Detection of erythromycin resistance genes by PCR indicated that, with the exception of one isolate with the CR phenotype, all M-phenotype isolates had the macrolide efflux (mefA) gene and all the MLSB-resistant isolates had the erythromycin resistance methylase (ermTR) gene; the isolate with the CR phenotype contained the ermB gene. No plasmid DNA could be isolated from the M-phenotype isolates, but the mefA gene was transferred by conjugation.

Kattar M.M. et al. *Application of 16S rRNA gene sequencing to identify Bordetella hinzii as the causative agent of fatal septicemia.* J Clin Microbiol. 2000; 38(2) : 789-94.p Abstract: We report on the first case of fatal septicemia caused by Bordetella hinzii. The causative organism exhibited a biochemical profile identical to that of Bordetella avium with three commercial identification systems (API 20E, API 20 NE, and Vitek GNI+ card). However, its cellular fatty acid profile was not typical for either B. avium or previously reported strains of B. hinzii. Presumptive identification of the patient's isolate was accomplished by traditional biochemical testing, and definitive identification was achieved by 16S rRNA gene sequence analysis. Phenotypic features useful in distinguishing B. hinzii from B. avium were production of alkali from malonate and resistance to several antimicrobial agents.

Katzer A. et al. *[Perioperative antibiotic prophylaxis in hip operations. Penetration into bone, capsule tissue and cartilage exemplified by cefuroxime].* Unfallchirurgie. 1997; 23(4) : 161-70.p Abstract: The most serious complication of accident surgery is postoperative osteitis. At the same time, perioperative antibiotic prophylaxis is generally recommended in order to reduce the rate of infection in joint surgery. The criteria for the suitability of a substance as prophylaxis include inter alia the activity spectrum with respect to the expected microorganisms, its retention time in the body and its ability to penetrate the endangered tissue. In the present study, the systemic and local activity levels after a single i.v. dose of 1500 mg cefuroxime was investigated in relation to the time of administration in 30 patients who had to undergo total hip replacement owing to a medial fracture of the neck of the femur. The tissue and serum samples were analyzed by high pressure liquid chromatography (HPLC). The results show that the tissue levels of the intermediary cephalosporin after an i.v. single shot dose are on average still several times higher than the minimum inhibitory concentration (MIC) of the most frequent bacterium. Staphylococcus aureus, as late as 4 hours after application. The optimal time for the administration form selected was immediately prior to the operation and the concentrations measured suggest that several repeat doses of cefuroxime for short-term prophylaxis are not necessary.

Kauffman C.A. et al. *Prospective multicenter surveillance study of funguria in hospitalized patients. The National Institute for Allergy and Infectious Diseases (NIAID) Mycoses Study Group.* Clin Infect Dis. 2000; 30(1) : 14-8.p Abstract: Although fungal urinary tract infections are an increasing nosocomial problem, the significance of funguria is still not clear. This multicenter prospective surveillance study of 861 patients was undertaken to define the epidemiology, management, and outcomes of funguria. Diabetes mellitus was present in 39% of patients, urinary tract abnormalities in 37.7%, and malignancy in 22.2%; only 10.9% had no underlying illnesses. Concomitant non-fungal infections were present in 85%, 90% had received antimicrobial agents, and 83.2% had urinary tract drainage devices. Candida albicans was found in 51.8% of patients and Candida glabrata in 15.6%. Microbiological and clinical outcomes were documented for 530 (61.6%) of the 861 patients. No specific therapy for funguria was given to 155 patients, and the yeast cleared from the urine of 117 (75.5%) of them. Of the 116 patients who had a catheter removed as the only treatment, the funguria cleared in 41 (35.3%). Antifungal therapy was given to 259 patients, eradicating funguria in 130 (50.2%). The rate of eradication with fluconazole was 45.5%, and with amphotericin B bladder irrigation it was 54.4%. Only 7 patients (1.3%) had documented candidemia. The mortality rate was 19.8%, reflecting the multiple serious underlying illnesses found in these patients with funguria.

Kaufman D. et al. *Antibiotic susceptibility in the surgical intensive care unit compared with the hospital-wide antibiogram.* Arch Surg. 1998; 133(10) : 1041-5.p Abstract: OBJECTIVE: To compare the antibiotic susceptibility of bacterial isolates from patients in the surgical intensive care unit (SICU) with hospital-wide bacterial susceptibility. DESIGN: Retrospective cohort analytic study. SETTING: Eight-bed SICU in a university-affiliated teaching hospital. PATIENTS: All hospitalized patients with culture results positive for microorganisms. INTERVENTIONS: None. MAIN OUTCOME MEASURES: Antibiotic susceptibility data were collected retrospectively for all bacterial isolates from SICU patients during July 1, 1994, to June 30, 1995. All duplicate and surveillance cultures were eliminated from the data set. Susceptibility testing was conducted using our standard laboratory methods. Results were compared with the hospital-wide antibiogram (HWA) for the same time period. Comparisons were made using the chi(2) test with Yates correction or the Fisher exact test, as appropriate. Staphylococcus aureus (HWA, n=494; SICU, n=71) was significantly less susceptible to oxacillin (51% vs 28%; P<.001), ciprofloxacin (50% vs 25%; P<.001), erythromycin (46% vs 23%; P<.001), and clindamycin (51% vs 27%; P<.001) in the SICU. Coagulase-negative staphylococci (HWA, n=339; SICU, n=37) were significantly less susceptible to oxacillin (33% vs 16%; P=.04) and clindamycin (57% vs 34%; P=.02). Pseudomonas aeruginosa (HWA, n=513; SICU, n=96) was less susceptible to imipenem (85% vs 74%, P=.01) and more susceptible to ticarcillin-clavulanic acid (88% vs 100%, P<.001) in the SICU. Escherichia coli (HWA, n=474; SICU, n=36) was more susceptible to most penicillin-derivative antibiotics in the SICU (ampicillin [68% vs 83%, P=.06], ticarcillin [65% vs 86%, P=.01], mezlocillin [76% vs 95%, P=.01], and ticarcillin-clavulanic acid [88% vs 100%, P=.02]). CONCLUSIONS: The 2 most commonly isolated bacterial pathogens in the SICU (S aureus and P aeruginosa) had significantly different susceptibility patterns compared with the HWA. Surprisingly, E coli isolated in the SICU tended to be more susceptible to penicillin-derivative antibiotics. These data indicate that empiric antibiotic choices in the SICU may be better guided by unit-specific antibiograms.

Kaye K.S. et al. *Pathogens resistant to antimicrobial agents. Epidemiology, molecular mechanisms, and clinical management.* Infect Dis Clin North Am. 2000; 14(2) : 293-319.p Abstract: The emergence of resistance to antimicrobial agents continues to be a major problem in the nosocomial setting and now in nursing homes and the community as well. Bacteria use a variety of strategies to avoid the inhibitory effects of antibiotic agents and have evolved highly efficient means

for the dissemination of resistance traits. Control of antibiotic-resistant pathogens provides a major challenge for both the medical community and society in general. To control the emergence of resistant pathogens, CDC and infection control guidelines must be adhered to, and antibiotics must be used more judiciously.

Kaye K.S. et al. *Risk factors for recovery of ampicillin-sulbactam-resistant Escherichia coli in hospitalized patients.* Antimicrob Agents Chemother. 2000; 44(4) : 1004-9.p Abstract: Ampicillin-sulbactam resistance in Escherichia coli is an emerging problem. This study determined risk factors for the recovery of ampicillin-sulbactam-resistant E. coli in hospitalized patients. A case-control design was used to compare two groups of case patients with control patients. The first group of case patients consisted of patients from whom nosocomially acquired ampicillin-sulbactam-resistant E. coli strains were isolated, and the second group of case patients consisted of patients from whom ampicillin-sulbactam-susceptible E. coli strains were isolated. Control patients were a random selection among 5% of all patients admitted during the same time period. Risk factors analyzed included antimicrobial drug exposure, comorbid conditions, and demographics. Univariate and multivariate analyses were performed. Ampicillin-sulbactam-resistant E. coli strains were isolated from 175 patients, and ampicillin-sulbactam-susceptible E. coli strains were isolated from 577 patients. Nine hundred thirty-four control patients were selected. Exposure to penicillin antibiotics as a class and to ampicillin and ampicillin-sulbactam individually were the only significant, independent risk factors associated with the isolation of ampicillin-sulbactam-resistant E. coli (odds ratio [OR] = 2.32 [P < 0.001], OR = 3.04 [P = 0.02], and OR = 1.72 [P = 0.04], respectively), but they were not associated with the isolation of ampicillin-sulbactam-susceptible E. coli. Interestingly, exposure to piperacillin-tazobactam tended to protect against the isolation of E. coli strains resistant to ampicillin-sulbactam, but this did not reach statistical significance (OR = 0.13; P = 0.11).

Kayser O. et al. *Antibacterial activity of extracts and constituents of Pelargonium sidoides and Pelargonium reniforme.* Planta Med. 1997; 63(6) : 508-10.p Abstract: The antibacterial activity of extracts and isolated constituents (scopoletin, umckalin, 5,6,7-trimethoxycoumarin, 6,8-dihydroxy-5,7-dimethoxycoumarin, (+)-catechin, gallic acid and its methyl ester) of Pelargonium sidoides and Pelargonium reniforme (Geraniaceae), plant species used in folk medicine by the Southern African native population, was evaluated against 8 microorganisms, including 3 Gram-positive (Staphylococcus aureus, Streptococcus pneumoniae, and beta-hemolytic Streptococcus 1451) and 5 Gram-negative bacteria (Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Haemophilus influenzae). Minimum inhibitory concentrations (MICs) varied with the preparation of the extracts and microorganisms tested, from about 0.6 mg/ml for aqueous phases to over 10 mg/ml for crude Pelargonium extracts. With the exception of the ineffective (+)-catechin, all the potentially active compounds exhibited antibacterial activities with MICs of 200-1000 micrograms/ml. The results provide for a rational basis of the traditional use of the titled Pelargonium species.

Kayser O. et al. *Antibacterial activity of simple coumarins: structural requirements for biological activity.* Z Naturforsch [C]. 1999; 54(3-4) : 169-74.p Abstract: The antibacterial activity of a series of simple coumarins was evaluated against 8 microorganisms, including three Gram-positive (Staphylococcus aureus, beta-hemolytic Streptococcus and Streptococcus pneumoniae) and five Gram-negative bacteria (Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis and Haemophilus influenzae), using the microdilution broth method. The coumarins tested showed broad diversity regarding growth inhibitory activity with minimum inhibitory concentrations ranging from 0.9 to > 12.4 microM. This study, presenting the first systematic analysis of structure-activity relationships among this group of coumarins, revealed some interesting structural requirements. While coumarins with a methoxy function at C-7 and, if present, an OH group at either the C-6 or C-8 position are invariably effective against the spectrum of tested standard bacteria (Gram-negative microorganisms including the Gram-positive bacterium Staphylococcus aureus), the presence of an aromatic dimethoxy arrangement is apparently favourable against those microorganisms which require special growth factors (beta-hemolytic Streptococcus, Streptococcus pneumoniae and Haemophilus influenzae). A combination of these structural features, two methoxy functions and at least one additional phenolic group as reflected by the highly oxygenated coumarins, identify promising candidates with antibacterial broad-spectrum activity.

Kazama H. et al. *Distribution of the antiseptic-resistance gene qacE delta 1 in gram-positive bacteria.* FEMS Microbiol Lett. 1998; 165(2) : 295-9.p Abstract: The distribution of the antiseptic-resistance genes qacE and qacE delta 1, originally isolated from Gram-negative bacteria, was studied in a large number of Gram-positive bacteria by a method that included the polymerase chain reaction. A total of 151 strains of Staphylococcus and Enterococcus, isolated from clinical sources and obtained from the Japanese Collection of Microorganisms, was used in this analysis. We found the qacE delta 1 gene in 36 of 103 strains of Staphylococcus and in nine of 48 strains of Enterococcus. All of the strains in which we detected the qacE delta 1 gene were clinical isolates. The qacE gene was not detected in any of the strains examined in this study. The nucleotide sequences of the qacE delta 1 genes from the strains of Staphylococcus and Enterococcus were identical to that of the gene located on integron InC in Pseudomonas aeruginosa. These results indicate that the antiseptic-resistance gene qacE delta 1 is present in Gram-positive, as well as Gram-negative, bacteria.

Kazama S. *[A new cardiovascular surgical instrument: cannula stabilizer].* Kyobu Geka. 2000; 53(3) : 209-11.p Abstract: A new instrument has been developed to safely keep the venous cannula out of the operative field during open heart surgery. This instrument is designed for holding the venous cannula in a curved state at a desired angle. It consists of four semicircular claws mounted on a bar. The size of the claws is tailored so that they comfortably accommodate the standard-size two-stage venous cannula. The bar is flexible enough to be bent manually to form the required curvature, and at the same time it is strong enough to resist the self-uncoiling force of the cannula. When in use, the bar is bent to form the desired curvature and then it is placed on the required portion of the venous cannula. The angle of its curvature and its location on the cannula can be adjusted easily as required during the course of the operative procedure. With this instrument the venous cannula can be easily held in a curved state without disturbing venous return so that the cannula does not come into the way of the surgeon's hands.

Keay S. et al. *A prospective study of microorganisms in urine and bladder biopsies from interstitial cystitis patients and controls.* Urology. 1995; 45(2) : 223-9.p Abstract: OBJECTIVES. Interstitial cystitis (IC) is a chronic inflammatory condition of the bladder of unknown etiology. We tested the hypothesis that a microorganism would be found at higher prevalence in urine or bladder tissue from women with IC than from control women. METHODS. Urine and bladder tissue were obtained at cystoscopy from 11 IC patients and 7 control subjects. These specimens were cultured for a variety of fastidious and nonfastidious bacteria, mycobacteria, fungi, and viruses. In addition, special staining techniques were used to examine biopsy specimens and cytospun urine, and tissue sections and outgrowths of explanted bladder cells were examined by electron microscopy. RESULTS. Cultures of urine from 6 of 11 IC patients grew five different bacteria (Corynebacterium sp. Klebsiella pneumoniae, Lactobacillus sp, Streptococcus constellatus, and Streptococcus morbillorum), human cytomegalovirus, or Torulopsis glabrata; one of these organisms (Lactobacillus sp) was found in urine from 2 patients. Although contamination by urethral organisms is possible, the prevalence of

microorganisms in urine of IC patients (6 of 11) was significantly greater than in urine of control subjects (0 of 7) ($P < 0.05$). Acridine orange staining revealed rods with appropriate morphology in urine from 4 of the 5 IC patients who had positive bacterial cultures and yeastlike organisms in urine and bladder tissue specimens that grew Torulopsis. Additionally, rodlike organisms were seen in urine from 2 IC patients with negative bacterial cultures and cocci were seen in the urine of 1 control patient. Biopsy specimens from 2 IC patients grew Torulopsis sp or Lactobacillus sp, in agreement with the results of acridine orange staining and culture of urine from these patients; in contrast, specimens from 3 control subjects grew small numbers of Pseudomonas sp or Staphylococcus epidermidis, but no organisms were cultured from urine or seen in acridine orange-stained tissue smears. All other cultures and stains were negative. CONCLUSIONS. These data do not provide evidence that IC is associated with infection or colonization by a single microorganism. However, they do generate the hypothesis that the prevalence of microorganisms, especially bacteria at low concentrations, is greater in the urine of IC patients than of control subjects. If these results are confirmed by other controlled studies, the question of whether the presence of these organisms is a cause or a result of IC should be addressed.

Keay S. et al. *Polymerase chain reaction amplification of bacterial 16S rRNA genes in interstitial cystitis and control patient bladder biopsies.* J Urol. 1998; 159(1) : 280-3.p Abstract: PURPOSE: Several characteristics of the chronic bladder disease called interstitial cystitis (IC) suggest an infectious etiology. However, a single causative organism has not been convincingly cultured in vitro, and DNA for a variety of microorganisms has been found inconsistently in bladder biopsies from IC patients. We therefore looked for a possible bacterial cause for IC by using a sensitive nested PCR assay on cystoscopic bladder biopsy specimens obtained from IC patients and controls. MATERIALS AND METHODS: Bladder biopsies were obtained at cystoscopy from 6 IC patients and 6 controls. DNA was extracted from these specimens and PCR with 2-round amplification performed using nested primers from a highly conserved region of the bacterial 16s rRNA gene. Amplified DNA was purified and sequenced using the Sequenase PCR Product Sequencing Kit, and the sequences obtained were compared with bacterial rRNA gene sequences recorded in GenBank. RESULTS: Biopsy specimens from all 6 patients and 6 controls were positive by PCR for DNA encoding bacterial 16s rRNA. Sequence data indicated a predominant microorganism in 10 of the 12 specimens, with > 95% homology to DNA from several different genera of bacteria including Acinetobacter, Propionobacterium, Salmonella, and Escherichia. None of the organisms identified by PCR had been cultured from tissue or urine obtained simultaneously from these persons, using sensitive culture techniques. CONCLUSIONS: These data indicate no difference between IC patients and controls in the proportion of bladder biopsies with PCR positivity or the type(s) of organism present, providing additional evidence that IC is not associated with infection by a particular type of bacterium.

Keck B. et al. *Salmonella typhimurium forms adenylcobamide and 2-methyladenylcobamide, but no detectable cobalamin during strictly anaerobic growth*. Arch Microbiol. 2000; 173(1) : 76-7.p Abstract: Under microaerophilic conditions Salmonella typhimurium LT2 synthesizes cobalamin, during which 5,6-dimethylbenzimidazole is formed from riboflavin. We report here that in an anoxic environment S. typhimurium did not form cobalamin, but rather adenylcobamide, 2-methyladenylcobamide, and cobyric acid. This indicated that S. typhimurium, like other microorganisms that synthesize 5,6-dimethylbenzimidazole from riboflavin, requires oxygen for the formation of the cobalamin base.

Kehl S.C. et al. *Prevalence of penicillin resistant and multi-drug resistant Streptococcus pneumoniae at a children's hospital*. WMJ. 1999; 98(3) : 42-5.p Abstract: Streptococcus pneumoniae isolated at Children's Hospital of Wisconsin during the winter of 1994 to 1995 and the winter of 1996 to 1997 were tested for susceptibility to penicillin, cephalosporins and other potentially therapeutically useful antimicrobial agents to determine the prevalence of penicillin and multidrug resistant isolates. During those years, the prevalence of S. pneumomiae not susceptible to penicillin was 27% and 28%, respectively, with 14% and 18%, respectively, of the respiratory isolates being high-level penicillin resistant. Despite the stable numbers of penicillin resistant isolates, there was evidence of significant increase in the resistance of these isolates to other antimicrobial agents. Respiratory isolates not susceptible to cefotaxime increased ($p = .01$; Fisher exact test) from 3% in 1995 to 20% in 1997. There was also a significant increase in the isolates not susceptible to erythromycin ($p = .09$; Fisher exact test) and trimethoprim/sulfamethoxazole ($p < .01$; Fisher exact test). This increase in resistance to multiple antimicrobial agents has significant implications for antibiotic therapy of children with infections likely to be due to Streptococcus pneumoniae.

Kelly C.G. et al. *Anti-adhesive strategies in the prevention of infectious disease at mucosal surfaces.* Expert Opin Investig Drugs. 2000; 9(8) : 1711-21.p Abstract: Binding of microbial cell surface adhesins to host receptor molecules is a critical early step in microbial infection and pathogenesis. Anti-adhesive strategies aimed at blocking this interaction offer an attractive means of preventing infection at an early stage. The strategy should reduce the likelihood of resistant strains of microorganisms emerging, since those that do not bind will not be subjected to sustained selective pressure, as may occur with antibiotic therapy. Three classes of adhesion-blocking agent have been investigated, namely anti-adhesin antibodies, adhesin analogues and receptor analogues. The effectiveness of a number of these adhesion-blocking compounds has been demonstrated in human and animal models of infection. Direct application to the tooth surface of anti-adhesin monoclonal antibody, or a synthetic peptide adhesion epitope, prevented infection with the oral pathogen, Streptococcus mutans in humans. Intranasal administration of a soluble receptor analogue significantly reduced virus production and symptoms following experimental infection with rhinovirus. Similarly, all three types of anti-adhesion agent protected against a variety of infections at other mucosal surfaces in animal models. A common finding from these studies is the long duration of protection, which cannot be due to persistence of the anti-adhesion agent, but may be the result of competitive exclusion by members of the normal flora at specific mucosal surfaces. Development of these novel antimicrobial agents is particularly timely in view of the increasing concern over the spread of antibiotic resistance.

Kelly C.G. et al. *A synthetic peptide adhesion epitope as a novel antimicrobial agent*. Nat Biotechnol. 1999; 17(1) : 42-7.p Abstract: The earliest step in microbial infection is adherence by specific microbial adhesins to the mucosa of the oro-intestinal, nasorespiratory, or genitourinary tract. We inhibited binding of a cell surface adhesin of Streptococcus mutans to salivary receptors in vitro, as measured by surface plasmon resonance, using a synthetic peptide (p1025) corresponding to residues 1025-1044 of the adhesin. Two residues within p1025 that contribute to binding (Q1025, E1037) were identified by site-directed mutagenesis. In an in vivo human streptococcal adhesion model, direct application of p1025 to the teeth prevented recolonization of S. mutans but not Actinomyces, as compared with a control peptide or saline. This novel antimicrobial strategy, applying competitive peptide inhibitors of adhesion, may be used against other microorganisms in which adhesins mediate colonization of mucosal surfaces.

Kelly-Wintenberg K. et al. *Room temperature sterilization of surfaces and fabrics with a one atmosphere uniform glow discharge plasma*. J Ind Microbiol Biotechnol. 1998; 20(1) : 69-74.p Abstract: We report the results of an interdisciplinary collaboration formed to assess the sterilizing capabilities of the One Atmosphere Uniform Glow Discharge Plasma (OAUGDP). This newly-invented source of glow discharge plasma (the fourth state of matter) is capable of operating

at atmospheric pressure in air and other gases, and of providing antimicrobial active species to surfaces and workpieces at room temperature as judged by viable plate counts. OAUGDP exposures have reduced log numbers of bacteria, Staphylococcus aureus and Escherichia coli, and endospores from Bacillus stearothermophilus and Bacillus subtilis on seeded solid surfaces, fabrics, filter paper, and powdered culture media at room temperature. Initial experimental data showed a two-log10 CFU reduction of bacteria when 2 x 10(2) cells were seeded on filter paper. Results showed > or = 3 log10 CFU reduction when polypropylene samples seeded with E. coli (5 x 10(4)) were exposed, while a 30 s exposure time was required for similar killing with S. aureus-seeded polypropylene samples. The exposure times required to effect > or = 6 log10 CFU reduction of E. coli and S. aureus on polypropylene samples were no longer than 30 s. Experiments with seeded samples in sealed commercial sterilization bags showed little or no differences in exposure times compared to unwrapped samples. Plasma exposure times of less than 5 min generated > or = 5 log10 CFU reduction of commercially prepared Bacillus subtilis spores (1 x 10(5)); 7 min OAUGDP exposures were required to generate a > or = 3 log10 CFU reduction for Bacillus stearothermophilus spores. For all microorganisms tested, a biphasic curve was generated when the number of survivors vs time was plotted in dose-response cures. Several proposed mechanisms of killing at room temperature by the OAUGDP are discussed.

Kenawy el-R et al. *Biologically active polymers: synthesis and antimicrobial activity of modified glycidyl methacrylate polymers having a quaternary ammonium and phosphonium groups.* J Controlled Release. 1998; 50(1-3) : 145-52.p Abstract: Polymers with antibacterial activity have been synthesized by chemical modification of poly(glycidyl methacrylate). The glycidyl methacrylate was polymerized by the free radical polymerization technique. The poly(glycidyl methacrylate) was hydrolyzed and was chloroacetylated using chloroacetyl chloride. The chloroacetylated product was modified to yield polymers with either quaternary ammonium or phosphonium salts. The antimicrobial activity of the modified glycidyl methacrylate polymers has been examined against a variety of test microorganisms by the cut plug and the viable cell counting methods using shake flask of ten times diluted nutrient broth medium. All three polymers obtained were inhibitory to the growth of Gram negative bacteria (Escherichia coli, Pseudomones aeruginosa, Shigella sp. and Salmonella typhae) and Gram positive bacteria (Bacillus subtilis and B. cereus) as well as the fungus (Trichophytun rubrum). It was found that the growth inhibitory effect varied according to the structure of the polymer and the composition of the active group and increased with increasing the concentration of the polymer. The tested polymers showed more antimicrobial activity against Gram negative bacteria and the fungus, whereas were less active against Gram positive bacteria.

Kennedy H.F. et al. *Origins of Staphylococcus epidermidis and Streptococcus oralis causing bacteraemia in a bone marrow transplant patient.* J Med Microbiol. 2000; 49(4) : 367-70.p Abstract: Coagulase-negative staphylococcal bacteraemia in immunocompromised patients is often associated with the use of central venous catheters, while the proposed origin of viridans streptococci causing bacteraemia in this patient group is the oral cavity. This report describes an episode of polymicrobial bacteraemia caused by Staphylococcus epidermidis and Streptococcus oralis followed by several further episodes of S. epidermidis bacteraemia in a 15-year-old boy after bone marrow transplantation. Pulsed-field gel electrophoresis (PFGE) of SmaI chromosomal DNA digests was used to compare blood culture and oral isolates of S. epidermidis and Str. oralis. The results indicated that the mouth was the source of both S. epidermidis and Str. oralis causing the first episode of bacteraemia. PFGE further demonstrated that the central venous catheter was the origin of a second strain of S. epidermidis responsible for subsequent episodes of staphylococcal bacteraemia. Both the oral mucosa and central venous lines should be considered as potential sources of organisms, including coagulase-negative staphylococci, associated with bacteraemia in immunocompromised patients.

Kern W.V. *[Antibiotics, new pathogens, new drug resistance].* Ther Umsch. 1999; 56(12) : 691-7.p Abstract: The 20th century is the century of the discovery of numerous pathogenic microorganisms. It is also the century of discovery of antimicrobial drugs and the beginning of the antibiotic era. While the development of antifungal drugs and of antivirals is on its rise, many infectious disease physicians and microbiologists feel that we might be on the edge of the beginning of the post-antibiotic era—50 years after antibiotic use in man and animals. Antibiotics have certainly been a major progress in modern medicine. Mortality and morbidity from many infectious diseases have been substantially reduced by effective antimicrobial therapy. The use of antibiotics has also been a prerequisite for major advances in clinical oncology, transplantation medicine, and surgery. The emergence and spread of resistant pathogens, however, has necessitated the development of broader and more active drugs and has resulted in excessive antimicrobial drug use with consequent selective pressure. Every 3rd patient admitted to a hospital is given antibiotics—often in the form of stepwise escalated therapy eventually including combinations of expensive agents. If the aim is to minimize the emergence of resistance and to contain costs, a much more critical indication for antimicrobial drug therapy will be necessary. Also, programmes on a local, regional, and perhaps even national level will be needed to help rationalize antimicrobial drug use.

Kerr J.R. *Cell adhesion molecules in the pathogenesis of and host defence against microbial infection.* Mol Pathol. 1999; 52(4) : 220-30.p Abstract: Eukaryotic cell adhesion molecules (CAMs) are used by various cells and extracellular molecules in host defence against infection. They are involved in many processes including recognition by circulating phagocytes of a site of inflammation, transmigration through the endothelial barrier, diapedesis through basement membrane and extracellular matrix, and release of effector mechanisms at the infected site. CAMs involved in leucocyte-endothelial cell interaction include the selectins, integrins, and members of the immunoglobulin superfamily. However, CAMs are also used by various microorganisms (protozoa, fungi, bacteria, and viruses) during their pathogenesis. For example, bacteria that utilise CAMs include Mycobacterium tuberculosis, Listeria monocytogenes, Yersinia spp, enteropathogenic Escherichia coli, Shigella spp, Neisseria spp, Bordetella spp, and Borrelia burgdorferi. In addition, CAMs are involved in the pathogenetic effects of the RTX toxins of Pasteurella haemolytica, Actinobacillus actinomycetemcomitans, and the superantigen exotoxins of Staphylococcus aureus and Streptococcus pyogenes. A recurrent and topical theme of potential importance within the bacterial group is the intimate relation between CAMs, bacterial protein receptors, and type III secretion systems. For example, the IpaBCD protein complex is secreted by the type III system of Shigella flexneri and interacts with alpha 5 beta 1 integrin on the eukaryotic cell surface, followed by Rho mediated internalisation; this illustrates the relevance of cellular microbiology. CAMs might prove to be novel therapeutic targets. Comparative genomics has provided the knowledge of shared virulence determinants among diverse bacterial genera, and will continue to deepen our understanding of microbial pathogenesis, particularly in the context of the interaction of prokaryotic and eukaryotic molecules.

Kertesz D.A. et al. *Invasive Streptococcus pneumoniae infection in Latin American children: results of the Pan American Health Organization Surveillance Study.* Clin Infect Dis. 1998; 26(6) : 1355-61.p Abstract: Protein-polysaccharide conjugate vaccines against Streptococcus pneumoniae promise to be an effective public health intervention for children, especially in an era of increasing antimicrobial resistance. To characterize the distribution of capsular types in Latin America, surveillance for invasive pneumococcal infection in children < or = 5 years of age was done in six countries between February 1993 and April 1996. Fifty percent of 1,649 sterile-site iso-

lates were from children with pneumonia, and 52% were isolated from blood. The 15 most common of the capsular types prevalent throughout the region accounted for 87.7% of all isolates. Overall, 24.9% of isolates had diminished susceptibility to penicillin: 16.7% had intermediate resistance and 8.3% had high-level resistance. Three customized vaccine formulas containing 7, 12, and 15 capsular types were found to have regional coverages of 72%, 85%, and 88%, respectively. This study emphasizes the need for local surveillance for invasive pneumococcal disease prior to the development and evaluation of protein-polysaccharide conjugate vaccines for children.

Kesah C.N. et al. *Prevalence, antimicrobial properties and beta-lactamase production of haemolytic enterobacteria in patients with diarrhoea and urinary tract infections in Legos, Nigeria.* Cent Afr J Med. 1996; 42(5) : 147-50.p Abstract: OBJECTIVE: To determine the prevalence, antimicrobial properties and beta-lactamase production of haemolytic enterobacteria in patients with diarrhoea and urinary tract infections in Lagos, Nigeria. DESIGN: Hospital based prospective study. SUBJECTS: Total of 324 patients comprising 194 diarrhoeal and 130 urinary tract infection (UTI) cases. MAIN OUTCOME MEASURES: Production of haemolysms. beta-lactamase and antibiograms of isolates. RESULTS: 186 (57.41 pc) of the 324 clinical specimens screened were positive for enterobacteria, out of which 29 (15.59 pc) were haemolytic. Proteus vulgaris (2.78 pc) Klebsiella spp. (1.85pc). Escherichia coli (1.23 pc). Pseudomonas spp. (0.93 pc). Yersinia enterocolitics and Morganella morganii (0.62 pc). Salmonella spp. Vibrio cholerae and Proteus mirabilis (0.31pc) were the haemolytic enterobacteria Isolated. The susceptibilities of haemolytic bacteria to eight antibotics determined by disc-agar diffusion technique revealed that all 29 (100 pc) haemolytic isolates were sensitive to gentamycin and streptomycin but showed varied susceptibilities to the other drugs. Eleven (37.9 pc) of the 29 isolates produced beta-lactamase. CONCLUSION: We conclude that gentamycin and streptomycin are effective drugs against haemolytic isolates from diarrhoea and UTI cases.

Ketai L. et al. *Is the stat Gram stain helpful during percutaneous image-guided fluid drainage?* Acad Radiol. 2000; 7(4) : 228-31.p Abstract: RATIONALE AND OBJECTIVES: The purpose of this study was to use logistic regression to analyze both Gram stain results and other clinical information to create a decision rule capable of predicting which abdominal or pelvic fluid collections would later prove to be infected and therefore require catheter drainage. MATERIALS AND METHODS: The authors retrospectively collected Gram stain results and clinical data (postoperative status and antibiotic use) regarding 124 abdominal or pelvic fluid drainage procedures performed between 1991 and 1996. They then analyzed these data by using logistic regression to create an equation that predicted the presence of fluid infection. Finally, they validated this equation by applying it to 39 abdominal or pelvic fluid drainage procedures performed in 1997. RESULTS: The resulting equation predicted that a fluid collection was likely to be infected if any of the following were present: Gram stain positive for bacteria, Gram stain showing moderate or many white blood cells, and purulent fluid at visual inspection. For the initial data set, the sensitivity of the decision rule was 91%, the specificity was 54%, and the overall accuracy was 77%. For the 1997 data set, the sensitivity of the decision rule was 88%, the specificity was 50%, and the accuracy was 77%. CONCLUSION: When combined with clinical information, Gram stain results are sensitive but nonspecific in the detection of abdominal or pelvic fluid infection. Use of the decision rule could prevent unnecessary catheter placement in a minority of patients with abdominal or pelvic fluid collections.

Keyf F. et al. *Persistence of 99mTc-labelled microorganisms on surfaces of impression materials.* J Nihon Univ Sch Dent. 1995; 37(1) : 1-7.p Abstract: Impression materials or prostheses can be contaminated with oral microflora and provide a significant source for cross-contamination. A study of such contamination was carried out using an approach different from that of infection control, which has often been investigated in previous studies. The study focused on microorganisms known to cause local and systemic diseases and which are normally found in the oral flora. The persistence of Streptococcus mutans (S. mutans), Escherichia coli (E. coli), Staphylococcus aureus and Candida albicans (C. albicans) on zinc-oxide eugenol, silicone rubber, irreversible hydrocolloid and polyether-rubber was investigated using 99mTc-labelled microorganisms. Ten specimens from each of the four impression materials were prepared as discs of 3 mm in height and 10 mm in diameter. After the specimens had been placed into a suspension of 99mTc-labelled microorganisms, remaining radioactivity was counted in a gamma counter. According to own findings, S. mutans was the most, and E. coli the least persistent on the specimen surfaces. The number of microorganisms removed after washing was less than the amount remaining on the surfaces. C. albicans was removed most easily from all impression surfaces that bore persistent microorganisms after washing. Other microorganisms showed various degrees of persistence according to the impression material.

Khan W.A. et al. *Randomised controlled comparison of single-dose ciprofloxacin and doxycycline for cholera caused by Vibrio cholerae 01 or 0139.* Lancet. 1996; 348(9023) : 296-300.p Abstract: BACKGROUND: Effective antimicrobial therapy can reduce the duration and volume of cholera diarrhoea by half. However, such treatment is currently limited by Vibrio cholerae resistance to the drugs commonly prescribed for cholera, and by the difficulties involved in the administration of multi-drug doses under field conditions. Because of its favourable pharmacokinetics we thought it likely that single-dose ciprofloxacin would be effective in the treatment of cholera. METHODS: In this double-blind study treatment was either a single 1 g oral dose of ciprofloxacin plus doxycycline placebo, or a single 300 mg oral dose of doxycycline plus ciprofloxacine placebo. 130 moderately or severely dehydrated men infected with V cholerae 01 and 130 infected with V cholerae 0139 were randomly assigned treatment. Patients stayed in hospital for 5 days. We measured fluid intake and stool volume every 6 h, and a sample of stool for culture was obtained daily. The primary outcome measures were clinical success—the cessation of watery stool within 48 h; and bacteriological success—absence of V cholerae from cultures of stool after study day 2. FINDINGS: Among patients infected with V cholerae 01, treatment was clinically successful in 62 (94%) of 66 patients who received ciprofloxacin and in 47 (73%) of 64 who receive doxycycline (difference 21% [95% Cl 8-33]); the corresponding proportions with bacteriological success were 63 (95%) and 44 (69%) (27% [14-39]). Among patients infected with V cholerae 0139, treatment was clinically successful in 54 (92%) of 59 patients who received ciprofloxacin and in 65 (92%) of 71 who received doxycycline (< 1% [-9 to 9]), and bacteriologically successful in 58 (98%) and 56 (79%), respectively (19% [9-30]). Total volume of watery stool did not differ significantly between ciprofloxacin-group and doxycycline-group patients infected with either V cholerae 01 or 0139. All but one of the V cholerae 01 and all of the 0139 isolates were susceptible in vitro to doxycycline, whereas 48 (37%) of the V cholerae 01 isolates and none of the 0139 isolates were resistant to tetracycline. Treatment clinically failed in 14 (52%) of 27 doxycycline-treated patients infected with a tetracycline-resistant V cholerae 01 strain, compared with three (8%) of 37 patients infected with a tetracycline-susceptible strain (44% [23-65]). INTERPRETATION: Single-dose ciprofloxacin is effective in the treatment of cholera caused by V cholerae 01 or 0139 and is better than single-dose doxycycline in the eradication of V cholerae from stool. Single-dose ciprofloxacin may also be the preferred treatment in areas where tetracycline-resistant V cholerae are common. In V cholerae, in-vitro doxycycline susceptibilities are not a useful indicator of the in-vivo efficacy of the drug.

Khardori N. et al. *Tolerance of Staphylococcus epidermidis grown from indwelling vascular catheters to antimicrobial agents.* J Ind Microbiol.

1995; 15(3) : 148-51.p Abstract: During a prospective study of indwelling vascular catheter-related infections, 134 isolates of Staphylococcus epidermidis were grown from 700 catheter tips. In vitro antimicrobial susceptibility testing of these isolates to oxacillin, vancomycin and ofloxacin was performed using the standard broth microdilution technique. These results were compared to those for the same organisms grown in biofilm before the addition of antimicrobial agents. In 96-well flat bottom microtiter plates, 10(4)-10(5) colony forming units of S. epidermidis in 0.1 ml broth were grown for 18 h at 37 degrees C, at which time a biofilm was observed for all isolates. Different concentrations of antimicrobial agents (0.1 ml) were then added to the plates. The plates were incubated for 18 h at 37 degrees C. Since MICs could not be estimated in these plates, all the wells were subcultured after mixing the biofilm with the broth. Minimum bactericidal concentrations (MBCs) were defined as 99.9% reduction in colony forming units. For organisms grown in suspension, 100% of the isolates were susceptible to vancomycin, 81% to ofloxacin and 40% to oxacillin. MBCs of susceptible isolates were within four-fold differences for vancomycin (53%), oxacillin (50%), and ofloxacin (51%). When grown as a biofilm, 78%, 93% and 71% of isolates had MBCs of > or = 2048 micrograms ml-1 of oxacillin, vancomycin and ofloxacin respectively. These data demonstrate the reduced bactericidal activity of antimicrobial agents against S. epidermidis in a biofilm and a simple method for its detection in the microbiology laboratory.

Khomenko A.G. et al. *[Diagnosis and treatment of acute progressive tuberculosis types].* Probl Tuberk. 1996; (5) : 21-3.p Abstract: An examination was made of 77 patients with extensive segmentary and lobular pulmonary tuberculous lesions: caseous pneumonia (n = 26), infiltrative caseous pneumonia (n = 18), fibrocavernous pneumonia complicated by caseous pneumonia (n = 16), and disseminated tuberculosis (n = 17). All patients had destructive changes; in 82.7% of patients the caverns were large and great in size. Bacteria were isolated in 94.8%, mycobacterial drug resistance was noted in 51.8%. Four variants of the course of a disease were identified: 1) that with predominance of the intoxication syndrome (41.6%); 2) that with respiratory failure (24.7%); 3) that with pulmonary hemorrhage (15.6%), 4) that added by secondary microorganisms (18.2%). Chemotherapy included a combination of 4 or 5 drugs along with pathogenetic tools, which stabilized a process in 80% of patients and arrested bacterial isolation in 69.5%. In 20%, the process continued to progress and in 3 of them died.

Kienzle N. et al. *Aeromonas wound infection in burns.* Burns. 2000; 26(5) : 478-82.p Abstract: Infection of burn patients with the Aeromonas organism is an uncommon event. This paper documents four cases of Aeromonas hydrophila and one case involving both A. hydrophila and A. caviae occurring in burn patients between 1990 and 1998 at the Royal Brisbane Hospital burns unit. The organism was isolated from either skin swabs, tissue samples, blood cultures or cultured lines. In all patients there was a history of immersion in water immediately post burn. There is one case of invasion and destruction of deeper tissues and one fatality. Appropriate management requires a high index of suspicion if a history of immersion in untreated water post burn is given and the treatment involves aggressive excision and antibiotic therapy.

Kikukawa M. et al. *[Infection in elderly leukemic patients].* Nippon Ronen Igakkai Zasshi. 1996; 33(1) : 17-21.p Abstract: Febrile episodes occurring in 29 elderly patients (mean age 75 years) with leukemia, from 1988 to 1993, were reviewed. A febrile episode was defined as a temperature of 38 degrees C or greater for at least 6 hours. The number of febrile episodes was 64. The average was 2.2 febrile episodes per patient. Seventy-two percent of febrile episodes occurred when the patients had neutropenia below 100/microliters, while 16% occurred with neutropenia of 101/microliters to 500/microliters. Causative microorganisms were identified in 48% of total febrile episodes. The most common infectious site was the urinary tract which accounted for 25% of total episodes. Pneumonia and septicemia accounted for 22% of total episodes, respectively. Gram-positive cocci were responsible for 66% of microbiologically documented febrile episodes, while 21% were caused by gram-negative bacilli. Gram-positive cocci, particularly staphylococcus aureus, coagulae-negative staphylococcus and enterococci increased compared with a decade ago in our department. Granulocyte colony-stimulating factor (G-CSF) was used 12 times for infection. No significant difference in fever amelioration was seen between G-CSF and non-G-CFS cases.

Kilian M. et al. *Biological significance of IgA1 proteases in bacterial colonization and pathogenesis: critical evaluation of experimental evidence.* APMIS. 1996; 104(5) : 321-38.p Abstract: IgA1 protease activity, which allows bacteria to cleave human IgA1 in the hinge region, represents a striking example of convergent evolution of a specific property in bacteria. Although it has been known since 1979 that IgA1 protease is produced by the three leading causes of bacterial meningitis in addition to important urogenital pathogens and some members of the oropharyngeal flora, the exact role of this enzyme in bacterial pathogenesis is still incompletely understood owing to lack of a satisfactory animal model. Cleavage of IgA1 by these post-proline endopeptidases efficiently separates the monomeric antigen-binding fragments from the secondary effector functions of the IgA1 antibody molecule. Several in vivo and in vitro observations indicate that the enzymes are important for the ability of bacteria to colonize mucosal membranes in the presence of S-IgA antibodies. Furthermore, the extensive cleavage of IgA sometimes observed in vivo, suggests that IgA1 protease activity results in a local functional IgA deficiency that may facilitate colonization of other microorganisms and the penetration of potential allergens. It has been hypothesized that IgA1 protease activity of Haemophilus influenzae, Neisseria meningitidis, and Streptococcus pneumoniae, under special immunological circumstances, allows these bacteria to take advantage of specific IgA1 antibodies in a strategy to evade other immune factors of the human body. The decisive factor is the balance between IgA antibodies against surface antigens of the respective bacteria and their IgA1 protease. Recent studies have shown that serine-type IgA1 proteases of H. influenzae, meningococci, and gonococci belong to a family of proteins used by a diverse group of Gram-negative bacteria for colonization and invasion.

Killgore G.E. et al. *A 5' nuclease PCR (TaqMan) high-throughput assay for detection of the mecA gene in staphylococci.* J Clin Microbiol. 2000; 38(7) : 2516-9.p Abstract: In an effort to find a rapid, efficient, and reliable method of screening large numbers of bacterial isolates for specific antimicrobial resistance genes, we compared conventional PCR results to the results generated using the TaqMan 5' nuclease PCR kit in conjunction with an ABI Prism 7700 Sequence Detector for detecting the mecA gene in various species of staphylococci. DNA was extracted using two techniques. The first used a high-salt extraction method suitable for conventional PCR but resulted in a 7.2% rate of PCR inhibition with the TaqMan technique. PCR inhibition could be overcome by diluting samples 1:5 prior to testing. The second method used the Qiagen QIAamp Tissue Kit; no instances of PCR inhibition were encountered with this method. A total of 197 (96%) of the 206 samples with no inhibition showed agreement between the two methods. Eight of the nine disagreements were likely the result of low-level DNA cross contamination caused by frequent specimen handling. Target DNA in all eight of these samples was first detected in the initial tests only after >30 PCR cycles, and all were negative upon repeat testing even after 40 PCR cycles using freshly extracted DNA. Among those positive samples in agreement, target DNA was invariably detected before 30 PCR cycles. The TaqMan assay eliminated the need to load, run, stain, and read agarose gels and provided the advantage of instant detection of PCR product by laser-activated fluorescence. Thus, final results were obtained 2 h after PCR was initiated, as opposed to a requirement of 2 days to examine 96 samples by

agarose gel electrophoresis.

Kim J.M. et al. *Vancomycin-resistant enterococcal infections in Korea.* Yonsei Med J. 1998; 39(6) : 562-8.p Abstract: Enterococci recently became the second-to-third most commonly isolated organism from nosocomial infections. Enterococci are intrinsically more resistant to many antimicrobial agents and often show acquired resistance to many antimicrobial agents including high-level aminoglycosides. With the increased use of vancomycin, vancomycin-resistant enterococci (VRE) has become an important nosocomial pathogen. In Korea, the proportion ofVRE among all enterococcal ofVRE is no longer low in some settings and recent observations of a sudden increase ofVRE isolation in several hospitals in Korea suggests that VRE infection may become a serious problem in the near future. The most important considerations are that vancomycin-resistant genes may spread to other highly virulent genera, such as MRSA, and that there are no approved and convincingly effective antibiotics for the treatment of VRE. Therefore, current efforts have concentrated on limiting the spread of these organisms within the hospital environment. Prudent use of antimicrobial agents and strict adherence to preventive measures such as aggressive communication, education, and infection control practices are essential to control the spread of this organism. However, hospital infection control protocols and the laboratory support they require are costly in terms of space and supplies, as well as in personnel resources. These factors add further pressure to already stretched hospital budgets. Nevertheless, policies or programs defining and managing VRE infection or colonization should be established and now is the time to enforce an overall management strategy against VRE.

Kim W.J. et al. *Bacterial resistance to antimicrobial agents: an overview from Korea.* Yonsei Med J. 1998; 39(6) : 488-94.p Abstract: Antimicrobial resistance of bacteria has become a worldwide problem. Available data suggest that the resistance problem is comparatively more serious in Korea. In large hospitals, the proportion of methicillin-resistant Staphylococcus aureus (MRSA) has been reported at over 70%, and of penicillin-nonsusceptible Streptococcus pneumoniae at around 70%. Infection or colonization of vancomycin-resistant enterococci has started to increase. Extended-spectrum beta-lactamase producing Escherichia coli and Klebsiella pneumoniae has become widespread and even carbapenem-resistant Pseudomonas aeruginosa has been increasing. Community-acquired pathogens such as Salmonella, Shigella and Neisseria gonorrhoeae are often resistant to various antimicrobial agents. The prevalence of resistant bacteria can lead to erroneous empirical selection of either noneffective or expensive drugs, prolonging hospitalization and higher mortality. The emergence and spread of resistant bacteria are unavoidable unless antimicrobial agents are not used at all. The high prevalence of resistant bacteria in Korea seems to be related to antibiotic usage: 1) easy availability without prescription at drug stores, 2) injudicious use in hospitals, and 3) uncontrolled use in agriculture, animal husbandry, and fisheries. Nosocomial infection is an important factor in the spread of resistant bacteria. Antimicrobial resistance problems should be regarded as the major public health concern in Korea. It is urgently required to ban the sale of antibiotics without prescription, to use antibiotics more judiciously in hospitals by intensive teaching of the principles of the use of antibiotics, and to establish better control measures of nosocomial infections. Regulation of antimicrobials for other than human use should also be required. These issues are not easy to address and require the collective action of governments, the pharmaceutical industry, health care providers, and consumers.

Kim Y.S. et al. *A Brassica cDNA clone encoding a bifunctional hydroxymethylpyrimidine kinase/thiamin-phosphate pyrophosphorylase involved in thiamin biosynthesis.* Plant Mol Biol. 1998; 37(6) : 955-66.p Abstract: We report the characterization of a Brassica napus cDNA clone (pBTHI) encoding a protein (BTHI) with two enzymatic activities in the thiamin biosynthetic pathway, thiamin-phosphate pyrophosphorylase (TMP-PPase) and 2-methyl-4-amino-5-hydroxymethylpyrimidine-monophosphate kinase (HMP-P kinase). The cDNA clone was isolated by a novel functional complementation strategy employing an Escherichia coli mutant deficient in the TMP-PPase activity. A biochemical assay showed the clone to confer recovery of TMP-PPase activity in the E. coli mutant strain. The cDNA clone is 1746 bp long and contains an open reading frame encoding a peptide of 524 amino acids. The C-terminal part of BTH1 showed 53% and 59% sequence similarity to the N-terminal TMP-PPase region of the bifunctional yeast proteins Saccharomyces THI6 and Schizosaccharomyces pombe THI4, respectively. The N-terminal part of BTH1 showed 58% sequence similarity to HMP-P kinase of Salmonella typhimurium. The cDNA clone functionally complemented the S. typhimurium and E. coli thiD mutants deficient in the HMP-P kinase activity. These results show that the clone encodes a bifunctional protein with TMP-PPase at the C-terminus and HMP-P kinase at the N-terminus. This is in contrast to the yeast bifunctional proteins that encode TMP-PPase at the N-terminus and 4-methyl-5-(2-hydroxyethyl)thiazole kinase at the C-terminus. Expression of the BTH1 gene is negatively regulated by thiamin, as in the cases for the thiamin biosynthetic genes of microorganisms. This is the first report of a plant thiamin biosynthetic gene on which a specific biochemical activity is assigned. The Brassica BTH1 gene may correspond to the Arabidopsis TH-1 gene.

King D.E. et al. *Community-acquired pneumonia in adults: initial antibiotic therapy.* Am Fam Physician. 1997; 56(2) : 544-50.p Abstract: Community-acquired pneumonia is a common infection encountered in clinical practice and is the leading cause of death due to infectious disease in the United States. To choose initial antimicrobial therapy appropriately, physicians must keep informed of recent developments in the epidemiology and clinical manifestations of atypical pathogens, antibiotic resistance and new antibiotics. Differentiating between "typical" and "atypical" pneumonia based on the initial clinical presentation is difficult. Primary treatment for community-acquired pneumonia in young adults without comorbidities is erythromycin. Older adults or those with comorbidities should be treated with erythromycin plus trimethoprim-sulfamethoxazole, a second- or third-generation cephalosporin, or a new macrolide. Empiric therapy for moderately or severely III hospitalized patients usually begins with erythromycin plus a second- or third-generation cephalosporin. Physicians should use initial antibiotic therapy for coverage of both typical and atypical pathogens.

Kinnaert P. et al. *Direct activation of human peritoneal mesothelial cells by heat-killed microorganisms.* Ann Surg. 1996; 224(6) : 749-54; discussion 754-5.p Abstract: OBJECTIVE:The aim of the study was to determine if human peritoneal mesothelial cells (HPMCs) can be activated directly by bacterial products contained in preparations of heat-killed Escherichia coli and staphylococci. SUMMARY BACKGROUND DATA: It has been shown recently that cytokine-activated HPMCs produce the inflammatory mediators, interleukin-1, interleukin-6, interleukin-8, and macrophage chemotactic protein-1. Studies concerning the effects of bacterial products on HPMCs are scarce and have not yielded conclusive results. METHODS: Growth-arrested HPMC monolayers were prepared from cell suspensions obtained by enzymatic disaggregation of small pieces of omentum. They were incubated for 24 hours with heat-killed E. coli (ATCC 25922), heat-killed staphylococci (ATCC 25933), or E. coli lipopolysaccharide, and the release of various cytokines in the culture media was measured by radioimmunoassays or enzyme-linked immunosorbent assays. Results were expressed as mean +/- standard error of the mean in picograms per milliliter of supernatant and analyzed with the Wilcoxon test; p values of less than 0.05 were considered significant. RESULTS: Baseline production of interleukin-6, interleukin-8, the chemokine "regulated upon activation, normal T cell expressed and secreted" (RANTES), and macrophage chemotactic protein-1 varied widely from one omental preparation to the other. E. coli increased the release of these mediators: from 1206 +/-

316 pg/mL to 8480 +/- 2189 pg/mL for interleukin-6, from 285 +/- 58 pg/mL to 3164 +/- 1053 pg/mL for interleukin-8, from 7 +/- 5 pg/mL to 684 +/- 264 pg/mL for RANTES, and from 2212 +/- 346 pg/mL to 7726 +/- 1473 pg/mL for macrophage chemotactic protein-1. Heat-killed staphylococci did not alter significantly the production of RANTES or macrophage chemotactic protein-1 but increased the production of the two other cytokines from 1325 +/- 389 pg/mL to 2206 +/- 523 pg/mL for interleukin-6 and from 318 +/- 70 pg/mL to 819 +/- 265 pg/mL for interleukin-8. CONCLUSIONS: The authors' results show that HPMCs are able to react to a direct stimulation with heat-killed microbes. They suggest that HPMCs, as well as resident macrophages, participate actively in the initiation and possibly in the modulation of intraperitonen inflammatory reactions.

Kinoshita M. et al. *Concept of segmentation in nosocomial epidemiology: epidemiological relation among antimicrobial-resistant isolates of Pseudomonas aeruginosa*. J Infect. 1997; 35(3) : 269-76.p Abstract: Typing studies on 271 clinical strains of Pseudomonas aeruginosa isolated from the University Teaching Hospital were conducted to obtain their serotypes, antimicrobial susceptibility patterns and plasmid profiles. These strain typing data were arranged through multivariate statistical analysis by computation to classify individual strains. Plots in the scatter diagrams obtained from both principal component analysis and quantification theory type III expressed the clinical strains of P. aeruginosa with various degrees of antimicrobial resistance. Epidemiological relation among these clinical strains was analysed in those scatter diagrams by segmentation, in combination with their epidemiological information (date and place of isolation, type of specimen, etc.). The results showed that the serotype E strains both with high-level resistance to gentamicin and with a plasmid of 3.9 x 10(6) dalton, and the strains resistant to more than five antimicrobial agents, were colonized and localized each in certain clinical wards for inpatients. It was suggested that segmentation analysis could be of practical use in the management of nosocomial infection control against P. aeruginosa with antimicrobial resistance.

Kinoshita S. et al. *[Antimicrobial activity of carbapenem antibiotics against gram-negative bacilli]*. Jpn J Antibiot. 1998; 51(9) : 551-60.p Abstract: Antimicrobial activities of meropenem (MEPM), imipenem (IPM), panipenem (PAPM), ceftazidime (CAZ), cefozopran (CZOP), aztreonam (AZT), norfloxacin (NFLX) and tetracycline (TC) against clinically isolated Gram-negative bacilli [271 strains of Enterobacteriaceae and 242 strains non-fermentative Gram-negative bacteria (NFB)] were investigated. Among carbapenem antibiotics, MEPM showed the lowest MIC90, which activity was about four-hold higher than those of IPM and PAPM. The activity of IPM was equal or slightly superior to that of PAPM. Resistance to IPM (> 16 micrograms/ml) was observed in 3 strains of Enterobacteriaceae (1.1%) and 14 strains of NFB (5.8%). It is conceivable that these strains produce metallo-beta-lactamase. Referring to the correlation among MICs of MEPM, IPM and PAPM, 3 strains in 3 species of Enterobacteriaceae showed cross resistance to carbapenems; while 14 strains of NFB showed cross resistance to MEPM and IPM, 15 strains to MEPM and PAPM, and 29 strains to IPM and PAPM, and all of these strains were Pseudomonas aeruginosa. Fifteen of 29 strains of IPM-resistant and 77 of 92 strains of PAPM-resistant P. aeruginosa were susceptible to MEPM. Thirty-three strains (12%) of the Enterobacteriaceae were resistant to CAZ and AZT (> or = 32 micrograms/ml) and these were considered as ESBL-producing strains.

Kiraz N. et al. *Case report. Rhodotorula rubra fungaemia due to use of indwelling venous catheters.* Mycoses. 2000; 43(5) : 209-10.p Abstract: Rhodotorula has been an infrequent cause of infection in humans but there have been some case reports about this systemic yeast infection. In this article, a Rhodotorula rubra fungaemia due to an indwelling catheter in a 23-year-old woman who had been diagnosed with non-Hodgkin's lymphoma grade IV B is described.

Kirton O.C. et al. *A prospective, randomized comparison of an in-line heat moisture exchange filter and heated wire humidifiers: rates of ventilator-associated early-onset (community-acquired) or late-onset (hospital-acquired) pneumonia and incidence of endotracheal tube occlusion*. Chest. 1997; 112(4) : 1055-9.p Abstract: PURPOSE: To compare the performance of an in-line heat moisture exchanging filter (HMEF) (Pall BB-100; Pall Corporation; East Hills, NY) to a conventional heated wire humidifier (H-wH) (Marquest Medical Products Inc., Englewood, Colo) in the mechanical ventilator circuit on the incidence of ventilator-associated pneumonia (VAP) and the rate of endotracheal tube occlusion. METHODS: This report describes a prospective, randomized trial of 280 consecutive trauma patients in a 20-bed trauma ICU (TICU). All intubated patients not ventilated elsewhere in the medical center prior to their TICU admission were randomized to either an in-line HMEF or a H-wH in the breathing circuit. Ventilator circuits were changed routinely every 7 days, and closed system suction catheters were changed every 3 days. HMEFs were changed every 24 h, or more frequently if necessary. A specific endotracheal tube suction and lavage protocol was not employed. Patients were dropped from the HMEF group if the filter was changed more than three times a day or the patient was placed on a regimen of ultra high-frequency ventilation. The Centers for Disease Control and Prevention (CDC) criteria for diagnosis of pneumonia were used; early-onset, community-acquired pneumonia was defined if CDC criteria were met in < or =3 days, and late-onset, hospital-acquired pneumonia was defined if criteria were met in >3 days. Laboratory and chest radiograph interpretation were blinded. RESULTS: The patient ages ranged from 15 to 95 years in the HMEF group and 16 to 87 years in the H-wH group (p=not significant), with a mean age of 46 years and 48 years, respectively. The male to female ratio ranged between 78 to 82%/22 to 18%, respectively, and 55% of all admissions were related to blunt trauma, 40% secondary to penetrating trauma, and 5% to major burns. There was no difference in Injury Severity Score (ISS) between the two groups. Moreover, there was no significant difference in mean ISS among those who did not develop pneumonia and those patients who developed either early-onset, community-acquired or late-onset, hospital-acquired pneumonia. The HMEF nosocomial VAP rate was 6% compared to 16% for the H-wH group ($p<0.05$), and total ventilator circuit costs (per group) were reduced. There were no differences in duration of ventilation (mean+/-SD) if the patient did not develop pneumonia or if the patient developed an early-onset, community-acquired or a late-onset, hospital-acquired pneumonia. Moreover, total TICU days were reduced in the HMEF group. In addition, the incidence of partial endotracheal tube occlusion was not significantly different between the H-wH and the HMEF groups. CONCLUSIONS: The HMEF used in this study reduced the incidence of late-onset, hospital-acquired VAP, but not early-onset, community-acquired VAP, compared to the conventional H-wH circuit. This was associated with a significant reduction in total ICU stay. Disposable ventilator circuit costs in the HMEF group were reduced compared to the H-wH group in whom circuit changes occurred at 7-day intervals. CLINICAL IMPLICATIONS: The use of the HMEF is a cost-effective clinical practice associated with fewer late-onset, hospital-acquired VAPs, and should result in improved resource allocation and utilization.

Kiska D.L. et al. *Comparison of antimicrobial susceptibility methods for detection of penicillin-resistant Streptococcus pneumoniae.* J Clin Microbiol. 1995; 33(1) : 229-32.p Abstract: We sought to determine if commercially available susceptibility tests were accurate in detecting penicillin resistance and relative resistance in Streptococcus pneumoniae. We compared the reference MIC method with oxacillin disk screening and three commercial tests, E-test (AB Biodisk), JustOne (Radiometer America), and MicroScan Pos MIC Panel Type 6 (Baxter Diagnostics), with 80 selected clinical isolates. Thirty-three additional isolates were tested by the reference method and the E-test to further validate the latter method. Oxacillin screening was effective in detecting all penicillin-resistant and relatively resistant

strains of S. pneumoniae. The MicroScan method was not effective in detecting penicillin resistance or relative resistance. The JustOne system classified only 6 (35%) of 17 resistant strains correctly, with 11 resistant strains classified as relatively resistant. The E-test correctly classified 30 (83%) of 36 resistant isolates, with 6 resistant isolates interpreted as relatively resistant. For determining penicillin MICs for S. pneumoniae, the E-test was the most accurate of the commercial systems that we studied.

Kiss L. et al. *Antibiotic resistance of Acinetobacter calcoaceticus strains isolated from patients treated in intensive care units.* Acta Microbiol Immunol Hung. 1995; 42(4) : 381-7.p Abstract: The distribution according to specimens and susceptibility to antimicrobial agents of 481 Acinetobacter calcoaceticus strains isolated from patients treated in intensive care units were studied. They occurred most frequently in tracheal specimens and pus. Using disk diffusion test the strains proved to be multiple resistant to ampicillin (86.3%), azlocillin (86.7%), mezlocillin (84.0%), cefamandole (99.7%), cefoxitin (94.1%), cefuroxime (90.6%), cefoperazone (84.9%), cefotaxime (82.0%), ceftriaxone (81.0%), tobramycin (71.2%), gentamicin (86.2%), chloramphenicol (90.5%) and tetracycline (89.8%). Based on the lowest incidence of resistant strains imipenem (0%), netilmicin (2.6%), amikacin (4.9%), ampicillin+sulbactam (8.9%), amoxicillin+clavulanic acid (29.4%), pefloxacin (26.2%), ciprofloxacin (30.1%), ofloxacin (34.3%), cotrimoxazole (41.6%), carbenicillin (41.2%) or ceftazidime (55.4%) may be the drug of choice in nosocomial A. calcoaceticus infections.

Klausner J.D. et al. *Correlates of gonococcal infection and of antimicrobial-resistant Neisseria gonorrhoeae among female sex workers, Republic of the Philippines, 1996-1997.* J Infect Dis. 1999; 179(3) : 729-33.p Abstract: From 1994 to 1997, the proportion of Neisseria gonorrhoeae highly resistant to ciprofloxacin (MIC >/=4 microg/mL) increased substantially among female sex workers (FSWs) in the Philippines. Among 1499 Filipina FSWs, we evaluated factors associated with gonococcal infection and with gonococcal antimicrobial resistance. By multivariate analysis, gonococcal infection was associated with sex with a new client, self-prescribed prophylactic antimicrobial use, work in a brothel, and inconsistent condom use and was negatively associated with registration status and vaginal hygiene practices. Factors associated with ciprofloxacin-resistant gonococci included: marital status, living alone, duration of sex work, and clinic site. Further, gonococci highly resistant to ciprofloxacin were isolated from 10 (11.5%) of 87 FSWs reporting self-prescribed antimicrobial use versus 44 (3.4%) of 1295 reporting no antimicrobial use (P<.001). Self-prescribed prophylactic antimicrobial use and inconsistent condom use could be important factors in the continued emergence of gonococcal antimicrobial resistance in the Philippines.

Klein G. et al. *Antibiotic resistance patterns of enterococci and occurrence of vancomycin-resistant enterococci in raw minced beef and pork in Germany.* Appl Environ Microbiol. 1998; 64(5) : 1825-30.p Abstract: The food chain, especially raw minced meat, is thought to be responsible for an increase in the incidence of vancomycin-resistant enterococci (VRE) in human nosocomial infections. Therefore, 555 samples from 115 batches of minced beef and pork from a European Union-licensed meat-processing plant were screened for the occurrence of VRE. The processed meat came from 45 different slaughterhouses in Germany. Enterococci were isolated directly from Enterococcosel selective agar plates and also from Enterococcosel selective agar plates supplemented with 32 mg of vancomycin per liter. In addition, peptone broth was used in a preenrichment procedure, and samples were subsequently plated onto Enterococcosel agar containing vancomycin. To determine resistance, 209 isolates from 275 samples were tested with the glycopeptides vancomycin, teicoplanin, and avoparcin and 19 other antimicrobial substances by using a broth microdilution test. When the direct method was used, VRE were found in 3 of 555 samples (0.5%) at a concentration of 1.0 log CFU/g of minced meat. When the preenrichment procedure was used, 8% of the samples were VRE positive. Our findings indicate that there is a low incidence of VRE in minced meat in Germany. In addition, the resistance patterns of the VRE isolates obtained were different from the resistance patterns of clinical isolates. A connection between the occurrence of VRE in minced meat and nosocomial infections could not be demonstrated on the basis of our findings.

Klein J.O. *Antimicrobial therapy issues facing pediatricians.* Pediatr Infect Dis J. 1995; 14(5) : 415-9.p Abstract: In the field of infectious diseases, the emergence of new pathogens or old diseases in newly recognized forms; changing virulence of pathogens; changing patterns of antimicrobial susceptibility; new diagnostic techniques, drugs or vaccines; changing concepts of chemoprophylaxis; controversies about medical vs. surgical techniques; and the challenge of care of children with infectious diseases within new guidelines of managed care are recently identified areas of change. The increased resistance of Streptococcus pneumoniae to many commonly used antimicrobials and the increased proportion of beta-lactamase-producing nontypable Haemophilus influenzae and Moraxella catarrhalis concern many practitioners. The decreased antibiotic susceptibility of S. pneumoniae is a relatively new phenomenon in the United States. Optimal therapy for mild, moderate or severe pneumococcal disease is dependent on current local susceptibility patterns. Group A streptococci are uniformly susceptible to readily achieved concentrations of all penicillins and cephalosporins. However, recent clusters of cases of rheumatic fever, increased recognition of toxic shock syndrome and bacteremic and localized severe pneumococcal disease have increased concern about the changing ecology of the Streptococcus and the implications for therapy. Finally recognition that many children with acute bacterial otitis media have resolution of disease without use of antimicrobial agents has led to more rigorous study designs for evaluating new drugs. (ABSTRACT TRUNCATED AT 250 WORDS).

Klein J.O. *Clinical implications of antibiotic resistance for management of acute otitis media.* Pediatr Infect Dis J. 1998; 17(11) : 1084-9; discussion 1099-100.p Abstract: Antibiotic resistance to available antimicrobial agents has been constant since the introduction of the sulfonamides in the 1930s. Multidrug-resistant Streptococcus pneumoniae and beta-lactamase-producing Haemophilus influenzae are a concern now because of the importance of these pathogens in infections of the respiratory tract in infants and children. Amoxicillin remains the drug of choice for initial episodes of acute otitis media (AOM) although increase of the dosage schedule to 80 mg/kg/day has been recommended by some investigators. There are 15 additional antimicrobial agents approved by the Food and Drug Administration for the indication of AOM. All approved drugs are clinically effective but some have been suggested to have priority for patients who fail amoxicillin: amoxicillin-clavulanate; an oral cephalosporin such as cefuroxime axetil; and intramuscular ceftriaxone. Management of the child with severe and recurrent disease should include antibiotic prophylaxis but the increased incidence of resistance requires selective use. Prevention of infection may be achieved by innovative techniques for interference with attachment of bacteria to the nasal mucosa such as administration of oligosaccharides in a nasal spray. The currently available polysaccharide pneumococcal vaccines have limited immunogenicity in infants, but the vaccine is useful in children 2 years of age and older who still have recurrent AOM. Children with frequent AOM during the prior respiratory season are candidates also for influenza virus vaccine. If medical management fails to prevent new episodes of AOM in children with severe and recurrent disease, placement of tympanostomy tubes and possible adenoidectomy should be considered.

Klein J.O. *Management of acute otitis media in an era of increasing antibiotic resistance.* Int J Pediatr Otorhinolaryngol. 1999; 49 Suppl 1 : S15-7.p Abstract: Development of resistance to available antimicrobial agents has been identified in every decade since the introduction of

the sulfonamides in the 1930s. Current concerns for management of acute otitis media (AOM) are multi-drug resistant Streptococcus pneumoniae and beta-lactamase producing Haemophilus influenzae and Moraxella catarrhalis. In the USA, amoxicillin remains the drug for choice for AOM. Increasing the current dose to 80 mg/kg/day in two doses provides increased concentrations of drug in serum and middle ear fluid and captures additional resistant strains of S. pneumoniae. For children who fail initial therapy with amoxicillin an expert panel convened by the Centers for Disease Control and Prevention suggested amoxicillin-clavulanate, cefuroxime axetil or intramuscular ceftriaxone. To protect the therapeutic advantage of antimicrobial agents used for AOM, it is important to promote judicious use of antimicrobial agents and avoid uses if it is likely that viral infections are the likely cause of the disease, to implement programs for parent education and to increase the accuracy of diagnosis of AOM. Conjugate polysaccharide pneumococcal vaccines are currently in clinical trial; early results indicate protective levels of antibody can be achieved with a three dosage schedule beginning at 2 months of age. Finally, alternative medicine remedies may be of value for some infectious diseases including AOM; garlic extract is bactericidal for the major bacterial pathogens of AOM but is heat- and acid-labile and loose activity when cooked or taken by mouth.

Klein J.O. *Management of otitis media: 2000 and beyond*. Pediatr Infect Dis J. 2000; 19(4) : 383-7.p Abstract: BACKGROUND: In the next few years what will alter our modes of diagnosis, choice of therapies and strategies for prevention of acute otitis media (AOM)? These issues, as well as whether antibiotic resistance will continue to threaten the efficacy of currently available antimicrobial agents, whether industry and academia will be able to respond to bacterial resistance with effective new antimicrobial drugs and whether the pneumococcal conjugate vaccine will substantially reduce the incidence of AOM provide a basis for discussing the problems and possible solutions related to AOM. ANTIMICROBIAL DRUGS: Bacteria and viruses will continue to find ways to survive the activity of currently available antimicrobial drugs. Among the new antibacterial drugs under consideration are ketolides, oxazolodinones and quinolones. Guidelines stress limiting usage of antimicrobial agents to diseases that are likely caused by bacterial pathogens. Antiviral drugs are now available against influenza virus and respiratory syncytial virus infections. DIAGNOSIS: Tympanometry and/or acoustic reflectometry are adjunctive techniques for assisting in the diagnosis of middle ear effusion in children whose otoscopic examination is ambiguous. Laser myringotomy has been used in several hundred children; however, there are no published studies of randomized trials. NEW VACCINES: Investigators have evaluated the safety and efficacy of a heptavalent pneumococcal polysaccharide vaccine conjugated with CRM197 (a diphtheria toxin mutant). The results showed a reduction in the overall burden of severe and recurrent AOM. Respiratory syncytial virus is the viral pathogen most frequently associated with AOM. For this reason safe and effective viral vaccines are needed to complement the efficacy of bacterial vaccines for prevention of AOM. CONCLUSIONS: Parents influence decisions by pediatricians to use antimicrobial agents and should be informed about the appropriate usage of antibiotics. Educators and public health officials must find techniques to distinguish WebSites that provide information of value from those that are not credible. Of paramount importance is the development of techniques to increase the accuracy of clinical and microbiologic diagnosis. Finally there is a need for studies of appropriate scientific design that can assess the efficacy and safety of alternative therapies.

Klein N.C. et al. *Tetracyclines.* Med Clin North Am. 1995; 79(4) : 789-801.p Abstract: Tetracyclines are relatively safe drugs with a broad antimicrobial spectrum. Doxycycline remains the preferred tetracycline agent for most indications. Doxycycline has a long half-life, which makes convenient twice-a-day dosing possible. It is well absorbed orally even in the presence of food, has excellent tissue penetration, and does not require a dose adjustment in renal insufficiency. Doxycycline is a useful agent for the treatment of atypical pneumonias, sexually transmitted diseases, traveler's diarrhea, rickettsial infections, and Lyme disease. Minocycline is the preferred drug for MRSA colonization/infection.

Klekamp J. et al. *The use of vancomycin and tobramycin in acrylic bone cement: biomechanical effects and elution kinetics for use in joint arthroplasty.* J Arthroplasty. 1999; 14(3) : 339-46.p Abstract: We examined the effects of vancomycin on the compressive strength and fatigue life of bone cement and the pharmacokinetics and antimicrobial activity against methicillin-resistant Staphylococcus aureus of vancomycin eluted from bone cement, both alone and in combination with tobramycin. Two cements, Palacos and Simplex, were tested. Three antibiotic preparations were tested: lyophilized vancomycin (vancomycin-L), vancomycin powder (vancomycin-P), and tobramycin powder (Lilly, Indianapolis, IN). Although antibiotics did not significantly affect compressive strength, the fatigue life of bone cement was significantly decreased with vancomycin. Thus, fatigue testing revealed effects on cement strength not apparent by compression testing. Vancomycin-P had a substantially less detrimental effect on fatigue strength than vancomycin-L. Vancomycin-P elutes less efficiently than tobramycin. Although relatively little vancomycin-P eluted from bone cement, it retained biologic activity.

Klempp-Selb B. et al. *Karyotyping of Candida albicans and Candida glabrata from patients with Candida sepsis.* Mycoses. 2000; 43(5) : 159-63.p Abstract: The aim of this study was to determine the relatedness of Candida strains from patients suffering from Candida septicaemia by typing of Candida isolates from blood cultures and different body sites by pulsed field gel electrophoresis (PFGE using a contour-clamped homogenous electric field, CHEF). We studied 17 isolates of Candida albicans and 10 isolates of Candida glabrata from six patients. Four patients suffered from a C. albicans septicaemia, one patient from a C. glabrata septicaemia, and one patient had a mixed septicaemia with C. albicans and C. glabrata. Eight isolates from blood cultures were compared with 19 isolates of other sites (stool six, urine four, genital swab four, tip of central venous catheter three, tracheal secretion one, sputum one). PFGE typing resulted in 10 different patterns, four with C. albicans and six with C. glabrata. Five of the six patients had strains of identical PFGE patterns in the blood and at other sites. Seven isolates of a 58-year-old female with a C. glabrata septicaemia fell into five different PFGE patterns. However, they showed minor differences only, which may be due to chromosomal rearrangements within a single strain. Thus it appears, that the colonizing Candida strains were identical to the circulating strains in the bloodstream in at least five of six patients.

Klepser M.E. et al. *Comparison of the bactericidal activities of piperacillin-tazobactam, ticarcillin-clavulanate, and ampicillin-sulbactam against clinical isolates of Bacteroides fragilis, Enterococcus faecalis, Escherichia coli, and Pseudomonas aeruginosa*. Antimicrob Agents Chemother. 1997; 41(2) : 435-9.p Abstract: Owing to the broad spectrum of activity afforded by beta-lactam-beta-lactamase inhibitor preparations, these agents are frequently selected as empiric therapy for the treatment of mixed infections such as intra-abdominal and diabetic foot infections, either alone or in combination with an aminoglycoside. Twelve healthy volunteers were enrolled in a randomized, open-label, four-way crossover trial comparing the bactericidal activities of piperacillin-tazobactam, ticarcillin-clavulanate, and ampicillin-sulbactam against microorganisms commonly isolated from mixed infections. Subjects received the following regimes: (i) 3.375 g of piperacillin-tazobactam intravenously (i.v.) every 6 h (q6h) (ii) 4.5 g of piperacillin-tazobactam i.v. q8h, (iii) 3.1 g of ticarcillin-clavulanate i.v. q6h, and (iv) 3.0 g of ampicillin-sulbactam i.v. q6h. Serum bactericidal titers were determined and used to calculate the duration of measurable bactericidal activity over the dosing interval of each of the regimens against two clinical isolates of Bacillus fragilis, Escherichia coli, Enterococcus faecalis, and Pseudomonas aeruginosa. The percentage of the dosing interval over which drug concentrations in serum

remained above the MIC for each organism was determined and compared with the observed duration of bactericidal activity was noted ($r = 0.78$; $P < 0.001$). All of the regimens demonstrated good activity against B. fragilis and E. coli. Against E. faecalis and P. aeruginosa, however, all of the regimens provided bactericidal activity for less than 50% of the respective dosing intervals. These data suggest that use of shorter dosing intervals or continuous-infusion regimens should be considered in combination with an aminoglycoside to improve the bactericidal profiles of these agents for E. faecalis and P. aeruginosa.

Klugman K.P. *The clinical relevance of in-vitro resistance to penicillin, ampicillin, amoxycillin and alternative agents, for the treatment of community-acquired pneumonia caused by Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis.* J Antimicrob Chemother. 1996; 38 Suppl A : 133-40.p Abstract: The documentation of antimicrobial resistance in respiratory pathogens, contained within the Alexander Project, does not necessarily translate into clinical resistance in the treatment of primary community-acquired pneumonia. There is, in particular, little evidence that penicillin resistance in pneumococci is clinically relevant for the treatment of pneumonia, and there is further evidence that the production of beta-lactamase by Haemophilus influenzae may not always be clinically relevant within this setting. beta-Lactamase producing H. influenzae and Moraxella catarrhalis should probably be treated with alternative agents when they cause exacerbations of chronic bronchitis. More studies are required to define the clinical breakpoints of macrolide and co-trimoxazole resistance in the treatment of pneumonia.

Klugman K.P. et al. *Penicillin- and cephalosporin-resistant Streptococcus pneumoniae. Emerging treatment for an emerging problem.* Drugs. 1999; 58(1) : 1-4.p Abstract: The global emergence of pneumococci resistant to antimicrobial therapy has led to dilemmas in the management of pneumococcal infections. The principles of pharmacodynamics predict that penicillin and cephalosporin therapy of pneumonia will be successful against pneumococci with minimum inhibitory concentrations of penicillin up to 4 micrograms/ml. These predictions are supported by the observations of a number of recent clinical studies. Otitis media therapy is influenced by penicillin-resistance and current recommendations are that amoxicillin is the drug of choice for this infection, given at a double dose of 80 to 90 mg/kg/day. For the therapy of meningitis, cefotaxime or ceftriaxone in maximal doses is recommended and vancomycin may be added if cephalosporin-resistant strains are encountered with reasonable frequency in the population. The new fluoroquinolones with excellent antipneumococcal activity may be considered for use in the setting of pneumonia caused by highly resistant pneumococci and are under evaluation for the management of meningitis.

Klugman K.P. et al. *Emergence of drug resistance. Impact on bacterial meningitis.* Infect Dis Clin North Am. 1999; 13(3) : 637-46, vii.p Abstract: Antimicrobial resistance has emerged among the three major bacterial pathogens causing meningitis. Chloramphenicol resistance in the meningococcus recently has been described, and although intermediate penicillin resistance is common in some countries, the clinical importance of penicillin resistance in the meningococcus has yet to be established. Beta-lactamase-producing Haemophilus influenzae are relatively common, and chloramphenicol resistance is emerging. Third-generation cephalosporins are required to treat meningitis caused by these resistant strains. Pneumococcus resistance to penicillin and to chloramphenicol is widespread, and resistance to third-generation cephalosporins is found in many parts of the world. Correct management of these strains includes the addition of vancomycin or rifampin to therapy with third-generation cephalosporins.

Knapp J.S. et al. *Plasmid-mediated antimicrobial resistance in Neisseria gonorrhoeae in Kingston, Jamaica: 1990-1991.* Sex Transm Dis. 1995; 22(3) : 155-9.p Abstract: BACKGROUND AND OBJECTIVES: Gonococcal infections caused by antimicrobial-resistant strains of Neisseria gonorrhoeae have spread into many geographic areas and have increased in prevalence since the mid 1970s. Surveillance of antimicrobial-resistant gonococcal strains of Jamaica from 1981 to 1983 indicated that fewer than 3% of strains of produced beta-lactamase (penicillinase-producing Neisseria gonorrhoeae); approximately 4% of strains were resistant to penicillin, and 12% were resistant to tetracycline. GOAL OF THIS STUDY: To measure the frequency and nature of antimicrobial resistance in Neisseria gonorrhoeae isolates in Kingston, Jamaica, from 1990 to 1991 and to assess the effectiveness of prescribed treatment regimens. STUDY DESIGN: Urethral isolates of Neisseria gonorrhoeae from 116 heterosexual men with uncomplicated gonorrhea, representing 7.1% (116/1633) men attending the STD Comprehensive Health Centre from October 1990 through March 1991 who had positive Gram-stained smears, were characterized by auxotype, serovar, presence of the TetM determinant, and plasmid content. Antimicrobial susceptibilities to penicillin, cefoxitin, ceftriaxone, ciprofloxacin, tetracycline, and spectinomycin were determined by an agar dilution method. RESULTS: A total of 80.2% (93/116) of the isolates exhibited plasmid-mediated resistance to penicillin, tetracycline, or both: penicillinase-producing Neisseria gonorrhoeae (13/116; 11.2%), tetracycline-resistant Neisseria gonorrhoeae (25/116; 21.6%), and penicillinase-producing/tetracycline-resistant Neisseria gonorrhoeae, (55/116;47.4%). Isolates with chromosomally mediated resistance to penicillin, tetracycline, or both, accounted for 5.2% (6/116) of the isolates. Penicillinase-producing Neisseria gonorrhoeae, tetracycline-resistant Neisseria gonorrhoeae, and penicillinase-producing/tetracycline-resistant Neisseria gonorrhoeae belonging to multiple auxotype/serovar classes were isolated repeatedly through the study period. CONCLUSIONS: Infections caused by Neisseria gonorrhoeae exhibiting plasmid-mediated resistance to penicillin, tetracycline, or both, have become prevalent and endemic in Kingston, Jamaica. Therefore, all gonococcal infections should be treated with antimicrobial therapies known to be active against penicillin-resistant and tetracycline-resistant organisms to reduce gonorrhea transmission.

Knapp J.S. et al. *Fluoroquinolone resistance in Neisseria gonorrhoeae.* Emerg Infect Dis. 1997; 3(1) : 33-9.p Abstract: Fluoroquinolones and broad-spectrum cephalosporins are the most effective antimicrobial agents for the treatment of gonorrhea. However, clinically significant resistance to fluoroquinolones has emerged in Neisseria gonorrhoeae. Fluoroquinolone-resistant strains account for approximately 10% of all gonococcal strains in Hong Kong and the Republic of the Philippines. As many as 50% of strains from some Far Eastern countries exhibit decreased susceptibility (intermediate resistance) to fluoroquinolones. Strains with intermediate resistance and clinically significant resistance are being isolated sporadically in North America, where resistant strains have been associated with an outbreak and with failure of infections to respond to treatment with doses of ciprofloxacin and ofloxacin recommended by the Centers for Disease Control and Prevention; strains exhibiting decreased susceptibility to these agents are endemic in at least one metropolitan area. Monitoring for fluoroquinolone resistance is now critical for ensuring adequate treatment of infections with resistant strains and for maximizing the time during which fluoroquinolones may be used to treat gonorrhea.

Knapp J.S. et al. *Molecular epidemiology, in 1994, of Neisseria gonorrhoeae in Manila and Cebu City, Republic of the Philippines.* Sex Transm Dis. 1997; 24(1) : 2-7.p Abstract: BACKGROUND AND OBJECTIVES: Failure of gonococcal infections to respond to 500 mg of ciprofloxacin or 400 mg of ofloxacin has been reported from Australia, the United Kingdom, and the United States. Recently, high rates of decreased susceptibility to the fluoroquinolones have been detected in penicillinase-producing Neisseria gonorrhoeae in the Republic of the Philippines. GOALS: To assess the diversity of antimicrobial-resistant gonococcal strains isolated from female sex

workers in Manila and Cebu City in the Republic of the Philippines in 1994. STUDY DESIGN: Isolates of N. gonorrhoeae isolated from 92 female sex workers in Manila (n = 28) and Cebu City (n = 64), respectively, were characterized by plasmid profile, auxotype/serovar class, and antimicrobial susceptibility profile. RESULTS: Plasmid-mediated resistance to penicillin or tetracycline was identified in 79.3% (73/92) of the isolates: penicillinase-producing N. gonorrhoeae (65/92; 70.7%), tetracycline-resistant N. gonorrhoeae (6/92; 6.5%), and penicillinase-producing/tetracycline-resistant N. gonorrhoeae (1/92; 1.1%). A beta-lactamase plasmid of 3.9 megadaltons was discovered. Of 54.3% (50/92) of strains resistant to nalidixic acid, 84% (42/50) of strains had minimum inhibitory concentrations of > or = 0.125 microgram/ml ciprofloxacin; penicillinase-producing N. gonorrhoeae (possessing the 3.05-, 3.2-, 3.9-, and 4.4-megadalton beta-lactamase plasmids, respectively) accounted for 68% (34/50) of these strains. CONCLUSIONS: In the Republic of the Philippines, gonococcal isolates resistant to penicillin or tetracycline accounted for 85.9% (79/92) of the isolates examined and included strains exhibiting resistance to fluoroquinolones. All gonococcal infections should be treated with antimicrobial therapies known to be active against all gonococcal strains to reduce the spread of strains exhibiting decreased susceptibilities to fluoroquinolones.

Knapp K.M. et al. *The approach to treatment of invasive pneumococcal disease in the 1990s.* J Ark Med Soc. 1997; 94(6) : 263-6.p Abstract: Streptococcus pneumoniae is the most common cause of pediatric invasive infections and an important cause of morbidity and mortality. In the past, S. pneumoniae responded universally to penicillin until nonsusceptible isolates were first noted in the 1960s. Before 1990, penicillin-nonsusceptible isolates remained a minor component of all reported isolates. Since that time, 20-30% of isolates in many centers in the United States and up to 50% of isolates in some other countries are penicillin-nonsusceptible. Of greater concern has been the development of isolates which are nonsusceptible to more than one antimicrobial agent. This review presents data on pediatric invasive pneumococcal disease in Arkansas and outlines the new treatment recommendations which have been developed in response to these problems. Streptococcus pneumoniae is an important pathogen worldwide and is considered the most common etiology of bacterial sinusitis, otitis media, pneumonia, meningitis and bacteremia. Before 1990, 95-96% of pneumococcal isolates were susceptible to penicillin. The first report of penicillin-nonsusceptible S. pneumoniae was made by Hansman and Bullen in 1967, who identified the strain in the sputum of a patient with hypogammaglobulinemia. Soon thereafter, penicillin-nonsusceptible pneumococci were reported in New Guinea and Australia as well. Over the last several years, the incidence of penicillin-nonsusceptible isolates has greatly increased. Of particular concern is the concomitant increase in the number of organisms that are nonsusceptible to more than one antimicrobial agent. Due to the development of such isolates, clinicians are having to approach patients with invasive disease due to pneumococci more cautiously. In an attempt to clarify confusion with terminology, the Centers for Disease Control and Prevention (CDC) have recommended the same nomenclature be used to classify resistance for all organisms: nonsusceptible organisms are those with an MIC (minimal inhibitory concentration) greater than or equal to that defined for the intermediate category of resistance and the term resistant should be reserved for those organisms with an MIC greater than or equal to that defined for the resistant category. Therefore, resistant isolates are a subgroup of the nonsusceptible isolates.

Knowles S. et al. *An outbreak of multiply resistant Serratia marcescens: the importance of persistent carriage.* Bone Marrow Transplant. 2000; 25(8) : 873-7.p Abstract: An outbreak of multi-resistant Serratia marcescens involving 24 patients occurred in a bone marrow transplant and oncology unit, from September 1998 to June 1999, of whom 14 developed serious infection. This is the first such outbreak described in a BMT unit. All isolates demonstrated the same antimicrobial susceptibility pattern and were the same unusual serotype O21:K14. The antimicrobial susceptibility profile showed reduced susceptibility to ciprofloxacin, gentamicin and piperacillin-tazobactam. As the latter two antimicrobials are part of our empiric therapy for febrile neutropenia, they were substituted with meropenem and amikacin during the outbreak. Investigation revealed breaches in infection control practices. Subsequently, the outbreak was contained following implementation of strict infection control measures. A prominent feature of the outbreak was prolonged carriage in some patients. These patients may have acted as reservoirs for cross-infection. This report also indicates that patients who become colonised with Serratia marcescens may subsequently develop invasive infection during neutropenic periods.

Ko G. et al. *Influence of relative humidity on particle size and UV sensitivity of serratia marcescens and mycobacterium bovis BCG aerosols.* Tuber Lung Dis. 2000; 80(4-5) : 217-28.p Abstract: Setting: A study of Serratia marcescens and BCG aerosols. Objective: To evaluate the effect of relative humidity (RH) on (1) the particle size and (2) sensitivity of 254nm germicidal ultraviolet (UV) irradiation. Methods: We built a RH controlled experimental chamber into which bacteria were aerosolized, exposed to varying amounts of UV irradiance over measured time periods, and quantitatively evaluated for viability. Aerosolized Serratia marcescens and bacille Calmette-Guerin (BCG) were subject to UV doses ranging from 57-829 &mgr;W. sec/cm(2), and sampled with a six-stage Andersen culture plate impactor at RHs ranging from 25-95%. Results: Percent survival for both organisms was inversely related to UV dose. Serratia marcescens was more susceptible to UV than BCG under all conditions. More than 95% of the bacterial aerosol particles were 1.1-4.7 &mgr;m in aerodynamic diameter, and particles sizes increased from low (25-36%) to high (85-95%) RH. The count median diameter ranged from 1.9-2.6 &mgr;m for Serratia marcescens and from 2.2-2.7 &mgr;m for BCG as RH increased. For both Serratia marcescens and BCG, resistance to UV increased as RH increased. The UV resistance of both Serratia marcescens and BCG aerosols dramatically increased at RH higher than 85%. Conclusions: Our results indicate that differences in UV dose, kinds of microorganisms, airborne particle size and RH affect UV susceptibility. Copyright 2000 Harcourt Publishers Ltd.

Ko W.C. et al. *Inducible beta-lactam resistance in Aeromonas hydrophila: therapeutic challenge for antimicrobial therapy.* J Clin Microbiol. 1998; 36(11) : 3188-92.p Abstract: Despite the abundant amount of knowledge about inducible chromosomally mediated beta-lactamases among Aeromonas species, extended-spectrum beta-lactam-resistant A. hydrophila strains selected in clinical practice were rarely reported. In the present study, two strains of A. hydrophila, A136 and A139, with markedly different susceptibilities to extended-spectrum cephalosporins were isolated from blood and the tip segment of an arterial catheter of a burn patient. Another strain (A136m) was selected in vitro by culturing A136 in a subinhibitory concentration of cefotaxime, the beta-lactam agent administered for the treatment of Aeromonas bacteremia in this patient. Typing studies by arbitrarily primed PCR and pulsed-field gel electrophoresis indicated a clonal relationship among strains A136, A136m, and A139. These strains were identified to be of DNA hybridization group 1. Wild-type strain A136 was resistant only to ampicillin and cephamycins, but A136m and A139 were highly resistant to the expanded- and broad-spectrum cephalosporins. The presence of increased beta-lactamase activity in A139 suggests that A139 is a derepressed mutant which overexpresses beta-lactamases. These results call attention to the use of beta-lactam agents for the treatment of invasive Aeromonas infections.

Kobashi Y. et al. *[Clinical analysis of the prognosis of severe pneumonia requiring mechanical ventilation].* Kansenshogaku Zasshi. 1999; 73(6) : 570-7.p Abstract: To determine which factors are important in pre-

dicting the outcome of patients with severe pneumonia requiring mechanical ventilation, we compared 43 surviving pneumonic patients with 37 non-surviving pneumonic patients. The following results were obtained. The following characteristics were noted in the non-surviving patients as compared with surviving patients; 1. a worsening of performance status in the background, 2. presence of physical signs such as hypotension and trachycardia, 3. abnormal laboratory data such as leukocytosis, lymphocytopenia, hypoalbuminemia, hepatorenal dysfunction and metabolic acidosis, 4. presence of massive pulmonary infiltrations on chest roentgenograms, 5. a prevalence of resistant microorganisms for many antibiotics such as MRSA (Methicillin resistant Staphylococcus aureus). These results suggest that the most important factor affecting the prognosis of patients with severe pneumonia requiring mechanical ventilation may by the condition of the host and of the microorganisms rather than antibiotic treatment.

Kobashi Y. et al. *[Clinical analysis of nursing home-acquired pneumonia in a community hospital].* Kansenshogaku Zasshi. 2000; 74(4) : 331-8.p Abstract: To clarify the characteristic features of nursing home-acquired pneumonia in our community hospital, we performed a clinical analysis of 86 patients with nursing home-acquired pneumonia. The patients were divided into young and elderly groups. In the young group cerebral palsy was the underlying disease. In the elderly group, it was cerebrovascular attack. Although there were no differences in ADL, the nutritional condition of the young group was comparatively good, the isolated microorganism consisted of mostly Mycoplasma pneumoniae and the prognosis was good. The elderly group where the nutritional condition was poor, the patients were detected by non-respiratory symptoms and risk factors such as obvious episodes of aspiration led us to be concerned about the risk factors for nursing home-acquired pneumonia. The microorganism isolated from the sputum of the elderly group was frequently a multidrug resistant microorganism such as Methicillin-resistant Staphylococcus aureus (MRSA) and polymicrobial infection. Their prognosis was poor despite treatment with multiple antibiotics. In the comparative study between survivors and non-survivors in the elderly group, risk factors such as hypotension, consciousness disturbance, the extension of infiltration shadows, respiratory failure, multiple organ failure and metabolic acidosis were influenced for the prognosis, but the isolated microorganisms and the antimicrobial agents were not concerned.

Kobashi Y. et al. *[Nosocomial pneumonia experienced in a community hospital].* Kansenshogaku Zasshi. 1998; 72(12) : 1253-60.p Abstract: To clarify the characteristic features of nosocomial pneumonia in a community hospital, we performed a clinical analysis of 147 patients (155 episodes) with nosocomial pneumonia. The following results were obtained. 1, Regarding the risk factors for nosocomial pneumonia, factors such as the patient whose age was over 65 years, a duration of admission of over one month, performance status 4 and underlying respiratory diseases associated with the appearance of nosocomial pneumonia. 2, The causative microorganism isolated from the sputum of the patient with nosocomial pneumonia was frequently a multi-drug resistant microorganism such as Methicillin-resistant Staphylococcus aureus (MRSA). 3, regarding treatment, although several antibiotics were administered for a long time, mechanical ventilation was used on 31% of the patients, and steroid pulse therapy was carried out on 24%. The clinical efficacy was poor with a 50% mortality rate. The reason why treatment of nosocomial pneumonia was difficult is thought to be been related to the general condition of these inpatients and to the appearance of a multidrug resistant, polymicrobial microorganisms.

Kobayashi K. *[Towards new strategies to combat mycobacterial diseases].* Nihon Hansenbyo Gakkai Zasshi. 1997; 66(3) : 191-8.p Abstract: Infectious diseases account for more than 30% of deaths throughout the world, and we are increasingly faced with new and reemerging disease challenges. Infections caused by mycobacteria are the leading cause of death from infectious diseases around the world. Leprosy/Hansen's disease, caused by Mycobacterium leprae, primarily involves the peripheral nervous system and skin. Tuberculosis remains an important global health problem with approximately 1.9 billion people presently infected with M. tuberculosis. Infections with nontuberculous mycobacteria such as M. avium complex (MAC) constitute an important health problem, because most strains of MAC are resistant to antituberculous drugs. Mycobacteria are intracellular microbial pathogens. The infect macrophages cause chronic inflammation, such as granulomatous inflammation, and progressive scarring. Host defense against mycobacterial infection is controlled predominantly by the macrophage-cytokine-type 1 helper T (Th1) cell axis resulting in the expression of cell-mediated immunity. Development of cell-mediated, Th1(1) protective immunity to mycobacteria is considered a two-edged response, contributing to both clearance of infecting agents and tissue damage. In the second half of the 20th century, the conceptual approach to the management of established infectious diseases is antimicrobial chemotherapy. However, the successful implementation of antimicrobial chemotherapy is becoming increasingly difficult because of (1) an epidemic of immunocompromised patients, for whom antimicrobial therapy is less effective; (2) the emergence of new pathogens and the reemergence of old pathogens; and (3) widespread drug resistance. Antiinfective immunotherapy will be a new control strategy for mycobacterial diseases. It is also conceivable that therapeutic interventions to enhance the host immunity will be as effective as and possibly synergistic with antimicrobial drugs. We believe that the immune-based strategies will contribute to elimination of mycobacterial diseases.

Koc E. et al. *Imipenem for treatment of relapsing Salmonella meningitis in a newborn infant.* Acta Paediatr Jpn. 1997; 39(5) : 624-5.p Abstract: Salmonella meningitis is a rare clinical entity that occurs mainly during early infancy. Treatment of Salmonella infections may be complicated by the bacteria's growing resistance to clinically important antimicrobial agents, especially third-generation cephalosporins. A report is presented of a newborn infant with Salmonella meningitis who relapsed after 4 weeks of cefotaxime treatment and was cured completely with imipenem cilastatin therapy.

Koc Y. et al. *Vancomycin-resistant enterococcal infections in bone marrow transplant recipients.* Bone Marrow Transplant. 1998; 22(2) : 207-9.p Abstract: Vancomycin-resistant enterococci (VRE) infections have been increasingly reported in immunosuppressed individuals over the past decade. Emergence of this pathogen in the bone marrow transplantation (BMT) setting, in the form of bacteremia or positive stool cultures, is of concern because of lack of effective antimicrobial therapy. We report episodes of vancomycin-resistant E. faecium bacteremia in two patients undergoing BMT including the first case of VRE meningitis observed in this setting. Since the outcome in these patients undergoing matched unrelated donor BMT was fatal, we believe that routine screening for VRE in high risk patients should be considered. Management of VRE carrier state in BMT candidates is unclear at present.

Koch A. et al. *Mycoplasma hominis and Ureaplasma urealyticum in patients with sexually transmitted diseases.* Wien Klin Wochenschr. 1997; 109(14-15) : 584-9.p Abstract : Mycoplasma hominis and Ureaplasma urealyticum can be isolated with considerable frequency from the human urogenital tract and are thought to cause various syndromes such as nongonococcal urethritis, pelvic inflammatory disease, pyelonephritis or infertility. The aim of this study was the evaluation of the presence of different genital pathogens in patients with sexually transmitted diseases (STD) and, in particular, the detection of mycoplasmas in individuals infected with genital microbes and an assessment of the presence of genital microorganisms in patients harbouring Mycoplasma hominis or Ureaplasma urealyticum. Furthermore, the occurrence of mycoplasmas in women with bacterial vaginosis was established. Specimens were

collected from a total of 41,980 persons attending the Outpatients' Centre for Infectious Venero-Dermatological Diseases in Vienna from 1994 to 1996. Of all genital pathogens, Ureaplasma urealyticum was cultured most frequently in men and women. Mycoplasma hominis and Ureaplasma urealyticum were detected more often in the vaginal fluid than in the male urethra. By contrast, infection rates with Neisseria gonorrhoeae and Chlamydia trachomatis were higher in men than in women. In both men and women, trichomoniasis increased colonisation with Mycoplasma hominis, while mycoplasmas occurred less frequently together with genital candidiasis. Mycoplasma hominis was cultivated significantly more often in women with bacterial vaginosis than in those without. In contrast to urethral infections in men, cervical infections with Neisseria gonorrhoeae or Chlamydia trachomatis raised the incidence of Mycoplasma hominis in the vaginal fluid.

Koeuth T. et al. *Differential subsequence conservation of interspersed repetitive Streptococcus pneumoniae BOX elements in diverse bacteria*. Genome Res. 1995; 5(4) : 408-18.p Abstract: Evolutionary conservation of an interspersed repetitive DNA sequence, BOX, from Streptococcus pneumoniae was investigated to explore the mosaic nature of these elements. BOX elements consist of various combinations of three subunits, boxA, boxB, and boxC. Eight oligonucleotide probes were designed based on consensus DNA sequences of boxA, boxB, and boxC subunits. DNA hybridization studies and PCR using these probes/primers demonstrate that oligonucleotide sequences within the boxA subunit appear to be conserved among diverse bacterial species. The boxB and boxC subunits show only limited, if any, sequence conservation in bacteria other than S. pneumoniae. Intact BOX elements with boxA, boxB, and boxC subunits were only present in high copy number in pneumococcal strains. This pattern of differential conservation lends support to the modular nature of BOX repetitive elements in that boxA-like subsequences are effectively independent of boxB-like or boxC-like subunits in bacteria other than S. pneumoniae. Furthermore, dendrograms derived from repetitive sequence-based PCR (rep-PCR) fingerprints of S. pneumoniae isolates using the BOXA1R primer yielded clustering patterns that were similar to those obtained previously by other methods, suggesting that these repetitive sequence-based DNA fingerprints represent intrinsic properties of an S. pneumoniae strain's genome. Our results indicate widespread conservation of boxA-like subsequences in the bacterial kingdom, lend support to the mosaic nature of BOX in S. pneumoniae, and demonstrate the utility of boxA-based primers for rep-PCR fingerprinting of many microorganisms.

Koga H. et al. *A rapid drug susceptibility test for Mycobacterium tuberculosis using the hybridization protection assay.* J Antimicrob Chemother. 1997; 40(2) : 189-94.p Abstract: The conventional drug susceptibility tests for Mycobacterium tuberculosis are time-consuming and the results are available only after 2-4 weeks. We have recently reported a new, simple and fast M. tuberculosis drug susceptibility test, using the hybridization protection assay (HPA), that allows the detection of isoniazid- or rifampicin-resistant strains of M. tuberculosis within 24 h of incubation. In the present study, the scope of application of our new test was extended to another two first-line antimycobacterial agents, namely ethambutol and streptomycin, and a quinolone antimicrobial agent, ciprofloxacin. The ethambutol-, streptomycin- and ciprofloxacin-resistance characteristics of M. tuberculosis were also delineated within 72 h of incubation with or without the drug. The results of our novel and rapid drug susceptibility test for M. tuberculosis were not only comparable to those determined by the conventional method, but became available within a few days of incubation. Our results also suggest that the drug susceptibility test using HPA might also be useful for detecting organisms resistant to antimicrobial agents other than antimycobacterials.

Koguchi M. et al. *[Antimicrobial activities of clarithromycin against clinical isolates]*. Jpn J Antibiot. 1996; 49(3) : 289-300.p Abstract: To examine the antimicrobial activity of clarithromycin (CAM) against strains clinically isolated from outpatients in 1994, minimum inhibitory concentrations (MICs) were determined for CAM and the control drugs. The results were as follows; 1. MIC50 and MIC90 of CAM were similar to those investigated in 1980's against many bacterial species. 2. CAM showed strong antimicrobial activities against beta-lactamase producing Moraxella subgenus Branhamella catarrhalis, Bordetella pertussis, Campylobacter jejuni subsp. jejuni and Peptostreptococcus spp. 3. It appears that resistance to MLs including CAM is increasing among Streptococcus pneumoniae.

Koguchi M. et al. *[Antimicrobial activities of clavulanic acid/amoxicillin against freshly isolated clinical strains from outpatients]*. Jpn J Antibiot. 1995; 48(12) : 1920-34.p Abstract: In order to investigate antimicrobial activities of clavulanic acid/amoxicillin (CVA/AMPC) against freshly isolated clinical strains obtained in 1995, beta-lactamase activities and minimum inhibitory concentration (MICs) were determined including those of the control drugs. The results are summarized as follows; 1. Detection frequencies of beta-lactamase producing strains were as follows: methicillin-susceptible Staphylococcus aureus subsp. aureus (MSSA, 90.0%), Haemophilus influenzae (22.0%), Moraxella subgenus Branhamella catarrhalis (100.0%), Escherichia coli (100.0%), Klebsiella pneumoniae subsp. pneumoniae (100.0%) and Neisseria gonorrhoeae (14.0%). It appeared that beta-lactamases produced by these strains were mostly penicillinase or enzyme of similar that. 2. Antimicrobial activities of CVA/AMPC against beta-lactamase producing strains were stronger than those of AMPC, and MIC90 of CVA/AMPC against benzylpenicillin (PCG)-insensitive or resistant Streptococcus pneumoniae was lower than those of sultamicillin, cefaclor and cefpodoxime. 3. CVA showed strong beta-lactamase inhibitory effect against M.(B.) catarrhalis of direct and indirect pathogenicity. We can expect CVA/AMPC to negate or decrease the influence of indirect pathogenicity.

Koguchi M. et al. *[Antimicrobial activities of norfloxacin against clinical isolates from ocular infections]*. Jpn J Antibiot. 1995; 48(8) : 1009-25.p Abstract: In order to evaluate antimicrobial activity of norfloxacin (NFLX), minimum inhibitory concentration (MICs) of NFLX and control drugs were determined against clinical isolates from ocular infections that were obtained in our laboratory from July, 1993 to December, 1994. The results are summarized as follows; 1. Compared to MIC distributions of NFLX against clinical isolates from ocular infections studied in 1986 and 1987, the MIC80 of NFLX against Corynebacterium spp., Enterobacter spp., Serratia spp., Burkholderia cepacia, Flavobacterium spp., Alcaligenes spp. increased 8 times. Almost all of NFLX-resistant strains among them were ofloxacin (OFLX)-resistant, new quinolones resistant strains, and a part of them were aminoglycosides, beta-lactams-resistant as well, thus all of these strains were multiple drug resistant. 2. MIC of NFLX against Pseudomonas aeruginosa were lower than that of OFLX. 3. NFLX showed strong antimicrobial activities against so-called "particular bacteria" including Staphylococcus aureus subsp. aureus, Moraxella spp., Haemophilus spp., and P. aeruginosa from ocular infections. And MIC80 of NFLX against these bacteria was 0.05-1.56 microgram/ml. We observed that NFLX eye drops was administered so that concentrations above the MIC against these clinical isolates were maintained.

Koh T.H. et al. *Increasing antimicrobial resistance in clinical isolates of Streptococcus pneumoniae.* Ann Acad Med Singapore. 1997; 26(5) : 604-8.p Abstract: The presence of antibiotic-resistant Streptococcus pneumoniae has become a major clinical problem in several parts of the world. However, there is a lack of data from Southeast Asia. We therefore initiated a study to determine the serogroups/serotypes and antimicrobial susceptibilities of clinical strains of S. pneumoniae isolated in our laboratory. In 1995, we isolated 144 strains of S. pneumoniae. Thirty-six (25.0%) strains were resistant to penicillin of which 19 (13.2%) were highly resistant

(minimal inhibitory concentration > 1.0 microgram/ml). Thirty-eight (26.4%) strains were resistant to erythromycin, 75 (52.1%) were resistant to tetracycline, 48 (33.3%) were resistant to sulfamethoxazole-trimethoprim and 29 (20.1%) were resistant to chloramphenicol. Twenty of the penicillin-resistant strains also had diminished susceptibility to ceftriaxone. Strains resistant to penicillin belonged to serogroups/serotypes 6 (n = 1), 9 (n = 1), 23 (n = 4), 14 (n = 6) and 19 (n = 20). Children under 5 years of age were more likely than older children and adults to have isolates resistant to penicillin (52.9% versus 16.2%, P = 0.00002). Penicillin-resistant strains were more likely than penicillin-susceptible strains to be multidrug-resistant (86.1% versus 7.4%, P < 0.000005). We concluded that there is a high prevalence of penicillin-resistant pneumococci in our isolates especially among very young children. Most penicillin-resistant strains belong to serogroup 19 and are also resistant to multiple drugs.

Kohler B. et al. *Mutans streptococci and dental caries prevalence in a group of Latvian preschool children.* Eur J Oral Sci. 1995; 103(4) : 264-6.p Abstract: Paraffin-stimulated saliva samples were collected from 140 children 3- and 4-yr old attending nine nursery schools in Latvia. The salivary levels of mutans streptococci were rated from zero to 3 after being cultured on a commercially available strip selective for these microorganisms. Of the children, 29.3% were rated at zero (approximately < 10(4) cfu per ml saliva). This group of children demonstrated the lowest mean caries prevalence dmfstot = 1.5 (SD 1.9). The highest dmfstot was found among children in class 2 (38.6%; approximately > 10(5)-10(6) cfu/ml) and class 3 (12.1%; approximately > 10(6) cfu/ml) with a mean caries prevalence of 6.5 (SD 5.8) and 6.4 (SD 6.0), respectively. The study demonstrates the association between high caries prevalence and high salivary levels of mutans streptococci in the young child. It is suggested that early identi-fication of mutans streptococci-colonized children might be of value in selecting at caries risk children for preventive measures.

Kohler J.R. et al. *Detecting legionellosis by unselected culture of respiratory tract secretions and developing links to hospital water strains.* J Hosp Infect. 1999; 41(4) : 301-11.p Abstract: For a 13-month period, all respiratory tract secretions submitted for routine bacteriology from a large hospital complex were cultured for legionella, irrespective of clinical diagnosis and laboratory requests. Ten cases of legionellosis were detected in this manner, three of which met a strict epidemiological definition of hospital-acquired. Therefore, the 16 warm-water systems of the hospitals, spread out over two locations, were examined for the presence of legionella. Legionella pneumophila was found in 15 warm water systems, with a distinct pattern of serogroups between the two locations. Legionella of the same serogroups as those isolated from patients were present in each hospital water supply. The isolates were further typed by monoclonal antibodies and by genomic macrorestriction analysis. Similarity between clinical and environmental isolates was found in seven cases. In these cases, acquisition from the hospital water supply appears very likely. The strains of the remaining three patients did not match those in hospital water, suggesting that community-acquired legionellosis was occurring as well. This study suggests that routinely culturing respiratory tract secretions of pneumonia patients for legionella can help diagnose unsuspected cases of legionellosis. Typing legionella strains beyond the serogroup level with tools such as macrorestriction analysis is useful to define sources of infection, which can then be targeted for control measures.

Kollef M.H. et al. *Predictive value of a rapid semiquantitative D-dimer assay in critically ill patients with suspected venous thromboembolic disease.* Crit Care Med. 2000; 28(2) : 414-20.p Abstract: OBJECTIVE: To evaluate the performance of a new, rapid semi-quantitative assay for the detection of circulating D-dimer in whole blood from critically ill patients with suspected venous thromboembolic disease. DESIGN: Prospective, blinded, single-center study. SETTING: Medical intensive care unit (ICU) of Barnes-Jewish Hospital, St. Louis, MO, a university-affiliated urban teaching hospital. PATIENTS: Two hundred thirty-nine adult patients with clinical suspicion of venous thromboembolic disease admitted to a medical ICU. INTERVENTIONS: Collection of blood samples within 24 hrs of clinical suspicion of venous thromboembolic disease. MEASUREMENTS AND MAIN RESULTS: The main outcome measures evaluated included the occurrence of venous thromboembolic disease (i.e., lower extremity venous thrombosis, pulmonary embolism, catheter-associated venous thrombosis) and hospital mortality. Fifty-seven patients (23.8%) were classified as having venous thromboembolic disease during their ICU stays (pulmonary embolism, 21 patients; lower extremity thrombosis, 44 patients; line-associated venous thrombosis, 3 patients). The semiquantitative whole-blood assay for circulating D-dimer had a 96.4% sensitivity and a negative predictive value of 92.1% for identifying patients with venous thromboembolic disease. The specificity of this assay was 19.7%, and its positive predictive value was 26.9%. There was a strong correlation between the semiquantitative assay for circulating D-dimer and the quantitative measurement of circulating D-dimer using an enzyme immunoassay (Spearman's correlation coefficient, 0.8643; p<.001). We also identified a strong correlation between both the quantitative and semiquantitative measurements of circulating D-dimer with the sepsis classification proposed by the American College of Chest Physicians/Society of Critical Care Medicine (i.e., systemic inflammatory response syndrome, sepsis, severe sepsis, septic shock) for patients without venous thromboembolic disease (n = 182; quantitative measure: Spearman's correlation coefficient, 0.207; p =.002; semiquantitative measure: Spearman's correlation coefficient, 0.3519; p<.001). CONCLUSIONS: These preliminary findings suggest that a rapid whole-blood assay for the semiquantitative detection of circulating D-dimer may be a useful diagnostic tool for the exclusion of venous thromboembolic disease among critically ill patients.

Kolodzeij H. et al. *Evaluation of the antimicrobial potency of tannins and related compounds using the microdilution broth method.* Planta Med. 1999; 65(5) : 444-6.p Abstract: The antimicrobial activity of a total of 27 tannins and related compounds was evaluated against 8 microorganisms, including 2 Gram-positive (Bacillus subtilis, Staphylococcus aureus), 4 Gram-negative bacteria (Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis), and 2 yeasts (Candida albicans, Cryptococcus neoformans). The compounds tested were generally found to possess only weak to moderate antibacterial, but fairly high anticryptococcal activities. Attention is given to structure-activity relationships with emphasis on simple galloyl esters, hydrolyzable tannins and proanthcyanidins among this class of secondary products.

Kondejewski L.H. et al. *Modulation of structure and antibacterial and hemolytic activity by ring size in cyclic gramicidin S analogs.* J Biol Chem. 1996; 271(41) : 25261-8.p Abstract: We have evaluated the effect of ring size of gramicidin S analogs on secondary structure, lipid binding, lipid disruption, antibacterial and hemolytic activity. Cyclic analogs with ring sizes ranging from 4 to 14 residues were designed to maintain the amphipathic character as found in gramicidin S and synthesized by solid phase peptide synthesis. The secondary structure of these peptides showed a definite periodicity in beta-sheet content, with rings containing 6, 10, and 14 residues exhibiting beta-sheet structure, and rings containing 8 or 12 residues being largely disordered. Peptides containing 4 or 6 residues did not bind lipopolysaccharide, whereas longer peptides showed a trend of increasing binding affinity for lipopolysaccharide with increasing length. Destabilization of Escherichia coli outer membranes was only observed in peptides containing 10 or more residues. Peptides containing fewer than 10 residues were completely inactive and exhibited no hemolytic activity. The 10-residue peptide showed an activity profile similar to that of gramicidin S itself, with activity against Gram-positive and Gram-negative microorganisms as well as yeast, but also showed high hemolytic activity. Differential activities were obtained by increasing the size of the ring to either 12 or 14

residues. The 14-residue peptide showed no antibiotic activity but exhibited increased hemolytic activity. The 12-residue peptide lost activity against Gram-positive bacteria, retained activity against Gram-negative microorganisms and yeast, but displayed decreased hemolytic activity. Biological activities in the 12-residue peptide were optimized by a series of substitutions in residues comprising both hydrophobic and basic sites resulting in a peptide that exhibited activities comparable with gramicidin S against Gram-negative microorganisms and yeast but with substantially lower hemolytic activity. Compared with gramicidin S, the best analog showed a 10-fold improvement in antibiotic specificity for Gram-negative microorganisms and a 7-fold improvement in specificity for yeast over human erythrocytes as determined by a therapeutic index. These results indicate that it is possible to modulate structure and activities of cyclic gramicidin S analogs by varying ring sizes and further show the potential for developing clinically useful antibiotics based on gramicidin S.

Konety B.R. et al. *Clinical usefulness of the novel marker BLCA-4 for the detection of bladder cancer.* J Urol. 2000; 164(3 Pt 1) : 634-9.p Abstract: PURPOSE: Previous studies at our laboratory identified 6 bladder cancer specific nuclear matrix proteins termed BLCA-1 to 6. We recently developed an immunoassay that detects the bladder cancer specific nuclear matrix protein BLCA-4. We analyzed urine samples from patients with bladder cancer, those with spinal cord injury and normal volunteers to determine the BLCA-4 level in these 3 groups. MATERIALS AND METHODS: Urine samples obtained from 51 normal controls, and 54 patients with bladder cancer and 202 with spinal cord injury were tested for BLCA-4. We evaluated the association of BLCA-4 level with tumor grade and stage, urine cytology and bladder cancer history in the nonspinal cord injured population. Similarly we compared parameters associated with BLCA-4, such as spinal cord injury duration, catheterization, history of urinary tract infection, smoking and urine culture, in spinal cord injured patients. RESULTS: We established a normal cutoff point of 13 optical density units per microg. protein for the BLCA-4 assay. The BLCA-4 level was less than the cutoff in all 51 normal controls, while in 53 of the 55 urine samples (96.4%) of patients with bladder cancer and 38 of the 202 (19%) of spinal cord injured patients urinary BLCA-4 was greater than the cutoff. There was no correlation of any individual factors studied in these cases, including urinary tract infection and urinary BLCA-4. CONCLUSIONS: Elevated urinary BLCA-4 levels may accurately identify bladder cancer and distinguish these patients from normal individuals. There is no correlation of urinary BLCA-4 with a history of urinary tract infection, smoking, catheterization or cystitis considered independently. Urinary BLCA-4 determination appears to have high potential as a test for screening and monitoring bladder cancer in the general population and in groups at high risk for the disease, such as those with spinal cord injury.

Konig B. et al. *Effects of Betaisodona on parameters of host defense.* Dermatology. 1997; 195 Suppl 2 : 42-8.p Abstract: The numbers of patients in intensive care units, with immunosuppression, and of elderly people increase in parallel with antibiotic-resistant microorganisms. Therefore the demand for an effective antisepsis increases. Moreover, it became evident that the pathophysiology and the outcome of infection are dependent on the properties of the microorganisms, e.g. synthesis of endo- and exotoxins, and on the host defense, the immune system. In addition to the microbicidal action, we studied the effects of povidone-iodine (PVP-I, Betaisodona) on the generation, release and activity of exotoxins (alpha-hemolysin, phospholipase C, lipase), as well as on granulocyte-derived tissue-destructive enzymes (elastase, beta-glucuronidase) and microbial-induced cytokine generation from human neutrophils. Our results clearly show that PVP-I does not only kill a wide range of bacteria but also inhibits the generation and release of bacterial exotoxins; furthermore, it also inactivates bacterial exotoxins as well as granulocyte-derived tissue-destructive enzymes and cytokines. These data support the usefulness and efficacy of PVP-I as an effective therapeutic agent to combat infection.

Konig F.A. et al. *[Pericardial tamponade during installation of a central venous catheter].* Chirurg. 2000; 71(1) : 98-100.p Abstract: A case report demonstrates the complication of pericardial tamponade during the installation of a central venous catheter via the subclavian vein. To reduce the high mortality of this rare complication, quickly applicable diagnostic measures and adequate therapy of pericardiocentesis are indicated. Prompt recognition and treatment of pericardial tamponade are imperative if a disastrous outcome is to be prevented.

Konishi M. et al. *[Clinical evaluation of lung abscess diagnosed by transtracheal aspiration].* Kansenshogaku Zasshi. 1998; 72(11) : 1193-6.p Abstract: We have diagnosed lung abscess according to findings of infiltration with cavity formation on chest X-ray and/or CT-scan and pathogens isolated from transtracheal aspirates. We evaluated the clinical features of 20 patients with lung abscess (18 males and 2 females, mean age; 54.3 years). Diabetus mellitus and periodontal diseases were prominent underlying diseases in patients with lung abscess. Cough was complained in 13 patients, chest or back pain in 9, purulent sputum in 8 and hemosputum in 5 when the patients admitted to our hospital. A temperature higher than 38 degrees C was present in 12 patients but temperature les than 37 degrees C in 2. Multiple microorganisms were cultured from TTA in 15 patients. A mean of 2.7 bacterial species per patient was isolated, aerobes alone being isolated in 2 patients, anaerobes alone in 3, and mixed aerobic and anaerobic isolates in 10. Seventeen strains of aerobes and 35 of anaerobes were isolated. Major pathogens were Streptococcus pneumoniae, Streptococcus intermedius and other in aerobes, and Peptostreptococcus micros, Fusobacterium necrophorum, Prevotella melaninogenica and others in anaerobes. Abnormality of chest X-ray was located on the right upper lobe in 6 patients, the right lower lobe in 6, the left upper lobe in 6, the left lower lobe in 4 and the right middle lobe in 1. All patients were cured only by treatment of antimicrobial agents, but cavity formation on chest X-ray remained in 4 patients after the treatment.

Koo H. et al. *In vitro antimicrobial activity of propolis and Arnica montana against oral pathogens.* Arch Oral Biol. 2000; 45(2) : 141-8.p Abstract: Arnica and propolis have been used for thousands of years in folk medicine for several purposes. They possess several biological activities such as anti-inflammatory, antifungal, antiviral and tissue regenerative, among others. Although the antibacterial activity of propolis has already been demonstrated, very few studies have been done on bacteria of clinical relevance in dentistry. Also, the antimicrobial activity of Arnica has not been extensively investigated. Therefore the aim here was to evaluate in vitro the antimicrobial activity, inhibition of adherence of mutans streptococci and inhibition of formation of water-insoluble glucan by Arnica and propolis extracts. Arnica montana (10%, w/v) and propolis (10%, w/v) extracts from Minas Gerais State were compared with controls. Fifteen microorganisms were used as follows: Candida albicans—NTCC 3736, F72; Staphylococcus aureus—ATCC 25923; Enterococcus faecalis—ATCC 29212; Streptococcus sobrinus 6715; Strep. sanguis—ATCC 10556; Strep. cricetus—HS-6; Strep. mutans—Ingbritt 1600; Strep. mutans—OMZ 175; Actinomyces naeslundii—ATCC 12104, W 1053; Act. viscosus OMZ 105; Porphyromonas gingivalis; Porph. endodontalis and Prevotella denticola (the last three were clinical isolates). Antimicrobial activity was determined by the agar diffusion method and the zones of growth inhibition were measured. To assess cell adherence to a glass surface, the organisms were grown for 18 h at 37 degrees C in test-tubes at a 30 degree angle. To assay water-insoluble glucan formation, a mixture of crude glucosyltransferase and 0.125 M sucrose was incubated for 18 h at 37 degrees C in test-tubes at a 30 degree angle. Arnica and propolis extracts (20 microl) were added to these tubes to evaluate the % of inhibition of cell adherence and water-insoluble glucan formation. The propolis extract significantly inhibited all the

microorganisms tested ($p < 0.05$), showing the largest inhibitory zone for Actinomyces spp. The Arnica extract did not demonstrate significant antimicrobial activity. Cell adherence and water-insoluble glucan formation were almost completely inhibited by the propolis extract at a final concentration of 400 microg/ml and 500 microg/ml, respectively. The Arnica extract showed slight inhibition of the adherence of the growing cells (19% for Strep. mutans and 15% for Strep. sobrinus) and of water-insoluble glucan formation (29%) at these same concentrations. Thus, the propolis extract showed in vitro antibacterial activity, inhibition of cell adherence and inhibition of water-insoluble glucan formation, while the Arnica extract was only slightly active in those three conditions.

Kornberg A. et al. *Inorganic polyphosphate: a molecule of many functions.* Annu Rev Biochem. 1999; 68 : 89-125.p Abstract: Inorganic polyphosphate (poly P) is a chain of tens or many hundreds of phosphate (Pi) residues linked by high-energy phosphoanhydride bonds. Despite inorganic polyphosphate's ubiquity—found in every cell in nature and likely conserved from prebiotic times—this polymer has been given scant attention. Among the reasons for this neglect of poly P have been the lack of sensitive, definitive, and facile analytical methods to assess its concentration in biological sources and the consequent lack of demonstrably important physiological functions. This review focuses on recent advances made possible by the introduction of novel, enzymatically based assays. The isolation and ready availability of Escherichia coli polyphosphate kinase (PPK) that can convert poly P and ADP to ATP and of a yeast exopolyphosphatase that can hydrolyze poly P to Pi, provide highly specific, sensitive, and facile assays adaptable to a high-throughput format. Beyond the reagents afforded by the use of these enzymes, their genes, when identified, mutated, and overexpressed, have offered insights into the physiological functions of poly P. Most notably, studies in E. coli reveal large accumulations of poly P in cellular responses to deficiencies in an amino acid, Pi, or nitrogen or to the stresses of a nutrient downshift or high salt. The ppk mutant, lacking PPK and thus severely deficient in poly P, also fails to express RpoS (a sigma factor for RNA polymerase), the regulatory protein that governs > or = 50 genes responsible for stationary-phase adaptations to resist starvation, heat and oxidant stresses, UV irradiation, etc. Most dramatically, ppk mutants die after only a few days in stationary phase. The high degree of homology of the PPK sequence in many bacteria, including some of the major pathogenic species (e.g. Mycobacterium tuberculosis, Neisseria meningitidis, Helicobacter pylori, Vibrio cholerae, Salmonella typhimurium, Shigella flexneri, Pseudomonas aeruginosa, Bordetella pertussis, and Yersinia pestis), has prompted the knockout of their ppk gene to determine the dependence of virulence on poly P and the potential of PPK as a target for antimicrobial drugs. In yeast and mammalian cells, exo- and endopolyphosphatases have been identified and isolated, but little is known about the synthesis of poly P or its physiologic functions. Whether microbe or human, all species depend on adaptations in the stationary phase, which is truly a dynamic phase of life. Most research is focused on the early and reproductive phases of organisms, which are rather brief intervals of rapid growth. More attention needs to be given to the extensive period of maturity. Survival of microbial species depends on being able to manage in the stationary phase. In view of the universality and complexity of basic biochemical mechanisms, it would be surprising if some of the variety of poly P functions observed in microorganisms did not apply to aspects of human growth and development, to aging, and to the aberrations of disease. Of theoretical interest regarding poly P is its antiquity in prebiotic evolution, which along with its high energy and phosphate content, make it a plausible precursor to RNA, DNA, and proteins. Practical interest in poly P includes many industrial applications, among which is the microbial removal of Pi in aquatic environments.

Kornelisse R.F. et al. *Intrathecal production of interleukin-12 and gamma interferon in patients with bacterial meningitis.* Infect Immun. 1997; 65(3) : 877-81.p Abstract: To assess the role of interleukin-12 (IL-12) and gamma interferon (IFN-gamma) in children with bacterial meningitis, bioactive IL-12 (p70) and the inactive subunit p40 and IFN-gamma were measured in serum and cerebrospinal fluid (CSF) from 35 children with bacterial meningitis and 10 control subjects. The production of IFN-gamma is induced by IL-12 with tumor necrosis factor alpha (TNF-alpha) as a costimulator and inhibited by IL-10. CSF concentrations of IL-12 p40 as well as those of IFN-gamma were markedly elevated, whereas IL-12 p70 was hardly detectable. Detectable CSF levels of IFN-gamma correlated positively with IL-12 p40 ($r = 0.40$, $P = 0.02$) and TNF-alpha ($r = 0.46$, $P = 0.04$) but not with IL-6, IL-8, or IL-10. In contrast to CSF levels of TNF-alpha, IL-12, and IL-10, those of IFN-gamma were significantly higher in patients with pneumococcal meningitis than in children with meningitis caused by Haemophilus influenzae and Neisseria meningitidis, presumably because of a high CSF TNF-alpha/IL-10 ratio in the former. We suggest that IL-12- and TNF-alpha-induced IFN-gamma production may contribute to the natural immunity against microorganisms in the CSF compartment during the acute phase of bacterial meningitis.

Korol S. et al. *[Water disinfection: comparative activities of ozone and chlorine on a wide spectrum of bacteria].* Rev Argent Microbiol. 1995; 27(4) : 175-83.p Abstract: Ozone and chlorine are agents that disinfect by destroying, neutralizing or inhibiting the growth of pathogenic microorganisms. The treatment of drinking water with ozone has shown to be more efficient against spores of Bacillus subtilis. It was observed that the ozone already in dose of 0.35 mg/l produced the reduction of at least 5 log in populations of approximately 1 x 10(6) cells/ml of Escherichia coli, Vibrio cholerae, Salmonella typhi, Yersinia enterocolitica, Pseudomonas aeruginosa, Aeromonas hydrophila, Listeria monocytogenes and Staphylococcus aureus. With a dose of 0.50 mg/l of chlorine, the reduction was much smaller for the tested microorganisms (except Vibrio cholerae), while the effect of 2 mg/l of chlorine was similar to the ozone treatment. For spores of Bacillus subtilis, the reduction observed with ozone concentrations of 0.35 and 0.70 mg/l was of almost 3 log, while no considerable effect was obtained with chlorine in the tested conditions. Our results have shown that both disinfectans were consumed during the treatment period, probably because of the own water demand and the added bacterial mass.

Korpan N.N. et al. *Clinical effects of continuous microwave for postoperative septic wound treatment: a double-blind controlled trial.* Am J Surg. 1995; 170(3) : 271-6.p Abstract: BACKGROUND: Continuous microwave (CM) has already been shown to be effective in treating various pathologic states. The aim of this trial was to study the curative effect of this new physical method on the course of postoperative suppurative and inflammatory processes in patients who underwent abdominal surgery. PATIENTS AND METHODS: In this study, 141 patients with postoperative purulent wounds (predominantly caused by pyogenic Staphylococcus aureus) were randomized into two groups: 71 patients received local CM therapy (group A), and the other 70 patients received a placebo treatment using a similar but ineffective device (group B, controls). In this double-blind study, criteria for wound healing in both patient groups were evaluated. RESULTS: Results demonstrated that wound clearance was significantly accelerated in group A (treated with CM) compared with group B (controls): 5.6 +/- 0.6 versus 10.2 +/- 0.5 days (mean +/- standard deviation), respectively. Similarly, initial epithelization was significantly forced in group A compared with group B: 7.0 +/- 0.4 versus 12.8 +/- 0.6 days, respectively; and granulation appeared after 4.9 +/- 0.2 versus 8.7 +/- 0.4 days of postoperative treatment, respectively. Daily decrease of wound surface area was significantly higher in group A than in group B (7.1% versus 3.2%). On the fifth postoperative day of treatment, the number of microorganisms was considerably lower (10(5) per gram of tissue) in patients treated with CM than in controls. CONCLUSIONS: The results of this controlled clinical trial suggest that low-intensity CM is an effective

postoperative treatment of purulent wounds after abdominal surgery. Further investigations may elucidate the underlying mechanisms in detail and optimize the curative effects in surgical practice.

Korshunov V.M. et al. *[The vaginal Bifidobacterium flora in women of reproductive age].* Zh Mikrobiol Epidemiol Immunobiol. 1999; (4) : 74-8.p Abstract: The composition of vaginal bifidoflora in 56 clinically healthy women of reproductive age was studied. The study revealed that four species of bifidobacteria, viz. Bifidobacterium bifidum, B. breve, B. adolescentis 2 and B. longum, dominated in the composition of this bifidobacterial population. Nine out of 11 isolated strains were found to be capable of inhibiting indicator microorganisms Staphylococcus aureus and Enterococcus faecalis when tested in vitro; in addition, strains B. adolescentis 2 F1, B. bifidum G1, B. breve P2 and B. longum Z4 inhibited Klebsiella ozaenae, Pseudomonas aeruginosa, Escherichia coli and were also active acid producers. Three of these 4 bifidobacterial strains were capable of adhesion to vaginal epitheliocytes, while B. bifidum G1 was practically incapable of adherence to these cells, similarly to B. bifidum strain 791 of intestinal origin. In addition, the spectra of antibiotic susceptibility varied from strain to strain, but all bifidobacterial strains were susceptible to benzylpenicillin and resistant to lomefloxacin, most of them being also resistant to cyprofloxacin and gentamicin. Thus the data presented in this work are indicative of the possibility and advantages of using bifidobacterial strains belonging to this ecological niche as probiotics for the correction of the microflora of the urogenital tract in females.

Korting H.C. et al. *Current antimicrobial susceptibility of cutaneous bacteria to first line antibiotics.* Int J Antimicrob Agents. 1998; 10(2) : 165-8.p Abstract: Antimicrobial susceptibility of common bacterial species occurring on human skin appears to be falling. Data for the antimicrobial susceptibility of major groups of bacteria isolated from human skin during routine cultures were complied and analysed over a period of 9 months. Routine diagnostics of specimens from skin lesions and normal human skin were analysed for the presence of specified groups of bacteria. The species were identified using standard methods. Anti-microbial susceptibility was determined using a broth microdilution system giving breakpoints, the Sensititre system. Of the 333 Staphylococcus aureus, 129 Streptococcaceae, 180 Enterobacteriaceae and 120 Pseudomonadaceae strains investigated more than 5% of Staphylococcus aureus strains were resistant to flucloxacillin and thus methicillin (MRSA). More than 25% of Staphylococcus aureus strains were resistant to tetracycline and erythromycin. Many MRSA strains were found multi-resistant. Gentamicin was active against a large majority of Enterobacteriaceae strains but many Pseudomonadaceae strains were resistant. Compared with previous corresponding surveys methicillin-resistant Staphylococcus aureus strains are clearly on the increase. To prevent a further increase of resistant strains a defined strategy for antibiotic use is needed in dermatology.

Kotilainen P. et al. *Testing of methicillin resistance by in vitro susceptibility and the presence of the mecA gene in clinical Staphylococcus aureus isolates in Finland.* Scand J Infect Dis. 1995; 27(5) : 475-9.p Abstract: A total of 140 epidemiologically unrelated Staphylococcus aureus strains collected in Finland between 1983 and 1994 were sent to the reference laboratory with verified or suspected methicillin resistance. These strains and 37 S. aureus strains previously identified as methicillin-susceptible were retested using 5 different susceptibility test methods including agar screening, disc diffusion, growth around methicillin (25 micrograms) test strips and minimal inhibitory concentration (MIC) determinations by an agar dilution method and E-test. The isolates were also analyzed for the presence of the mecA gene by the polymerase chain reaction (PCR). Based on in vitro susceptibility, 69 strains were identified as methicillin-resistant and were positive for the mecA gene in PCR, while 84 strains were methicillin-susceptible and negative for this gene. Susceptibility testing gave conflicting results for 24 (14%) strains. When the tests were repeated in triplicate for each isolate, discrepant results were still achieved with 18 of the 24 strains in at least 2 different tests. Thus, based on in vitro susceptibility, these strains could not be definitely classified as resistant or susceptible to methicillin. Yet 7 of them were positive for the mecA gene as an indication of genetic resistance to methicillin. Corroborating earlier studies, these results illustrate the difficulty of detecting methicillin resistance/susceptibility based only on susceptibility testing and underscore the importance of confirming methicillin resistance in S. aureus in specialized laboratories.

Kotterman M.J. et al. *Successive mineralization and detoxification of benzo[a]pyrene by the white rot fungus Bjerkandera sp. strain BOS55 and indigenous microflora.* Appl Environ Microbiol. 1998; 64(8) : 2853-8.p Abstract: White rot fungi can oxidize high-molecular-weight polycyclic aromatic hydrocarbons (PAH) rapidly to polar metabolites, but only limited mineralization takes place. The objectives of this study were to determine if the polar metabolites can be readily mineralized by indigenous microflora from several inoculum sources, such as activated sludge, forest soils, and PAH-adapted sediment sludge, and to determine if such metabolites have decreased mutagenicity compared to the mutagenicity of the parent PAH. 14C-radiolabeled benzo[a]pyrene was subjected to oxidation by the white rot fungus Bjerkandera sp. strain BOS55. After 15 days, up to 8.5% of the [14C]benzo[a]pyrene was recovered as 14CO2 in fungal cultures, up to 73% was recovered as water-soluble metabolites, and only 4% remained soluble in dibutyl ether. Thin-layer chromatography analysis revealed that many polar fluorescent metabolites accumulated. Addition of indigenous microflora to fungal cultures with oxidized benzo[a]pyrene on day 15 resulted in an initially rapid increase in the level of 14CO2 recovery to a maximal value of 34% by the end of the experiments (>150 days), and the level of water-soluble label decreased to 16% of the initial level. In fungal cultures not inoculated with microflora, the level of 14CO2 recovery increased to 13.5%, while the level of recovery of water-soluble metabolites remained as high as 61%. No large differences in 14CO2 production were observed with several inocula, showing that some polar metabolites of fungal benzo[a]pyrene oxidation were readily degraded by indigenous microorganisms, while other metabolites were not. Of the inocula tested, only PAH-adapted sediment sludge was capable of directly mineralizing intact benzo[a]pyrene, albeit at a lower rate and to a lesser extent than the mineralization observed after combined treatment with white rot fungi and indigenous microflora. Fungal oxidation of benzo[a]pyrene resulted in rapid and almost complete elimination of its high mutagenic potential, as observed in the Salmonella typhimurium revertant test performed with strains TA100 and TA98. Moreover, no direct mutagenic metabolite could be detected during fungal oxidation. The remaining weak mutagenic activity of fungal cultures containing benzo[a]pyrene metabolites towards strain TA98 was further decreased by subsequent incubations with indigenous microflora.

Kotulova D. et al. *[Bacterial virulence factors and their role in the pathogenesis of pyogenic infections of the abdominal cavity and mediastinum].* Bratisl Lek Listy. 1995; 96(5) : 241-4.p Abstract: Purulent peritonitis are caused predominantly by anaerobic bacteria which come from physiological intestinal flora. Mediastinitis is caused amidst other etiologic factors also by bacteria inhabiting the oropharyngeal region, as well as microorganisms causing diseases localized in the proximity of mediastinum. Anaerobic sporulating bacteria both Gram positive and negative cause often miscellaneous infections due to Staphylococcus aureus, Enterobacteriacae, Streptococcus, Enterococcus. It involves a group of bacteria which are able to produce a fibrin network in their proximity, to resist phagocytosis by their structures, to distruct the components of the complement system and immunoglobulins, to impair membranes of cells which leads by means of their factors of virulence to formation of defectuous immunity. Microbiological examination requires the material to be sent for anaerobic cultivation and the antimicrobial therapy must take into account its polymicrobic etiology. (Ref. 23.).

Kotzekidou P. *Microbial stability and fate of Salmonella enteritidis in halva, a low-moisture confection*. J Food Prot. 1998; 61(2) : 181-5.p Abstract: A traditional low-moisture confectionery, halva, was studied with respect to microbial stability over prolonged storage. It was kept under refrigeration or at room temperature in air-sealed or vacuum packaging in moisture-proof material. Microbial stability of commercial samples was evaluated with regard to the following groups of microorganisms: aerobic plate count, Enterobacteriaceae, enterococci, sulfite-reducing clostridia, aerobic mesophilic and thermophilic sporeformers, staphylococci, Staphylococcus aureus, Salmonella spp., lipolytic microorganisms, yeasts and molds. In all samples tested the above microorganisms were in acceptable levels, while sulfite-reducing clostridia, Salmonella spp., and molds were not detected. The potential for survival of Salmonella Enteritidis in the product was evaluated by artificial contamination. Inoculum surviving after the immediate significant decrease was still recovered after 8 months of storage. The reduction of salmonellae during storage cannot be predicted on the basis of the aw alone.

Kouda M. et al. *[Evaluation of the activity and effects of combinations of various antibacterial agents against methicillin-resistant Staphylococcus aureus in vitro]*. Jpn J Antibiot. 2000; 53(3) : 171-8.p Abstract: MICs of various antibacterial agents against methicillin-resistant Staphylococcus aureus (MRSA) were measured. Furthermore, we evaluated the effects of combinations of antibacterial agents against MRSA in vitro. In 24 cases out of 37, in which MRSA was isolated from inpatients, other microorganisms, such as Candida spp., Entrococcus spp., and Pseudomonas aeruginosa, were simultaneously isolated. From the results of minimum inhibitory concentrations (MICs), obtained from micro broth-dilution method, of various antibacterial agents against MRSA, range of MICs of arbekacin (ABK), vancomycin (VCM) and teicoplanin (TEIC) were < or = 0.25-4.0, 0.5-1.0 and 0.25-4.0 micrograms/ml respectively, and no strains of MRSA showed resistance to ABK, VCM and TEIC, so that we concluded that these three antibacterial agents were effective for MRSA infection. On the in vitro study of combination-effect of antibacterial agents, significant synergistic effects were achieved in the combination of VCM and flomoxef (FMOX) (Synergism rate was 97.3%) or VCM and imipenem (IPM) (Synergism rate was 97.2%). From the results that the fractional inhibitory concentration index in the combination of VCM with IPM was smaller than that with FMOX and that P. aeruginosa or Enterococcus spp. were simultaneously isolated in high frequency in the MRSA-isolated cases, we thought that the combination of VCM with IPM is more useful, because IPM is effective against P. aeruginosa but FMOX is not.

Kouda M. et al. *[Reliability of disc-diffusion susceptibility testing for arbekacin, vancomycin and teicoplanin against methicillin-resistant Staphylococcus aureus]*. Jpn J Antibiot. 1999; 52(12) : 681-9.p Abstract: We investigated the differences in judgments among four disc-diffusion methods on susceptibility testing of arbekacin (ABK), vancomycin (VCM) and teicoplanin (TEIC) against 37 strains of methicillin-resistant Staphylococcus aureus (MRSA). These results were compared with minimum inhibitory concentrations (MICs) obtained from micro broth-dilution method. A marked difference was noted in the judgment of susceptibility to TEIC in Tri-disc method, that is 2 strains (5.4%) fell into sensitive (+3) 34 strains (91.9%) into moderately sensitive (+2) and 1 strain (2.7%) into moderately resistant (+), while in Sensi-disc method all strains fell into sensitive (S). According to the MICs, no strain of the MRSA tested revealed resistance to ABK, VCM and TEIC. Consequently, these three antimicrobial agents were thought to be effective on MRSA infections. From these results, we concluded that Tri-disc method for glycopeptide against MRSA, especially for TEIC, is not recommendable as a disc-diffusion method in susceptibility testing.

Kozlov K.K. et al. *[Catheterization of the subclavian vein in patients with combined trauma in emergency situations]*. Vestn Khir Im I I Grek. 2000; 159(2) : 65-6.p Abstract: The authors describe a simplified method of catheterization of the subclavian vein available in all medical institutions and in any situation.

Kraus D. et al. *Complementary recognition of alternative pathway activators by decay-accelerating factor and factor H*. Infect Immun. 1998; 66(2) : 399-405.p Abstract: The alternative complement pathway (ACP) functions as a surveillance mechanism by which microorganisms are opsonized with C3b in the absence of specific antibodies. The effectiveness of the ACP relies on its ability to distinguish self from nonself. This recognition function is mediated by C3 regulatory proteins including serum factor H, membrane cofactor protein (MCP), and membrane decay-accelerating factor (DAF). H activity against bound C3b can be increased by host components such as sialic acid and decreased by microbial polysaccharides. DAF and MCP may also recognize cell surface changes such as the presence of viral glycoproteins, since some virus-infected and tumor cells activate the ACP. In the present study, liposomes containing wild-type and mutant Salmonella minnesota lipopolysaccharide (LPS) were tested for ACP activation in serum. LPS-containing liposomes with bound C3b were then tested for their susceptibility to C3 convertase regulation by H and membrane DAF and for the sensitivity of their bound C3b to the cofactor activity of H. The results indicate that while the shortest mutant, Re595 LPS, did not induce ACP activation, R7 LPS containing an additional disaccharide did. This activation was poorly regulated by DAF but was inhibited by H. The regulatory activity of H for liposome-bound C3b, however, decreased when LPS of greater polysaccharide size was present in the membrane. In contrast the ACP activation induced by the phospholipid phosphatidylethanolamine was effectively inhibited by DAF but only poorly inhibited by H.

Krause K.H. *Professional phagocytes: predators and prey of microorganisms.* Schweiz Med Wochenschr. 2000; 130(4) : 97-100.p Abstract: Phagocytosis is an ancient cellular function. However, professional phagocytes have evolved only in higher organisms, where they play an important role in host defence. Professional phagocytes are capable of engulfing relatively large microorganisms and killing them with a combination of various microbicidal systems. Crucial killing mechanisms of phagocytes include superoxide generation by phagocyte NADPH oxidase and release of microbicidal proteins through exocytosis of performed granules. Phagocytes are also able to interfere with microbial growth through alteration of the phagosomal ionic environment (acidification, iron depletion). While the microbicidal mechanisms of phagocytes are extremely efficient and capable of killing most microorganisms, pathogenic microorganisms have developed mechanisms to resist phagocytes. Microorganisms capable of surviving within phagocytes are rare, but represent very successful pathogens, such as Mycobacterium tuberculosis. Other pathogens, such as S. aureus, have developed strategies to evade phagocytosis. How microorganisms are phagocytosed and killed, and why certain pathogens resist these mechanisms, are crucial questions for an understanding of the pathogenesis of infectious diseases and the development of innovative treatment approaches.

Krause M. *[Infectious diarrhea]*. Schweiz Rundsch Med Prax. 1996; 85(40) : 1249-52.p Abstract: Infectious diarrhea is a very common, usually self-limited disease. Among travellers to developing countries, diarrhea is by far the most common medical problem. The intake of sufficient glucose-electrolyte solutions is the most important step to prevent dehydration. Loperamide may be prescribed as a valuable antimotility agent: however, this drug should not be used in patients with high fevers, bloody diarrhea and severe abdominal cramps. Stool cultures are recommended in cases without improvement, when clostridium difficile is suspected and when multiple cases occur. Antibiotics are indicated for treatment of certain microorganisms, for patients with immunosuppression and in dysenteric syndromes. They are not recommended for prophylaxis on a routine basis.

Krcmery V. et al. *Nosocomial bacterial and fungal meningitis in children; an eight year national survey reporting 101 cases. Pediatric Nosocomial Meningitis Study Group.* Int J Antimicrob Agents. 2000; 15(2) : 143-7.p Abstract: One hundred and one cases of nosocomial meningitis in children from a national survey over 8 years have been analyzed for risk factors and outcome. From 101 cases, 115 organisms were isolated. Seventy six were Gram-positive bacteria, 29 were Gram-negative and there were ten fungal isolates. Major risk factors for acquisition of nosocomial meningitis were neurosurgery (70.2%), ventriculoperitoneal shunt (42.9%), prior therapy with broad spectrum antibiotics (64.1%), central venous catheter (94.5%), premature neonates with very low birth weight (32.8%) and total parenteral nutrition (68.8%). Overall attributable mortality was 14. 9%; in bacterial infection it was 13.2% and in fungal nosocomial meningitis, 30.0%. Higher mortality was significantly related to perinatal pathology with CNS abnormality, prematurity polymicrobial infection with Enterobacteriaceae and concomitant bacteraemia. Prematurity in neonates, very low birth weight and infection with Enterobacteriaceae were significantly associated with a worse outcome.

Krcmery V. Jr. *Cancer departments as a source of resistant bacteria and fungi?* Neoplasma. 1999; 46(1) : 3-6.p Abstract: Antimicrobial resistance increases worldwide. Among many factors, such as clonal spread of genes of resistance among and intra species, local epidemiology, nosocomial transmission, also consumption of antimicrobials may be responsible. Cancer departments, mainly in centers treating hematologic malignancies and organizing bone marrow transplantation (BMT) are known to have extensive consumption of either prophylactically or therapeutically administered antibiotics and antifungals. It is worthy to remember, that first strains of quinolone resistant E. coli, vancomycin resistant enterococci and staphylococci and fluconazol-resistant Candida albicans appeared in the patients treated for cancer with antineoplastic chemotherapy, resulting in profound granulocytopenia. Therefore, assessment of risks of antibiotic prophylaxis with quinolones and azoles and extensive use of empiric therapy with glycopeptides and polyenes needs to be considered. Intensive prophylactic strategies should be limited to group of high risk, leukemic patients or BMT recipients.

Krcmery V. Jr. *The use of quinolones as therapy in granulocytopenic cancer patients. Comparison with other antimicrobials.* Drugs. 1995; 49 Suppl 2 : 139-43.p Abstract: Quinolones are valuable antimicrobial agents for prevention and therapy of febrile neutropenia. However, as with other groups of antibacterials, there are limitations to the use of quinolones in immunocompromised hosts: they should not be used in those neutropenic patients receiving ciprofloxacin or ofloxacin for prophylaxis, because of the risk of infection with resistant Gram-negative, or less susceptible Gram-positive, organisms. There are also insufficient data to support monotherapy of febrile neutropenia with quinolones, although some studies using higher ciprofloxacin dosages have reported encouraging results. More data on this issue, including use in paediatric cancer patients, are required. Quinolones are indicated for empirical therapy in combination with agents active against Gram-positive organisms, such as broad spectrum penicillins with or without beta-lactamase inhibitors, or in combination with vancomycin or teicoplanin. Some studies have shown that a combination of cefotaxime or ceftriaxone may provide better coverage against streptococci, but there are insufficient data on the combination of quinolones with third generation cephalosporins. A specific group of patients with low risk mild to moderate neutropenia with solid tumours may benefit from oral therapy with quinolones in combination with either an aminopenicillin with a beta-lactamase inhibitor or clindamycin. After 10 years of quinolone use in febrile neutropenia, these agents can still be regarded as valuable drugs of choice; however, the incidence of resistance among staphylococci and Pseudomonas spp., especially in centres using quinolones as prophylaxis, is increasing.

Kreitlow S. et al. *Cyanobacteria—a potential source of new biologically active substances.* J Biotechnol. 1999; 70(1-3) : 61-3.p Abstract: Hydrophilic and lipophilic extracts of twelve cyanobacterial strains, isolated from fresh and brackish water, and two waterblooms, collected during the summer from the Baltic Sea, were investigated for their antibiotic activities against seven microorganisms. No inhibitory effects were found against the three Gram-negative bacteria Escherichia coli, Proteus mirabilis and Serratia marcescens and the yeast Candida maltosa. Of all cyanobacterial samples, extracts from seven species inhibited the growth of at least one of the Gram-positive bacteria Micrococcus flavus, Staphylococcus aureus and Bacillus subtilis. M. flavus proved to be the most sensitive bacterium in the agar diffusion test system. In particular, the hexane and dichlormethane extracts showed antimicrobial effects. But only one water extract, prepared from material of a natural waterbloom, was found to be active.

Krensky A.M. *Granulysin: a novel antimicrobial peptide of cytolytic T lymphocytes and natural killer cells.* Biochem Pharmacol. 2000; 59(4) : 317-20.p Abstract: Granulysin is a novel antimicrobial protein produced by human cytolytic T lymphocytes and natural killer cells. It is active against a broad range of microbes, including Gram-positive and Gram-negative bacteria, fungi, and parasites. The fact that it kills Mycobacterium tuberculosis is particularly important, since the current vaccine (Bacille Calmette-Guerin, BCG) is of limited efficacy and antibiotic resistance is increasing. Although functionally related to other antibacterial peptides, defensins and magainins, granulysin is structurally distinct. Like porcine NK lysin and amoebapores made by Entamoeba histolytica, granulysin is related to saposins, small lipid-associated proteins present in the central nervous system. The identification of this novel molecule indicates a broader and perhaps more significant role for T lymphocytes in both innate and acquired antimicrobial defenses.

Krepel C.J. et al. *Surgical sepsis: constancy of antibiotic susceptibility of causative organisms.* Surgery. 1995; 117(5) : 505-9.p Abstract: BACKGROUND. It is well documented that antibiotic therapy exerts selective pressure on bacteria. Conversion of bacteria from susceptible to resistant to antibiotics has been observed often during antimicrobial therapy. It has been postulated that human intestinal reservoirs facilitate communication of transposons that can transfer resistance determinants among various bacterial species. METHODS. This study examined the susceptibilities of organisms isolated from infected abdomens to a number of antibiotic agents during a 12-year time interval. Analysis included 1102 isolates recovered from 255 specimens, representing the following genera: Bacteroides, Clostridium, Gemella, Fusobacterium, Peptostreptococcus, Porphyromonas, Prevotella, Enterococcus, Staphylococcus, Streptococcus, Pseudomonas, and Enterobacteriaceae. Strains were tested against beta-lactam agents, beta-lactams in combination with beta-lactamase inhibitors, first, second, and third generation cephalosporins, aminoglycosides, clindamycin, metronidazole, chloramphenicol, and imipenem. RESULTS. The results indicated that during a time period of more than a decade essentially no change occurred in the antibiotic susceptible fraction of all species tested. CONCLUSIONS. Abdominal sepsis is caused by leakage of endogenous intestinal flora. This study suggests that the intestinal flora is not permanently affected by short-term antibiotic therapy and that older antibiotics are appropriate first-line therapeutic agents for community-acquired infections caused by normal intestinal flora.

Kresken M. et al. *Drug resistance among clinical isolates of frequently encountered bacterial species in central Europe during 1975-1995. Study Group Bacterial Resistance of the Paul-Ehrlich-Society for Chemotherapy.* Infection. 1999; 27 Suppl 2 : S2-8.p Abstract: A multicenter study for monitoring antimicrobial drug resistance in clinical isolates of the family Enterobacteriaceae, Pseudomonas aeruginosa, Staphylococcus and Enterococcus species in central Europa conducted by the Study

Group Bacterial Resistance of the Paul-Ehrlich-Society for Chemotherapy has been ongoing since 1975. Between 1975 and 1995 susceptibility data on almost 60,000 bacteria, which were isolated and sampled under a common protocol by laboratories from Austria, Germany and Switzerland, were collected. These bacterial isolates were known by the respective investigators to have caused infections. From 1975 to the mid-80s none of the bacterial species examined showed an increase in resistance. The frequency of resistance in klebsiellae and Staphylococcus aureus to some antibiotics even declined. In 1990 and particularly in 1995, a clear increase in resistance for a number of antibiotic-organism pairs was observed. Resistance rates to fluoroquinolones increased in all species under investigation. In Escherichia coli the increase of resistance to ampicillin, co-trimoxazole and gentamicin was remarkable. Resistance to imipenem increased in P. aeruginosa. Resistance to cephalosporins, on the other hand, remained largely unchanged in gram-negative bacilli. Between 1990 and 1995, the prevalence of oxacillin resistance increased from 1.7 to 12.9% in S. aureus and from 15.8 to 55.8% in coagulase-negative staphylococci, whereas staphylococcal and enterococcal resistance to glycopeptides was still rare.

Krieger J.N. et al. *Prokaryotic DNA sequences in patients with chronic idiopathic prostatitis.* J Clin Microbiol. 1996; 34(12) : 3120-8.p Abstract: Half of all men experience symptoms of prostatitis at some time in their lives, but the etiology is unknown for more than 90% of patients. Optimal clinical and culture methods were used to select 135 men with chronic prostatitis refractory to multiple previous courses of antimicrobial therapy. The subjects had no evidence of structural or functional lower genitourinary tract abnormalities of bacteriuria or bacterial prostatitis by traditional clinical tests, or of urethritis or urethral pathogens by culture. Specific PCR assays detected Mycoplasma genitalium, Chlamydia trachomatis, or Trichomonas vaginalis in 10 patients (8%). Broad-spectrum PCR tests detected tetracycline resistance-encoding genes, tetM-tetO-tetS, in 25% of patients and 16S rRNA in 77% of subjects. The tetM-tetO-tetS-positive cases constituted a subset of the 16S rRNA-positive cases. Patients with 16S rRNA were more likely to have > or = 1,000 leukocytes per mm3 in their expressed prostatic secretion than men whose prostate biopsy specimens were negative for 16S rRNA ($P < 0.001$). Based on direct sequencing and repetitive cloning, multiple sources of 16S rRNA were observed in individual patients. Sequences of 29 cloned PCR products revealed 16S rRNAs distinct from those of common skin and gut flora. These findings suggest that the prostate can harbor microorganisms that are not detectable by traditional approaches. These organisms may be associated with inflammation in the expressed prostatic secretions. Molecular methods hold great promise for identifying culture-resistant microorganisms in patients with chronic prostatitis.

Krimmer V. et al. *Detection of Staphylococcus aureus and Staphylococcus epidermidis in clinical samples by 16S rRNA-directed in situ hybridization.* J Clin Microbiol. 1999; 37(8) : 2667-73.p Abstract: Staphylococcus epidermidis and Staphylococcus aureus are the most common causes of medical device-associated infections, including septicemic loosenings of orthopedic implants. Frequently, the microbiological diagnosis of these infections remains ambiguous, since at least some staphylococci have the capacity to reduce their growth rate considerably. These strains exhibit a small-colony phenotype, and often they are not detectable by conventional microbiological techniques. Moreover, clinical isolates of S. aureus and S. epidermidis adhere to polymer and metal surfaces by the generation of thick, multilayered biofilms consisting of bacteria and extracellular polysaccharides. This study reports improved detection and identification of S. aureus and S. epidermidis by an in situ hybridization method with fluorescence-labeled oligonucleotide probes specific for staphylococcal 16S rRNA. The technique has proven to be suitable for the in situ detection of staphylococci, which is illustrated by the identification of S. epidermidis in a connective tissue sample obtained from a patient with septicemic loosening of a hip arthroplasty. We also show that this technique allows the detection of intracellularly persisting bacteria, including small-colony variants of S. aureus, and the differentiation of S. epidermidis from other clinically relevant staphylococci even when they are embedded in biofilms. These results suggest that the 16S rRNA in situ hybridization technique could represent a powerful diagnostic tool for the detection and differentiation of many other fastidious microorganisms.

Kristiansen J.E. et al. *The potential management of resistant infections with non-antibiotics.* J Antimicrob Chemother. 1997; 40(3) : 319-27.p Abstract: The antimicrobial activity of synthetic, non-chemotherapeutic compounds, such as the phenothiazine, methylene blue, has been known since the time of Ehrlich (1854-1915). In this context the term 'non-antibiotics' is taken to include a variety of compounds which are employed in the management of pathological conditions of a non-infectious aetiology, but which modify cell permeability and have been shown to exhibit broad-spectrum antimicrobial activity. The antimicrobial properties of compounds such as phenothiazines, as well as those of other neurotropic compounds, have only been investigated sporadically, and their application to management of microbial infections has not been evaluated. A review of the literature, coupled with a number of more recent investigations, suggests that some of these and other membrane-active compounds enhance the activity of conventional antibiotics, eliminate natural resistance to specific antibiotics (reversal of resistance) and exhibit strong activity against multi-drug resistant forms of Mycobacterium tuberculosis. Thus non-antibiotics may have a significant role in the management of certain bacterial infections.

Kristinsson K.G. *Effect of antimicrobial use and other risk factors on antimicrobial resistance in pneumococci.* Microb Drug Resist. 1997; 3(2) : 117-23.p Abstract: Penicillin-resistant and multi-resistant pneumococci have spread globally and reached high prevalence in many countries. Antimicrobial use is considered a major driving force for resistance, although the influence in the community has not been as clearly demonstrated. Other risk factors may be important, and only with a clear understanding of the risk factors can effective control measures be introduced. The main habitat of the pneumococcus is the nasopharynx of children. Carriage increases from birth and is maximal at pre-school age. Antimicrobial use in children is likely to have a significant influence on the susceptibility of pneumococci. Most studies looking for risk factors for resistance in pneumococci have identified antimicrobial use as a risk factor, especially the following aspects: ongoing, recent, repeated, frequent, and prophylactic antibiotic use. The effect of individual classes of antimicrobials has not been studied in detail but use of beta-lactam antibiotics and trimethoprim-sulpha has been associated with increased risk. Other risk factors are young age, nosocomial acquisition, prior hospitalization, and HIV infection. Day-care centers can facilitate the spread of resistant pneumococci and an Icelandic study showed that carriage of resistant pneumococci was associated with young age, domicile in an area with high antimicrobial consumption, recent antimicrobial use, frequent antimicrobial use, and use of trimethoprim-sulpha. The rapid increase of penicillin-resistant pneumococci in Iceland was met with propaganda against overuse of antimicrobials, which lead to reduction of antimicrobial use and subsequently a reduced incidence of penicillin-resistant pneumococci. This reduction may be related to reduced antimicrobial use. Reducing antimicrobial use should be considered important for programs aimed at reducing antimicrobial resistance.

Kristinsson K.G. *Epidemiology of penicillin resistant pneumococci in Iceland.* Microb Drug Resist. 1995; 1(2) : 121-5.p Abstract: The prevalence of penicillin-resistant pneumococci (PRP) has been increasing, with the highest levels reported from countries with relatively unrestricted antimicrobial use. It has been low in northern Europe except Iceland, which is disconcerting as antimicrobial use in Iceland has been relatively restricted. This suggests that other factors may facilitate their spread. By studying their epidemiology and possible

risk factors for carriage, we have attempted to explain their rapid spread in Iceland. The incidence of infections caused by PRP (as percentage of infections considered due to pneumococci) has increased from 0% in 1988 to 2.3% in 1989, 2.7% in 1990, 8.4% in 1991, 16.3% in 1992, and 19.8% in 1993. The infections have mainly affected 0- to 3-year-old children (71.4%), and the PRP belonged almost exclusively to serogroups 6, 19, and 23 (98.8%). Most were serotype 6B multiresistant (75%; resistant to penicillin (MIC = 1.0), cephalothin, erythromycin, clindamycin, tetracycline, chloramphenicol, fusidic acid, sulfonamides, and trimethoprim), and believed to belong to a single clone originating from Spain. The PRP have been prevalent in healthy children, 0-10% nasopharyngeal carriage, especially in day-care centers, with the highest prevalence in areas that had the highest antimicrobial consumption. Recent antimicrobial consumption, especially of trimethoprim-sulfa, appeared to increase PRP carriage. The rapid spread of PRP in Iceland may have been facilitated by high antimicrobial consumption in day-care centers (especially of trimethoprim-sulfa) which are attended by the majority of Icelandic children.

Kruse H. et al. *A transferable multiple drug resistance plasmid from Vibrio cholerae O1.* Microb Drug Resist. 1995; 1(3) : 203-10.p Abstract: Ten multiple antimicrobial-resistant isolates of Vibrio cholerae O1 isolated from patients in Uganda were characterized, and the transferability of resistance to bacteria of diverse origins was investigated. The isolates were toxigenic and belonged to biotype E1 Tor, serotype Ogawa, and ribotype 8, and possessed a 130-MDa plasmid of incompatibility group 6-C. This plasmid, designated pRVC1, was shown to confer resistance to trimethoprim (mediated by a dhfrI gene), sulfonamides (a sulI gene), tetracycline [a tet(C) gene], chloramphenicol (a catI gene), ampicillin (a beta-lactamase gene other than blaTEM or blaSHV), and streptomycin. pRVC1 proved to be transmissible at frequencies between 1 x 10(-1) and 5 x 10(-6) transconjugants per recipient to a variety of bacterial pathogens, including those of humans, animals, and fish. Most efficient transfer was observed from V. cholerae to strains of Shigella flexneri, Escherichia coli, Vibrio parahaemolyticus, and three Aeromonas species. The present in vitro study suggests that pRVC1 may spread from V. cholerae to other bacteria pathogenic to man, animals, and fish in natural environments.

Krzeminski Z. et al. *[The presence of staphylococci in the vagina of pregnant women].* Ginekol Pol. 1998; 69(2) : 82-6.p Abstract: We were investigating the colonisation rate as well as the quantity of staphylococci in the vagina of women with physiological and complicated pregnancy. We have found high frequency of staphylococci (coagulase-negative and/or coagulase-positive). Vaginal carriage rate amount 90%. According to our results neither the presence nor the quantity of these microorganisms were related to the presence or the number of lactobacilli, among them to the hydrogen peroxide producing ones. We have also assumed that neither colonisation nor the quantity of staphylococci have any influence on the course of pregnancy.

Kubota T. et al. *Prevalence of human papillomavirus infection in women attending a sexually transmitted disease clinic.* Kansenshogaku Zasshi. 1999; 73(3) : 233-8.p Abstract: The purpose of this study was to determine the prevalence of infection due to human papillomavirus (HPV) types of high and intermediate oncogenic risk, which was most frequently associated with uterine cervical neoplasia. The subjects were 236 prostitutes who visited a sexually transmitted diseases (STD) clinic in a metropolitan area in 1998. Another 95 women who visited a university hospital were selected as a normal control group. A swab sample collected from the uterine cervix and external os was subjected to hybrid capture assays for low-oncogenic-risk HPV types (HPV A; including types 6, 11, 42, 43 and 44) and high- and intermediate-oncogenic-risk HPV types (HPV B; including 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68). Chlamydia trachomatis and Neisseria gonorrhoeae. Fisher's exact test was used for statistical analyses. Among the microorganisms tested, the positive rate for HPV B was the highest both in the women attending the STD clinic (STD group) and in the control group. The positive rate for HPV B in the STD group was 47.5% (112 of 236), and this was significantly higher than the 5.3% (5 of 95) in the control group ($p < 0.0001$). These findings suggest that HPV examination is recommended for women who visit an STD clinic to assess the future risk of cervical neoplasia.

Kuchta T. et al. *Analysis of hopanoids in bacteria involved in food technology and food contamination.* FEMS Microbiol Lett. 1998; 159(2) : 221-5.p Abstract: Hopanoids are pentacyclic triterpenoids which are believed to act as reinforcers of membranes in certain prokaryotic microorganisms. A rapid and sensitive method for their screening in bacteria was elaborated, involving extraction of nonsaponifiable lipids and the analysis by gas chromatography-mass spectrometry, selectively monitoring the ion of m/z = 191. Using the method, hopanoids were detected in strains of Acetobacter pasteurianus, but were found to be absent in lactic acid bacteria (Lactobacillus spp., Lactococcus spp.) and in food-contaminating bacteria (Salmonella spp., Listeria spp., Yersinia spp. and others).

Kugler K.C. et al. *Serious streptococcal infections produced by isolates resistant to streptogramins (quinupristin/dalfopristin): case reports from the SENTRY antimicrobial surveillance program.* Diagn Microbiol Infect Dis. 2000; 36(4) : 269-72.p Abstract: The emergence and sustained prevalence of Gram-positive organisms resistant to antimicrobials has been of interest for over a decade. Quinupristin/dalfopristin (formerly RP 59500 or Synercid) is a new injectable streptogramin combination that has been reported to have activity against Gram-positive organisms, even those with documented MLS(B) resistance. However, the two case reports presented here illustrate three well-documented Streptococcus spp. strains (S. mitis, S. pneumoniae) to be resistant to quinupristin/dalfopristin (MICs at 3, 8, and 12 microg/ml) following referral as routine isolates in the SENTRY Antimicrobial Surveillance Program. The S. pneumoniae pleural fluid isolate was cross-resistant to erythromycin. Both bacteremic S. mitis strains were resistant to macrolides (erythromycin, azithromycin, clarithromycin), lincosamides (clindamycin), and fluoroquinolones. Patient histories indicated no prior use of MLS class antimicrobials for the S. mitis case, but the patient having the S. pneumoniae isolate did receive prior treatment of erythromycin and clindamycin. All isolates had modestly increased penicillin MICs of 0.12 microg/ml. The mode of resistance to quinupristin/dalfopristin was not evident (sat A-negative by PCR); and these cases illustrate the existence of streptogramin-resistant isolates before the introduction of this antimicrobial class into human clinical practice.

Kujdych N. *Prescribing trends in the treatment of acute otitis media. Reining in resistant bacteria.* Adv Nurse Pract. 1999; 7(10) : 30-5.p Abstract: Several factors influence antimicrobial selection when treating otitis media. In addition to good in vitro activity against common pathogens, the drug should be well-absorbed with high serum concentrations and good penetration to the site of infection. Oral amoxicillin dosed at 40 mg/kg/day to 50 mg/kg/day every 8 hours for 10 days remains first-line therapy for uncomplicated AOM. Second-line agents to treat AOM can include second- and third-generation cephalosporins. The rapid emergence of antibiotic-resistant bacteria represents a particular problem because these pathogens cause not only otitis media but more serious and invasive bacterial infections such as pneumonia, bacteremia and meningitis.

Kulak Y. et al. *Existence of Candida albicans and microorganisms in denture stomatitis patients.* J Oral Rehabil. 1997; 24(10) : 788-90.p Abstract: The aetiology of denture stomatitis is not clear from the literature. Some studies show its aetiology as Candida albicans, while other reports point out the significance of microorganisms. In this study the existence of C. albicans and microorganisms was investigated in subjects with and without denture stomatitis. The results showed that a

combination of C. albicans and microorganisms is more likely to be responsible for denture stomatitis.

Kumamoto Y. et al. *[Comparative studies on activities of antimicrobial agents against causative organisms isolated from patients with urinary tract infections (1996), III. Secular changes in susceptibility].* Jpn J Antibiot. 1998; 51(3) : 143-236.p Abstract: Susceptibilities to various antimicrobial agents were examined for Enterococcus faecalis, Staphylococcus aureus, Escherichia coli, Klebsiella spp., and Pseudomonas aeruginosa that were isolated from patients with urinary tract infections (UTIs) in 10 hospitals during June 1996 to May 1997, and the results were compared with those obtained during the same period in earlier years. 1. E. faecalis Among E. faecalis strains, those with high susceptibilities to ampicillin and minocycline appeared to have decreased in the latest study period. 2. S. aureus To almost antimicrobial agents, S. aureus isolated from uncomplicated UTIs showed low susceptibilities. But the MIC50s of those agents for S. aureus from complicated UTIs have changed better state. Particularly, the MIC50s of imipenem and clindamycin were 0.125 microgram/ml or below in the latest period for the first time in our history. 3. E. coli The susceptibilities to piperacillin and quinolones of E. coli isolated from uncomplicated UTIs were better than those isolated from complicated UTIs. 4. Klebsiella spp. The susceptibilities to almost antimicrobial agents of Klebsiella spp. have been better during the latest period, compared to those during period of 1995-1996, but to ofloxacin and ciprofloxacin have appeared to have been lower. 5. P. aeruginosa The susceptibilities to quinolones of P. aeruginosa have been better during the latest period compared those during periods of 1995-1996. But, the susceptibilities to cefozopran, carbapenems and monobactams of P. aeruginosa isolated from complicated UTIs appeared to have been lower. These susceptibility changes should be utilized in determining clinical treatments.

Kumarasinghe G. et al. *In vitro activity of cefoperazone-sulbactam: Singapore experience.* Southeast Asian J Trop Med Public Health. 1996; 27(4) : 734-7.p Abstract: In vitro activity of commonly used antimicrobial agents against consecutively isolated 521 strains of Gram negative bacilli causing serious infections in the National University Hospital, Singapore were tested in parallel with cefoperazone-sulbactam combination. With the combination complete resistance of 2% and intermediate resistance of 5% were noted among the 521 strains tested. Resistance to imipenem was low (5%) but resistance against other antimicrobial agents varied from 12% (amikacin) to 80% (ampicillin). In vitro data demonstrated a possible future role for cefoperazone-sulbactam in the treatment of sepsis caused by Gram negative bacilli in our hospital.

Kumarasinghe G. et al. *Antimicrobial resistance problem in a university hospital.* Pathology. 1995; 27(1) : 67-70.p Abstract: In a study conducted in 1991 in the National University Hospital, Singapore, the susceptibilities of a total of 2156 recent clinical isolates were tested against 25 antimicrobial drugs. The organisms were those isolated from routine specimens received in the microbiology laboratory. About 40% Staphylococcus aureus isolations in the hospital were resistant to methicillin. A high incidence of the resistance was noted among Staphylococcus aureus and coagulase negative staphylococci to antistaphylococcal drugs. Acinetobacter sp. and Klebsiella sp. are becoming major threats with regard to antimicrobial treatment as they are multi-drug resistant. Pseudomonas aeruginosa did not show a resistance problem except to pefloxacin (74%). Ampicillin resistance of Acinetobacter sp. (93%) was reduced to 71% by ampicillin/clavulanic acid and to 7% by ampicillin/sulbactam. With regards to the urinary isolates higher rates of resistance were noticed with Pseudomonas aeruginosa to antipseudomonas drugs and for co-trimoxazole with other Gram negative organisms, compared to non-urinary isolates.

Kume A. et al. *Gene therapy for chronic granulomatous disease.* J Lab Clin Med. 2000; 135(2) : 122-8.p Abstract: Recent progress in the development of gene therapy for chronic granulomatous disease (CGD), an inherited immunodeficiency syndrome, is reviewed. This disorder results from defects in any of the four genes encoding essential subunits of respiratory burst oxidase, the superoxide-generating enzyme complex in phagocytic leukocytes. The absence of respiratory burst oxidants results in recurrent bacterial and fungal infections and can also be complicated by the formation of inflammatory granulomas. Although current management, including prophylactic use of antimicrobial agents and interferon-gamma, has significantly improved its prognosis, CGD continues to be associated with significant morbidity and mortality from life-threatening infections and complications. Allogeneic bone marrow transplantation can provide a life-long cure of the disease, but difficulty in finding suitable donors and risks associated with this procedure have limited its application. Recently CGD has emerged as a promising candidate for gene therapy targeted at the hematopoietic system. CGD mouse models have been developed with gene targeting technology, and preclinical studies in these animals with recombinant retroviral vectors have demonstrated the appearance of functionally normal neutrophils and increased resistance against pathogens such as Aspergillus. Although the murine studies have provided a promise of long-term cure of patients by gene transfer, phase I clinical studies in a limited number of patients with CGD with such vectors have yet to produce a clinically relevant number of corrected neutrophils for extended time periods. Efforts are ongoing to improve gene transfer efficiency into human hematopoietic stem/progenitor cells and to achieve better engraftment of the gene-corrected stem cells.

Kunaratanapruk S. et al. *Unnecessary hospital infection control practices in Thailand: a survey.* J Hosp Infect. 1998; 40(1) : 55-9.p Abstract: The high prevalence of hospital-acquired infection has a significant impact on the operating cost of hospitals in Thailand. A nationwide questionnaire survey was conducted to determine how frequently unnecessary infection control procedures were performed. Nearly 17% of hospitals routinely cleaned floors with disinfectants; 48% installed ultraviolet lights in the operating room; 57% performed routine environmental cultures; 68% reported fogging of the operating theatres and the isolation rooms; wearing a protective gown in the intensive care units was routine in 57% of the surveyed hospitals; 30% of hospital laundries set temperatures unnecessarily high and sterile gloves were overused in 25% of hospitals. Large cost reduction can be achieved by discontinuing these practices.

Kunugita C. et al. *Characterization of a new plasmid-mediated extended-spectrum beta-lactamase from Serratia marcescens.* J Antibiot (Tokyo). 1995; 48(12) : 1453-9.p Abstract: A new extended spectrum beta-lactamase was detected in Serratia marcescens 42039 that was isolated from urine of patients with complicated urinary tract infection in Japan. This stain produced three different beta-lactamase types (TEM-1, a cephalosporinase, and a new beta-lactamase: CKH-1). The TEM-1 and CKH-1 encoding genes were conjugated from S. marcescens 42039 to Escherichia coli K-12 at frequencies of 10(-5) to 10(-6). The MICs of beta-lactams against the transconjugant were: ampicillin > 1600, piperacillin 800, cephalothin 1600, ceftazidime 6.25, cefotaxime 100, and ceftriaxone 200 micrograms/ml. The CKH-1 enzyme was purified to more than 90% by ion-exchange chromatography. The molecular weight of purified CKH-1 was 30 K dalton and the isoelectric point was 8.2. Relative Vmax/Km values (cephaloridine = 100) of penicillin G, cephalothin, and oxyiminocephalosporins such as cefuroxime, ceftriaxone, and cefotaxime, were 256, 226, 116, 87, and 49, respectively. The I50 values of tazobactam, BRL-42715, and clavulanic acid against CKH-1 enzyme were 0.0011, 0.0002, and 0.097 microM respectively. The enzymatic activity of CKH-1 was not inhibited by EDTA and anti-TEM-1 serum. These findings indicate that CKH-1 is a member of the groups of class A beta-lactamases. This is the first report of a plasmid-mediated oxyiminocephalosporin hydrolyzing broad-spectrum beta-lactamase from clinical isolates of S. marcescens.

Kupferwasser I. et al. *Clinical and morphological characteristics in Streptococcus bovis endocarditis: a comparison with other causative microorganisms in 177 cases.* Heart. 1998; 80(3) : 276-80.p Abstract: AIM: To compare the clinical and morphological characteristics of patients with Streptococcus bovis endocarditis with those of patients with endocarditis caused by other microorganisms. METHODS: 177 consecutive patients (Streptococcus bovis, 22; other streptococci, 94; staphylococci, 44; other, 17) with definite infective endocarditis according to the Duke criteria were included. All patients underwent transthoracic and transoesophageal echocardiography. In 88 patients, findings from surgery/necropsy were obtained. RESULTS: S bovis endocarditis was associated with older patients, with a higher mortality ($p = 0.04$), and with a higher rate of cardiac surgery ($p < 0.001$) than other microorganisms, although embolic events were observed less often ($p = 0.02$). Pathological gastrointestinal lesions were detected in 45% of the patients. Multiple valves were affected in 68% of the patients with S bovis endocarditis and in 20% of those with other organisms ($p < 0.001$). Moderate or severe regurgitation occurred more often in S bovis endocarditis than with other microorganisms ($p = 0.05$). When surgery or necropsy was performed, infectious myocardial infiltration of the left ventricle was confirmed histopathologically in 36% of the patients with S bovis endocarditis and in 10% of those with other organisms ($p = 0.002$). CONCLUSIONS: S bovis endocarditis is a severe illness because of the more common involvement of multiple valves, and of the frequent occurrence of haemodynamically relevant valvar regurgitation and infectious myocardial infiltration.

Kupper T. et al. *Morphological study of bacteria of the respiratory system using fluorescence microscopy of Papanicolaou-stained smears with special regard to the identification of Mycobacteria sp.* Cytopathology. 1995; 6(6) : 388-402.p Abstract: In Papanicolaou-stained smears certain structures such as nucleoli, Pneumocystis carinii, Charcot-Leyden crystals, bacteria and fungi show a brilliant fluorescence. The morphological characteristics of microorganisms which can be detected by this system, especially mycobacteria, are described. This screening method offers the possibility of providing the clinician with a provisional diagnosis within hours. Proof of the nature of the organisms should be obtained by culture.

Kurenkov V.V. et al. *[Effects some drugs of re-epithelialization in the early postoperative period after photorefraction keratectomy].* Vestn Oftalmol. 1999; 115(6) : 38-40.p Abstract: Terms of re-epithelialization, severity of the painful syndrome, intensity of corneal "crepe" (opacity) are assessed in myopic patients treated by maxitrol, eubetal, colbiocin ointments and maxitrol eyedrops in the early postoperative period after photorefraction keratectomy. The crepe intensity was assessed routinely according to a clinical score: 0) transparent cornea, 1) trace crepe; 2) moderate crepe; and 3) intensive crepe. Biomicroscopy on day 4 after photorefraction keratectomy showed complete epithelialization in 91.7% patients after colbiocin ointment, in 91.% after maxitrol eyedrops, 87% after eubetal ointment, and 82.6% after maxitrol ointment. The least corneal opacity (0 and 0-1) was observed after eubetal ointment and maxitrol eyedrops. The mean score for pain was virtually the same in all groups; in the colbiocin ointment group more patients complained of pain for more than 24 h in comparison with other groups.

Kuriyama T. et al. *Past administration of beta-lactam antibiotics and increase in the emergence of beta-lactamase-producing bacteria in patients with orofacial odontogenic infections.* Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2000; 89(2) : 186-92.p Abstract: OBJECTIVE: The purpose of this study was to determine the current status of beta-lactamase-producing bacteria in orofacial odontogenic infections. STUDY DESIGN: Microbiologic data regarding purulent exudate from 111 cases with orofacial odontogenic infections were analyzed in relation to the past administration of beta-lactams. RESULTS: beta-lactamase-producing bacteria were isolated more frequently from the beta-lactam-administered group (38.5%) than from the beta-lactam-nonadministered group (10.9%; $P < .005$), and they were isolated more frequently as the duration of administration increased. The predominant bacteria isolated included Prevotella (the most frequent isolate), viridans streptococci, Peptostreptococcus, and Fusobacterium, and 7.1% of total isolates produced beta-lactamase. Penicillin and cefazolin worked well with beta-lactamase-nonproducing Prevotella but were remarkably affected by beta-lactamase-producing Prevotella. Cefmetazole, sulbactam/cefoperazone, and imipenem worked well against both types of Prevotella. CONCLUSIONS: beta-lactams are still suitable for the first antimicrobial therapy in the treatment of these infections. However, because past beta-lactam administration increases the emergence of beta-lactamase-producing bacteria, beta-lactamase-stable antibiotics should be prescribed to patients with unresolved infections who have received beta-lactams.

Kurlaev P.P. et al. *[Prognosis of postinjection abscesses course with use of mathematical model].* Khirurgiia (Mosk). 1999; (7) : 46-8.p Abstract: Virulent and persistent characteristics of staphylococci isolated from 100 patients with various types of course of the abscessed forms of postinjection suppuration were defined. Comparative analysis of 11 biological characteristics of the microorganisms was carried out. An important role of the complex of properties of Staphylococcus aureus was established, including lysozyme, proteolytic, fibrinolytic activities, ability for inactivation of immunoglobulins through their Fc-receptors' binding to protein A, antilysozyme, "antiinterferon", anticomplement activities in determination of protracted character of festering and inframmatory process initiated by them. The model for prognosis of the course of postinjection abscesses was developed with the help of discriminant analysis, being based on the analysis of the informative properties of the pathogen.

Kurlaev P.P. et al. *[The connection between the duration of the course of postinjection abscesses and the biological characteristics of the causative microorganisms].* Vestn Khir Im I I Grek. 1996; 155(6) : 54-6.p Abstract: An analysis of results of treatment of 100 patients with postinjectional abscesses (PA) has shown their tendency to continuous inflammation in (23.9 +/- 5.4)% of the cases. Under condition of long duration of PA microorganisms of Staphylococcus aureus species have been isolated which possess 2-6 times greater capacity for inactivating the natural antiinfectious resistance factors: lysozyme, complement, immunoglobulins, bacterial component of the interferon. The inclusion of oxytocin preparation into the scheme of treatment which inhibits manifestations of antilysozymal activity of staphylococci allowed the frequency of prolonged unfavourable periods of PA to be reduced to 10.9%.

Kurlandsky L.E. et al. *In vitro activity of minocycline against respiratory pathogens from patients with cystic fibrosis.* Pediatr Pulmonol. 2000; 29(3) : 210-2.p Abstract: Our objective was to determine the in vitro activity of minocycline against isolates of Burkholderia cepacia (BC), Stenotrophomonas maltophilia (SM), and Pseudomonas aeruginosa (PA) cultured from the respiratory tract of patients with cystic fibrosis (CF). Cultures of BC, SM, and PA were isolated in a hospital bacteriology laboratory from the sputum or oropharyngeal cultures obtained from patients attending a Cystic Fibrosis Center, and were prospectively tested for in vitro sensitivity to minocycline by Kirby-Bauer disk diffusion. From January 1994 to July 1995, 116 cultures from 61 patients had at least one of the three pathogens; 9/61 (15%) patients had an isolate of BC, and 7/9 (78%) had an initial isolate sensitive to minocycline, of which 3 were sensitive only to minocycline; 2 cultures were resistant to all antibiotics. Four of 7 patients with BC were treated with minocycline; 3 patients developed resistant isolates 3-13 months after therapy. Five of 61 patients (8%) had an isolate of SM: 4/5 (80%) of these isolates were sensitive to minocycline, of which 1 was sensitive only to minocycline. Fifty-five of 61 patients (90%) had at least one PA isolate, with 112 morphotypes recovered from 90 cultures: 40/112 morphotypes (36%) were sensitive to minocycline, 65 (58%) were resistant, and 7 (6%)

were intermediate in sensitivity. We conclude that the marked in vitro activity of minocycline against BC and SM isolated from patients with CF suggests that minocycline may have an adjunct role in the antimicrobial therapy of multidrug resistant, respiratory pathogens in CF. Copyright 2000 Wiley-Liss, Inc.

Kurokawa I. et al. *Antimicrobial susceptibility of Propionibacterium acnes isolated from acne vulgaris.* Eur J Dermatol. 1999; 9(1) : 25-8.p Abstract: Systemic and topical antimicrobial treatment for acne vulgaris remains the mainstay method of therapy in Japan. Strains of Propionibacterium acnes (P. acnes) resistant to erythromycin (EM), clindamycin (CLDM), tetracycline (TC), doxycycline (DOXY) and minocycline (MINO) have been reported. The aim of the present study was to examine the antimicrobial susceptibility to 10 currently used antimicrobial agents of 50 strains of P. acnes isolated from acne lesions and identified using a Rap ID ANA II panel. Minimum inhibitory concentrations (MIC) were determined by the agar dilution method according to the criteria of the Japan Society of Chemotherapy. EM, ampicillin (ABPC), and CLDM were the most potent drugs, followed by MINO, nadifloxacin (NDFX), cephalexin (CEX), DOXY, ofloxacin (OFLX), and TC. In terms of the MIC80, EM and ABPC were the most potent, followed by CLDM, NDFX, MINO, CEX, DOXY, OFLX, TC and gentamycin (GM). Although most of the strains used were susceptible to the antimicrobial agents tested, strains of P. acnes resistant (MIC 12.5 mug/ml) to EM (4%), CLDM (4%), DOXY (2%) and TC (2%) were observed. In this study, no strains of P. acnes resistant to MINO were seen, suggesting that oral MINO is the most useful treatment for acne vulgaris with minimal risk of bacterial resistance.

Kuroyama M. et al. *[A consideration on the results of nationwide surveillance of antimicrobial susceptibilities—gram-negative bacilli].* Jpn J Antibiot. 1999; 52(4) : 333-52.p Abstract: The results of the semi-annual nationwide surveillance of antimicrobial susceptibilities, conducted by the Japanese Ministry of Health and Welfare during the period of January 1993 to July 1995, were analyzed for typical Gram-negative bacilli in the purpose of provision of an index for antimicrobial selection. During these 3 years, Escherichia coli, Citrobacter freundii, Enterobacter aerogenes and Proteus mirabilis showed slightly increasing tendency in susceptibility to fosfomycin (FOM) and Citrobacter freundii. Klebsiella pneumoniae and Enterobacter aerogenes showed slightly increasing tendency to minocycline (MINO). While Haemophilus influenzae and Haemophilus parainfluenzae showed slightly decreasing tendency to cefmetazole (CMZ). However, these annual changes were almost negligible. Generally, these microorganisms showed relatively good susceptibilities, every year, to the principal antimicrobial agents being approved for use against Gram-negative bacilli. However, Enterobacter cloacae, Enterobacter aerogenes, Serratia marcescens and Pseudomonas aeruginosa showed tendencies of decreased susceptibility to some of the antimicrobial agents. On the other hand, sulfamethoxazole-trimethoprim (ST), CMZ, latamoxef (LMOX), gentamicin (GM) and amikacin (AMK) showed good activities against some of the Gram-negative bacilli to which no indications are approved. In conclusion, bedside the identification of the causative microorganisms and the performance of antimicrobial susceptibility testing, such analyses (graphics of susceptibility tendency of clinical isolates to variety of antimicrobial agents) could be used as an index for selection of antimicrobial agents, when emergent and urgent selection of antimicrobial agents is necessary.

Kwon H.H. et al. *Distribution and characterization of beta-lactamases of mycobacteria and related organisms.* Tuber Lung Dis. 1995; 76(2) : 141-8.p Abstract: SETTING: The detailed distribution and precise features of mycobacterial beta-lactamases urgently need to be elucidated. OBJECTIVE: To study the distribution pattern of beta-lactamases among mycobacteria, their enzymatic profiles and degree of contribution to the expression of drug resistance of some mycobacteria to beta-lactam antibiotics. DESIGN: Cell-associated beta-lactamase was measured by nitrocefin disc method. beta-lactamases obtained from some mycobacteria were studied for their substrate specificity, metal ion-dependency and isoelectric focusing (IEF) patterns. Changes in the minimum inhibitory concentrations (MICs) of beta-lactams for rapidly growing mycobacteria due to the combined use of tazobactam were measured. RESULTS: In slow growers, Mycobacterium tuberculosis complex possessed strong and M. kansasii showed strong to intermediate beta-lactamase activity, while M. avium complex lacked such an activity. All the rapid growers possessed strong to intermediate activity. The beta-lactamases of test organisms including M. tuberculosis, M. kansasii, M. fortuitum etc, exerted both penicillinase and cephalosporinase activities and were not metalloenzymes. M. tuberculosis, M. kansasii, and M. smegmatis exhibited the species-specific IEF patterns of beta-lactamases. Tazobactam potentiated the in vitro antimicrobial activities of some beta-lactams against M. fortuitum and M. chelonae. CONCLUSION: Many mycobacteria possessed peculiar beta-lactamases and the enzymes were partly attributable to their drug resistance to certain beta-lactam antibiotics.

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Labbe A.C. et al. *Trends in antimicrobial resistance among clinical isolates of the Bacteroides fragilis group from 1992 to 1997 in Montreal, Canada.* Antimicrob Agents Chemother. 1999; 43(10) : 2517-9.p Abstract: The objective of the present study was to analyze the susceptibility profiles of 911 clinical strains of the Bacteroides fragilis group isolated from 1992 to 1997 in our institution in order to monitor susceptibility changes over time. Whereas the rates of resistance to metronidazole, imipenem, piperacillin-tazobactam, ticarcillin-clavulanic acid, penicillin, piperacillin, and cefoxitin remained essentially unchanged, there was a significant increase in the rates of resistance to clindamycin, which rose from 8.2% in 1992 to 19.7% in 1997 ($P < 0.0004$).

LaClaire L. et al. *Antimicrobial susceptibilities and clinical sources of Facklamia species.* Antimicrob Agents Chemother. 2000; 44(8) : 2130-2.p Abstract: Facklamia spp. are gram-positive cocci, arranged in short chains or diplos, and resemble viridans streptococci on 5% sheep blood agar. Eighteen strains representing four species of Facklamia were isolated from blood cultures, an abscess, bone, cerebrospinal fluid, gall bladder, vaginal swab, and one unknown source. Cultures were tested against 15 antimicrobial agents by using the broth microdilution MIC method. Reduced susceptibilities to the beta lactams, erythromycin, clindamycin, trimethoprim-sulfamethoxazole, and tetracycline were found. These results indicate that the susceptibilities of the Facklamia species are varied and that some strains have resistance patterns which may present difficulty in managing systemic infections in patients.

Lacroix J.M. et al. *Detection and incidence of the tetracycline resistance determinant tet(M) in the microflora associated with adult periodontitis.* J Periodontol. 1995; 66(2) : 102-8.p Abstract: Subgingival plaque samples were collected from 68 patients with adult periodontitis, enumerated on Trypticase-soy blood agar plates, with and without tetracycline at 4 micrograms/ml, and incubated anaerobically for 5 days. Each different colony morphotype was enumerated, and a representative colony was subcultured for identification and examined for the tetracycline resistance gene tet(M). Both PCR amplification and DNA hybridization, using a fragment of tet(M) from Tn1545, were used to detect tet(M). The PCR primers (5'-GACACGCCAGGACATATGG-3' and 5'-TGCTTTC-CTCTTGTTCGAG-3') were chosen to amplify a 397 bp region of tet(M). Tetracycline-resistant bacteria represented approximately 12% of the total viable count. The percentage of tet(M)-positive bacteria in the tetracycline resistant microflora varied from < or = 0.05 to 83% (mean of 10%). tet(M) was detected in 60% of 204 tetracy-

cline-resistant strains subcultured and identified. The tet(M) containing strains consisted of streptococci (55%, mainly S. intermedius, S. oralis, S. sanguis, and Streptococcus SM4), Actinomyces D01 (14%), Bifidobacterium D05 (11%), and Veillonella spp. (10%). Tetracycline-resistant strains in which tet(M) was not detected included the Prevotella and Bacteroides species (41%, mainly Bacteroides D28, P. intermedia, P. nigrescens, and P. oris). These results suggest that tet(M) is widely spread in the adult periodontal microflora, but it appears, with the exception of S. intermedius, to be mainly associated with microorganisms not considered to be periodontopathogens. Assessment of other tetracycline-resistant genes in oral organisms is needed to fully evaluate the nature of resistance to this antibiotic in the oral flora.

Ladd M.E. et al. *Reduction of resonant RF heating in intravascular catheters using coaxial chokes.* Magn Reson Med. 2000; 43(4) : 615-9.p Abstract: The incorporation of RF coils into the tips of intravascular devices has been shown to enable the localization of catheters and guidewires under MR guidance. Furthermore, such coils can be used for endoluminal imaging. The long cable required to connect the coil with the scanner input inadvertently acts as a dipole antenna which picks up RF energy from the body coil during transmit. Currents are induced on the cable which can lead to localized heating of surrounding tissue. Cables of various lengths were measured to determine if a resonance in the heating as a function of cable length could be found. Coaxial chokes with a length of lambda/4 were added to coaxial cables to reduce the amplitude of the currents induced on the cable shield. A 0.7-mm diameter triaxial cable, small enough to fit into a standard intravascular device, was developed and measured both with and without a coaxial choke. It is demonstrated that resonant heating does occur and that it can be significantly reduced by avoiding a resonant length of cable and by including coaxial chokes on the cable.

Laessig K.A. et al. *The role of resistance testing in clinical trial design and product labelling: a regulatory perspective.* Antivir Ther. 2000; 5(1) : 77-83.p Abstract : Assays that attempt to characterize HIV susceptibility or resistance are among the latest technologies that are likely to impact HIV clinical trial design, antiretroviral drug development and patient management. However, at present the Food and Drug Administration (FDA) have yet to approve any phenotypic or genotypic HIV resistance assay and the role of resistance testing in clinical management of patients and in drug development is ill defined. In November 1999, the Division of Antiviral Drug Products at the FDA convened a meeting of its advisory committee to consider the available information about HIV resistance testing, and to generate some recommendations about how these assays could be utilized in antiretroviral drug development. In addition, the committee was presented with several hypothetical regulatory scenarios in order to illustrate how HIV resistance testing might be incorporated in antiretroviral drug development and drug labelling. In this article, we discuss the regulatory history of resistance testing in antimicrobial drug development, the current use of resistance testing for antiretrovirals, as well as a summary of the hypothetical scenarios that were presented to the committee and the discussion of the committee members regarding those scenarios.

Laguna P. et al. *[Abscess of the psoas muscle: analysis of 11 cases and review of the literature].* Enferm Infecc Microbiol Clin. 1998; 16(1) : 19-24.p Abstract: BACKGROUND: Abscess of the psoas muscle (AP) is an infrequent disease of difficult diagnosis, developing spontaneously (primary AP) or by extension of a subjacent infection (secondary AP). In recent years changes have been observed in its etiology, advances in its diagnosis and modifications in the treatment schedules. METHODS: The cases of AP diagnosed from 1983-1996 were retrospectively studied. RESULTS: The cases included 11 AP, 5 (45%) primary and 6 (55%) secondary, of which the source of origin were: spondylitis in four, sacroiliac arthritis in one and intestinal in another. The clinical presentation was characterized by its prolonged course (evolution of symptoms greater than 30 days in 64% of the cases), with the most frequent symptoms being flank/abdominal pain (82%) and hip/inguinal pain (45%), with fever being presented in only 36%. The diagnostic profitability of echography and computerized tomography (CT) were 57% (4/7) and 91% (10/11), respectively. One case was diagnosed with magnetic resonance. The causal microorganisms were: Mycobacterium tuberculosis (36% of the cases), Staphylococcus aureus (18%), polymicrobian flora (18%) and Salmonella enteritidis, Streptococcus intermedius and Escherichia coli in 9% each. Eight cases (73%) underwent percutaneous (5 cases) and surgical (3 cases) drainage, with the evolution being favorable in 10 (91%) and death in one despite adequate medicosurgical treatment. CONCLUSIONS: The clinical presentation of AP is often unspecific, thereby delaying its diagnosis, and thus, CT is the procedure of choice. The tuberculous etiology continues to be frequent in our environment. Ultrasonographic or CT guided percutaneous drainage is a valid therapeutic alternative versus surgery.

Laguno M. et al. *Pacemaker-related endocarditis. Report of 7 cases and review of the literature.* Cardiology. 1998; 90(4) : 244-8.p Abstract: We report on 7 patients with pacemaker endocarditis diagnosed during the workup of long-standing fever. Persistent positive blood cultures and echocardiography led to the diagnosis in 6 patients whereas autopsy was diagnostic in another. Causative microorganisms were Staphylococcus epidermidis (3), Staphylococcus lugdunensis (1), Pseudomonas aeruginosa (1), Streptococcus bovis (1), and Streptococcus mitis-Streptococcus sanguis (1). Pulmonary embolism was present in nearly 50% of the cases, a figure clearly higher than previously reported. In all but 1 case the initial medical approach was not successful, and thus the pacing system was finally removed. None of the cases relapsed after the removal. We have reviewed the literature regarding pacemaker endocarditis, particularly with respect to treatment.

Lai K.K. *Treatment of vancomycin-resistant Enterococcus faecium infections.* Arch Intern Med. 1996; 156(22) : 2579-84.p Abstract: OBJECTIVE: To define the clinical characteristics of patients infected with vancomycin-resistant enterococci (VRE) and the outcome of the infections without the availability of effective antimicrobial therapy. METHODS: Charts of 28 patients with VRE infections were reviewed for demographics, clinical findings at the time of isolation of VRE, underlying medical problems, surgical procedures, invasive devices, treatment with antimicrobial agents, microbiological data, and patients' responses and outcomes. RESULTS: The infections included 6 cases of bacteremia, 9 surgical site infections (SSIs), 4 cases of peritonitis, 2 pelvic abscesses, 7 urinary tract infections (UTIs), and 2 soft tissue infections (STIs). Four of the 6 bacteremia cases were central-line related and resolved with line removal alone; 1 was treated with a combination product of quinupristin and dalfopristin (Synercid) and 1 had persistent bacteremia in the presence of a ventriculoperitoneal shunt. Seven of 9 SSIs resolved with surgical debridement and 2 of the 9 patients received antibiotics for organisms other than VRE. Similarly, 2 patients with STIs were treated with local debridement and antibiotics directed at organisms other than VRE and 2 patients with pelvic abscesses were treated with drainage and surgical debridement with antibiotics directed at other organisms; the infections resolved completely. Patients with peritonitis were treated with removal of their Tenckhoff catheters, drainage, and irrigation and 1 patient was treated with quinupristin-dalfopristin; 3 of 4 patients were cured. Two of 7 patients with UTIs were treated with nitrofurantoin and their urine cultures showed no growth after treatment; however, most patients with UTIs experienced resolution despite a lack of specific antimicrobial therapy. CONCLUSIONS: Although no antimicrobial agents are currently available for VRE infections, VRE line-related bacteremias could be treated by line removal alone. Surgical site infections, STIs, and abscesses could be managed by surgical debridement and drainage without specific antimicrobial agents against VRE and UTIs could

be resolved with nitrofurantoin or removal of Foley catheters. Removal of foreign devices, debridement, and surgical drainage seemed to be important in the resolution ofVRE infections.

Lai S.W. et al. *Acinetobacter baumannii bloodstream infection: clinical features and antimicrobial susceptibilities of isolates.* Kao Hsiung I Hsueh Ko Hsueh Tsa Chih. 1999; 15(7) : 406-13.p Abstract: The number of nosocomial infections caused by Acinetobacter baumannii has increased in recent years. The purposes of this study are to discover the risk factors of transmission to prevent the nosocomial infection of A. baumannii. We retrospectively studied 36 patients with A. baumannii bacteremia at China Medical College Hospital from January 1996 to December 1997. There were 23 males and 13 females. All bacteremia were acquired nosocomially. Malignancy (n = 8) and intracranial hemorrhage (n = 6) were the most common underlying diseases. Only one patient on arterial line disclosed intraarterial catheter-related A. baumannii bacteremia and 3 patients had evidence of A. baumannii pneumonia. Twenty-one patients (58%) had central venous catheters in place at the onset of bacteremia, but none was proven to be catheter-related infection. There were 32 patients (89%) with unknown portal of entry. Multivariate logistic regression analysis revealed that potential risk factors related to A. baumannii bacteremia were prior antimicrobial therapy ($P < 0.05$). The most common clinical features of A. baumannii bacteremia were, in descending order, fever, leukocytosis, thrombocytopenia and hypotension. Eleven patients (30.6%) died directly from A. baumannii bacteremia. All isolates were resistant to ampicillin, cephalothin, cefonicid and moxalactam. The most alarming evidence was that 19% of isolates showed resistance to imipenem. Our findings emphasized that A. baumannii bacteremia had the following characteristics: usually acquired nosocomially, unknown portal of entry, and high multiresistance, especially the increasing resistance rate to imipenem. Imipenem must be reserved as a last-line agent to treat A. baumannii infections, so we want to suggest that the treatment of choice for A. baumannii is gentamicin, amikacin or ceftazidime.

Laing F.P. et al. *Molecular epidemiology of Xanthomonas maltophilia colonization and infection in the hospital environment.* J Clin Microbiol. 1995; 33(3) : 513-8.p Abstract: Between April 1992 and December 1993, 80 Xanthomonas maltophilia isolates were collected from 63 patients in three acute-care hospitals in Calgary, Alberta, Canada. On the basis of Centers for Disease Control and Prevention definitions, 48 patients had nosocomial and 15 had community-acquired X. maltophilia. Thirty-eight of the patients were colonized and 25 were infected. Sixty-four percent of patients who acquired X. maltophilia in the intensive care unit (ICU) became infected, whereas 32% of patients in a non-ICU setting became infected. ICU patients tended to be hospitalized for a shorter period of time than non-ICU patients before the onset of X. maltophilia infection. Regardless of being colonized or infected, all patients had debilitating conditions, with respiratory disease being the most common underlying illness (35%). Forty-two patients (88%) with hospital-acquired X. maltophilia received prior antibiotic therapy which included gentamicin, tobramycin, ceftazidime, piperacillin, and imipenem. Agar dilution MICs showed that patient isolates were resistant to these antimicrobial agents that patients had received. Pulsed-field gel electrophoresis of SpeI-digested genomic DNA revealed that six epidemiologically linked patient isolates from the ICU of one acute-care hospital had identical DNA profiles. In contrast, isolates from patients from the other two hospitals had unique genotype profiles (n = 57) regardless of the presence or absence of an epidemiologic association. In these patients there was genetic evidence against the acquisition of a resident hospital clone. These results indicate that pulsed-field gel electrophoresis can resolve genotypically distinct strains of X. maltophilia and, consequently, is a useful tool for evaluating nosocomial infections caused by X. maltophilia.

Lalitha M.K. et al. *E test as an alternative to conventional MIC determination for surveillance of drug resistant Streptococcus pneumoniae.* Indian J Med Res. 1997; 106 : 500-3.p Abstract: A commercial E test was compared with the standard agar dilution method for the determination of minimum inhibitory concentration (MIC) of penicillin, erythromycin, chloramphenicol and cefotaxime for 36 strains of Streptococcus pneumoniae from patients with invasive diseases. Additional strains were tested for MIC values for penicillin (6), erythromycin (14) and cefotaxime (13) for a better statistical evaluation. Besides, 5 reference standards with predetermined MIC values obtained from WHO pneumococcal reference center at Copenhagen, Denmark were tested for penicillin and erythromycin, for quality assessment using both agar dilution as well as E test methods. An overall agreement within +/- 2 dilutions was noted for 97 per cent of the strains tested for all the antimicrobials. A high degree of correlation was noted for erythromycin (r = 1), penicillin (r = 0.99), chloramphenicol (r = 0.95) and cefotaxime (r = 0.9). In MIC determination of a single antimicrobial for diagnostic purpose, E test was found to be more cost effective than conventional agar dilution method. E test was simple to perform, easy to interpret and a valid method for MIC determination of antimicrobials for S. pneumoniae in our center.

Lam S. et al. *The challenge of vancomycin-resistant enterococci: a clinical and epidemiologic study.* Am J Infect Control. 1995; 23(3) : 170-80.p Abstract: BACKGROUND: Vancomycin-resistant enterococci have been recovered with increasing frequency from hospitalized patients. Risk factors, mode of nosocomial transmission, extent of colonization in hospitalized patients, and treatment options for these organisms have not been completely delineated. METHODS: We studied 53 patients (group A) with vancomycin-resistant enterococci isolated from various clinical specimens and also surveyed for vancomycin-resistant enterococci in stool specimens submitted for Clostridium difficile toxin assays (group B). Stool specimens submitted for identification of bacterial pathogens and stool specimens from hospital employees were also analyzed for vancomycin-resistant enterococci. RESULTS: Seventy-six isolates of vancomycin-resistant enterococci were recovered in group A. Five of these patients harbored vancomycin-resistant enterococci on admission. Fifty-three of 289 group B stool specimens submitted for C. difficile toxin assays yielded vancomycin-resistant enterococci. Cephalosporins and vancomycin were the most common antimicrobial agents received by both groups of patients. Enterococcus faecium isolates were more resistant than Enterococcus faecalis isolates to antimicrobial agents. All isolates exhibited high-level aminoglycoside resistance and were not beta-lactamase producers. There were at least 15 different molecular clones of E. faecium and three of E. faecalis. Vancomycin-resistant enterococcal bacteremia was associated with a 100% in-hospital mortality rate. CONCLUSIONS: Multidrug-resistant and vancomycin-resistant enterococci have become important nosocomial pathogens that are difficult to treat. Vancomycin-resistant enterococcal bacteremia was associated with a poor prognosis. We found a high rate of colonization in patients with suspected C. difficile toxin colitis. Judicious use of vancomycin and broad-spectrum antibiotics is recommended, and strict infection control measures must be implemented to prevent nosocomial transmission of these organisms.

Lamari F. et al. *Determination of slime-producing S. epidermidis specific antibodies in human immunoglobulin preparations and blood sera by an enzyme immunoassay: correlation of antibody titers with opsonic activity and application to preterm neonates.* J Pharm Biomed Anal. 2000; 23(2-3) : 363-74.p Abstract: Slime-producing Staphylococcus epidermidis is responsible for severe infections in immunocompromised patients and, particularly, in premature infants who are transiently deficient in IgG. A sulfated polysaccharide with molecular mass of 20-kDa (20-kDa PS) has been recognized as the major polysaccharide component and antigenic determinant of S. epidermidis extracellular slime layer. The presence of adequate amounts of antibodies to 20-kDa PS in patients' sera would be of importance to prevent or treat slime-producing S. epidermidis bacteremia. Administration of intravenous immunoglobulin (IVIG) is considered to be a reasonable IgG

replacement therapy and has been widely used to prevent or treat neonatal sepsis. Clinical trials have shown conflicting results on the efficacy of IVIGs and this phenomenon has been attributed to the variability of IVIG preparations in the content and opsonic activity of IgG against microorganisms of clinical importance. Monitoring of antibodies to distinct bacterial macromolecules, which are species-specific and responsible for bacterial infections, has not been performed previously. A highly precise and repeatable enzyme immunoassay was developed to determine quantitatively the levels of antibodies against the 20-kDa PS of S. epidermidis slime. The amount of 20-kDa PS specific antibodies found in 27 lots of an IVIG preparation (Sandoglobulin) correlated well with their in vitro opsonic activity against slime-producing S. epidermidis. The majority of lots (75%) having titers higher than 200 units/ml showed significant opsonic activity (50-75%) towards slime-producing S. epidermidis. Sandoglobulin lots with titers higher than 200 units/ml of 20-kDa PS specific IgG were administered as a prophylactic agent to low-birth weight (lower than 1700 g) preterm neonates immediately after birth. The levels of total and 20-kDa PS specific IgG in neonates' blood sera were significantly higher than those found in the control group, even 10 days after the last infusion. The rate of slime-producing S. epidermidis bacteremia in neonates who received IVIG was also considerably lower than those in the control group. The results of this study suggest that specific IgG titers estimated by the developed enzyme immunoassay may well be indicative of the IVIG opsonic activity against slime-producing S. epidermidis. Furthermore, administration of Sandoglobulin with titers higher than a cut-off value of 200 units/ml may significantly protect preterm neonates against slime-producing S. epidermidis bacteremia.

Lamas C.C. et al. *Hospital acquired native valve endocarditis: analysis of 22 cases presenting over 11 years.* Heart. 1998; 79(5) : 442-7.p Abstract: OBJECTIVE: To analyse hospital acquired infective endocarditis cases with respect to age, sex, clinical, laboratory, and echocardiographic features, predisposition, complications, surgery, mortality, and diagnostic criteria. DESIGN: Prospective cohort study. SETTING: Teaching hospital. PATIENTS: A series of 200 patients with infective endocarditis presenting over 11 years, 168 with native valve infective endocarditis, of whom 22 acquired this infection in hospital. RESULTS: 22 (14%) of the 168 cases of native valve infection were hospital acquired. The most common pathogens were staphylococci (77%). Two thirds of patients had no cardiac predisposition; one third had end stage renal disease. The most common source of infection was vascular access sites (73%). Eleven patients died. In 11 cases, infective endocarditis was proven pathologically (six at necropsy, five during surgery) and analysis of these showed that 45% were classed as probable by the Beth Israel criteria, 73% as definite by the Duke criteria, and 91% as definite by our suggested modifications of the Duke criteria. Figures for the 11 cases not proven pathologically were 27%, 73%, and 91%, respectively. Five of the 22 cases (22%) were rejected by the Beth Israel criteria but none were rejected by the Duke criteria with or without our modifications. CONCLUSIONS: Hospital acquired infective endocarditis is difficult to diagnose. The Duke criteria have improved diagnostic sensitivity and our modifications have improved it further. Mortality is high but has been reduced by surgery. This serious infection could, in many cases, be prevented by improved care of intravascular lines and prompt removal when obviously infected.

Lambotte O. et al. *Nosocomial bacteremia in HIV patients: the role of peripheral venous catheters.* Infect Control Hosp Epidemiol. 2000; 21(5) : 330-3.p Abstract: A retrospective case-control study compared 40 human immunodeficiency virus (HV)-infected patients with 43 nosocomial bacteremias (NB) to 77 HIV-infected patients without NB. Presence of a peripheral venous catheter (PVC) was associated with occurrence of NB and was significantly more frequent in NB without an identified source. PVCs probably are an underestimated source of NB in HIV-infected patients.

Lamp K.C. et al. *Pharmacokinetics and pharmacodynamics of the nitroimidazole antimicrobials.* Clin Pharmacokinet. 1999; 36(5) : 353-73.p Abstract: Metronidazole, the prototype nitroimidazole antimicrobial, was originally introduced to treat Trichomonas vaginalis, but is now used for the treatment of anaerobic and protozoal infections. The nitroimidazoles are bactericidal through toxic metabolites which cause DNA strand breakage. Resistance, both clinical and microbiological, has been described only rarely. Metronidazole given orally is absorbed almost completely, with bioavailability > 90% for tablets; absorption is unaffected by infection. Rectal and intravaginal absorption are 67 to 82%, and 20 to 56%, of the dose, respectively. Metronidazole is distributed widely and has low protein binding (< 20%). The volume of distribution at steady state in adults is 0.51 to 1.1 L/kg. Metronidazole reaches 60 to 100% of plasma concentrations in most tissues studied, including the central nervous system, but does not reach high concentrations in placental tissue. Metronidazole is extensively metabolised by the liver to 5 metabolites. The hydroxy metabolite has biological activity of 30 to 65% and a longer elimination half-life than the parent compound. The majority of metronidazole and its metabolites are excreted in urine and faeces, with less than 12% excreted unchanged in urine. The pharmacokinetics of metronidazole are unaffected by acute or chronic renal failure, haemodialysis, continuous ambulatory peritoneal dialysis, age, pregnancy or enteric disease. Renal dysfunction reduces the elimination of metronidazole metabolites; however, no toxicity has been documented and dosage alterations are unnecessary. Liver disease leads to a decreased clearance of metronidazole and dosage reduction is recommended. Recent pharmacodynamic studies of metronidazole have demonstrated activity for 12 to 24 hours after administration of metronidazole 1 g. The post-antibiotic effect of metronidazole extends beyond 3 hours after the concentration falls below the minimum inhibitory concentration (MIC). The concentration-dependent bactericidal activity, prolonged half-life and sustained activity in plasma support the clinical evaluation of higher doses of metronidazole given less frequently. Metronidazole-containing regimens for Helicobacter pylori in combination with proton pump inhibitors demonstrate higher success rates than antimicrobial regimens alone. The pharmacokinetics of metronidazole in gastric fluid appear contradictory to these results, since omeprazole reduces peak drug concentration and area under the concentration-time curve for metronidazole and its hydroxy metabolite; however, concentrations remain above the MIC. Other members of this class include tinidazole, ornidazole and secnidazole. They are also well absorbed and distributed after oral administration. Their only distinguishing features are prolonged half-lives compared with metronidazole. The choice of nitroimidazole may be influenced by the longer administration intervals possible with other members of this class; however, metronidazole remains the predominant antimicrobial for anaerobic and protozoal infections.

Landa A.S. et al. *Recalcitrance of Streptococcus mutans biofilms towards detergent-stimulated detachment.* Eur J Oral Sci. 1999; 107(4) : 236-43.p Abstract: The biofilm mode of growth protects the plaque microorganisms against environmental attacks, such as from antimicrobials or detergents. Detergents have a demonstrated ability to detach initially adhering bacteria from enamel surfaces, but the ability of detergent components to detach plaque bacteria is not always obvious from in vivo experiments and reports on their clinical efficacy are inconsistent. It is likely that antimicrobials or detergents are unable to penetrate the plaque and reach the bacteria that actually link the plaque mass to the substratum surface. Attenuated total reflectance/Fourier transform infrared spectroscopy was used to measure the transport of sodium lauryl sulphate (SLS) through Streptococcus mutans HG 985 biofilms. The transport of SLS to the base of the S. mutans biofilms was not hindered, while moreover an accumulation of SLS near the base of the biofilms was found, suggesting that SLS was adsorbed to biofilm components. X-ray photoelectron spectroscopy confirmed the ability of S. mutans, grown on sucrose supplemented medium, to adsorb SLS, and simultaneously

indicated that exposure of cells to SLS might lead to a loss of surface proteins. Furthermore, experiments in a parallel-plate flow chamber demonstrated that initially adhering S. mutans HG 985 could be stimulated to detach by SLS, but that, depending on the growth stage of the biofilm, only maximally 27% of biofilm bacteria could be stimulated to detach by a 4% (w/v) SLS solution.

Landyshev S.I.u. *[Changes in the microflora of the sputum and the bronchoalveolar fluid in patients with acute and protracted pneumonias].* Probl Tuberk. 1996; (4) : 41-3.p Abstract: A quantitative technique was used to microbiological study of sputum in 110 patients with acute pneumonia and 56 with advanced pneumonia, in 38 of them, their bronchoalveolar lavage fluid was simultaneously examined. In acute pneumonia, Pneumococcus was most commonly (71.8%) cultured, frequently in combination with other microorganisms, mainly with Neisseria and Enterobacteriaceae. These patients were found to have higher pneumococcal cultivation rates (83.0%) in the bronchoalveolar lavage fluid. Following 3 weeks of etiotropic therapy, the pneumococcal cultivation rates dropped to 10.8%. Pneumococcus also occupied the leading place (69.6%) in the etiology of advanced pneumonia, Mycoplasma pneumoniae was detected by the indirect immunofluorescence test in 28.5% of patients. After 3-week therapy, the cultivation rates for Pneumococcus decreased to 23.0%, its association with other microbes being more frequently observed. At the same time there was a rise in the detection rate of Mycoplasma antigen, which could cause advanced pneumonia.

Langevin P.B. et al. *The potential for dissemination of Mycobacterium tuberculosis through the anesthesia breathing circuit.* Chest. 1999; 115(4) : 1107-14.p Abstract: BACKGROUND: Respiratory pathogens that pass through the anesthesia breathing system potentially can infect other patients. This study was designed to determine if bacteria can pass through contemporary anesthesia breathing systems and if the environment within the machine is hostile to these organisms. METHODS: Staphylococcus aureus, Pseudomonas aeruginosa, and Mycobacterium tuberculosis were nebulized into the expiratory limb of an anesthesia breathing circuit and collected from the inspiratory and expiratory limbs in an impinger system that provided a quantitative determination of the number of organisms entering the circuit and the number that would reach the patient in the inspiratory gas. Bacteria were collected before, during, and after nebulization. A second experiment determined if a saturated solution of soda lime was bactericidal. RESULTS: When the gas flow through the circuit was interrupted for < 1 h following the nebulization period, large numbers of microorganisms (1 x 10(3) to 1 x 10(5), around 100% of the nebulized organisms) were collected from the inspiratory gas. Soda lime itself was not bactericidal for any of the organisms tested, but solutions of this material with a pH of 12 were bactericidal. CONCLUSION: Cross contamination between patients may occur unless the gas flow through the anesthesia breathing system is interrupted for > 1 h.

LaPointe G. et al. *Use of a polymerase-chain-reaction-amplified DNA probe from Pseudomonas putida to detect D-hydantoinase-producing microorganisms by direct colony hybridization.* Appl Microbiol Biotechnol. 1995; 42(6) : 895-900.p Abstract: Pseudomonas putida strain DSM 84 produces N-carbamyl-D-amino acids from the corresponding D-5-monosubstituted hydantoins. The sequence of the D-hydantoinase gene from this strain (GenBank accession number L24157) was used to develop a DNA probe of 122 base pairs (bp) that could detect D-hydantoinase genes in other bacterial genera by DNA and by colony hybridization. Under conditions tolerating 32% mismatch, the probe was specific for all strains that expressed D-hydantoinase activity. These include Pseudomonadaceae of all rRNA groups, and bacteria belonging to the genera Agrobacterium, Serratia, Corynebacterium, and Arthrobacter. Environmental sampling was simulated by screening a mixture of unknown microorganisms from commercial inocula for the biodegradation of industrial, municipal and domestic wastes. The 122-bp probe was specific for microorganisms that subsequently demonstrated D-hydantoinase activity. Bacterial species from four different genera were detected, which were Pseudomonas, Klebsiella, Enterobacter, and Enterococcus.

Lara Sánchez J. et al. *Prevalencia de la infección por el virus de la hepatitis B (VHB) en mujeres embarazadas / Prevalence of the hepatitis B virus infection in pregnant women.* Enferm. Infecc. Microbiol. 1995; 15(2) : 68-71.p Abstract: De los diferentes virus de la hepatitis, el tipo B (VHB) es el que presenta una mayor transmisión perinatal. Una característica importante de la infección vertical por el VHB es el alto riesgo de progresar hasta una infección crónica. Se estudiaron los sueros de mujeres embarazadas que acudieron para realizarse estudios básicos de laboratorio de control prenatal, en b£squeda de marcadores serológicos de infección por el VHB. Se analizaron 1,443 sueros, identificándose cuatro positivos para el AgsHB y 28 con anticuerpos IgG contra el Ag core, lo que proporcionó una prevalencia de madres portadoras de la AgsHB del 0.27% y de pacientes con antiHBc de 1.95%. No se detectó ninguna mujer con Ige ni con anticuerpos IgM contra el Ag core. La importancia del escrutinio de embarazadas en b£squeda del AgsHB es identificar a las pacientes cuyos recién nacidos deben ser inmunizados contra el VHB y así reducir la posibilidad de transmisión(AU).

Laraki N. et al. *Structure of In31, a blaIMP-containing Pseudomonas aeruginosa integron phyletically related to In5, which carries an unusual array of gene cassettes.* Antimicrob Agents Chemother. 1999; 43(4) : 890-901.p Abstract: The location and environment of the acquired blaIMP gene, which encodes the IMP-1 metallo-beta-lactamase, were investigated in a Japanese Pseudomonas aeruginosa clinical isolate (isolate 101/1477) that produced the enzyme. In this isolate, blaIMP was carried on a 36-kb plasmid, and similar to the identical alleles found in Serratia marcescens and Klebsiella pneumoniae clinical isolates, it was located on a mobile gene cassette inserted into an integron. The entire structure of this integron, named In31, was determined. In31 is a class 1 element belonging to the same group of defective transposon derivatives that originated from Tn402-like ancestors such as In0, In2, and In5. The general structure of In31 appeared to be most closely related to that of In5 from pSCH884, suggesting a recent common phylogeny for these two elements. In In31, the blaIMP cassette is the first of an array of five gene cassettes that also includes an aacA4 cassette and three original cassettes that have never been described in other integrons. The novel cassettes carry, respectively, (i) a new chloramphenicol acetyltransferase-encoding allele of the catB family, (ii) a qac allele encoding a new member of the small multidrug resistance family of proteins, and (iii) an open reading frame encoding a protein of unknown function. All the resistance genes carried on cassettes inserted in In31 were found to be functional in decreasing the in vitro susceptibilities of host strains to the corresponding antimicrobial agents.

Lark R.L. et al. *Antimicrobial resistance in community-acquired respiratory tract pathogens.* Compr Ther. 1999; 25(1) : 20-9.p Abstract: Antimicrobial resistance among common respiratory pathogens has become a significant problem. However, there remain multiple treatment options, including the newer macrolides, third-generation cephalosporins, beta-lactam/beta-lactamase inhibitor antibiotics, and the newer fluoroquinolones.

Larsen T. et al. *Evaluation of a new device for sterilizing dental high-speed handpieces.* Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1997; 84(5) : 513-6.p Abstract: Dental high-speed turbines and handpieces can take up and expel microorganisms during operation and thus need regular sterilization. This study established a method for validating devices used to sterilize high-speed turbines and handpieces. The air and water channels and turbine chambers were contaminated with suspensions of Streptococcus salivarius or endospores of Bacillus stearothermophilus. The effect of flushing and/or autoclaving performed by a new device combining both procedures was evaluated by counting the number of viable bacteria recovered from

these devices. Further, the effect on clinically used handpieces was evaluated. In an initial experiment, the device partially reduced S. salivarius, and the endospores survived. In a second experiment, a 5 to 6 log reduction of S. salivarius in air and water channels was obtained. No growth was observed in clinically used high-speed handpieces, and both S. salivarius and endospores were eliminated from the turbine chambers. Thus, the method of validation proved capable of discriminating between different levels of bacterial reduction.

Larsen T. et al. *Development of a flow method for susceptibility testing of oral biofilms in vitro.* APMIS. 1995; 103(5) : 339-44.p Abstract: Bacteria in biofilms are known to be more resistant than bacteria in batch cultures to antimicrobial agents. The purpose of the present study was to develop a flow method for formation of oral biofilms permitting susceptibility testing of plaque bacteria. A brain heart infusion (BHI) Streptococcus sanguis 804 culture was pumped through a modified Robbins Device (MRD) with 25 exchangeable silicone disks at 40 ml/h. After 24-48 h disks were removed and biofilm cells dispersed by vortex mixing and low-output ultrasonication. Colony forming units (cfu)/cm2 were determined after aerobic incubation on blood agar plates. Optimal biofilm formation was found after growth for 48 h at 37 degrees C in BHI + 1% sucrose, using saliva-coated silicone disks in inverted MRDs, yielding on average 4.4 x 10(5) cfu/cm2. Similar results were obtained for S. sanguis ATCC 10556 and five clinical isolates. Testing the susceptibility of S. sanguis to chlorhexidine gluconate showed increased resistance of biofilms compared to batch culture. Thus an appropriate biofilm model for susceptibility testing of oral microorganisms has been established.

Larson E.L. et al. *Changes in bacterial flora associated with skin damage on hands of health care personnel.* Am J Infect Control. 1998; 26(5) : 513-21.p Abstract: In a prospective observational study of 40 nurses (20 with diagnosed hand irritation and 20 without), nurses with damaged hands did not have higher microbial counts (P =.63), but did have a greater number of colonizing species (means: 3.35 and 2.63, P =.03). Although numbers were small, nurses with damaged hands were significantly more likely to be colonized with Staphylococcus hominis (P =.03). Fifty-nine percent of S hominis isolates from nurses with damaged hands were resistant to methicillin compared with 27% of isolates from those with healthy skin (P =.14). Twenty percent of nurses with damaged hands were colonized with Staphylococcus aureus compared with none of the nurses with normal hands (P =.11). Nurses with damaged hands were also twice as likely to have gram-negative bacteria (P =.20), entercocci (P =.13), and Candida (P =.30) present on the hands. Antimicrobial resistance of the coagulase-negative staphylococcal flora (with the exception of S hominis) did not differ between the 2 groups, nor did a trend toward increasing resistance exist when compared with other studies during the past decade. Skin moisturizers and protectant products were used almost universally by nurses at work, primarily products brought from home. Efforts to improve hand condition are warranted because skin damage can change microbial flora. Such efforts should include assessment or monitoring of hand care practices, formal institutional policy adoption and control of use of skin protectant products or lotions, and prudent use of latex gloves or more widespread use of powder-free and nonlatex products.

Larson M.J. et al. *Can urinary nitrite results be used to guide antimicrobial choice for urinary tract infection?* J Emerg Med. 1997; 15(4) : 435-8.p Abstract: Enterococcus is unable to reduce nitrates and is also considered clinically resistant to trimethoprim/sulfamethoxazole (TMP/SMX), the drug of choice for uncomplicated urinary tract infection (UTI). The purpose of this study was to determine whether urinalysis nitrite results can be used to guide antimicrobial therapy when treating UTI in the emergency department (ED). A retrospective chart review examined 159 university hospital ED outpatients who had signs or symptoms of UTI and had a urinalysis with positive culture. Patients were categorized into two groups based on nitrite results. The proportion of isolates sensitive to TMP/SMX in each group was compared by using a two-sample z-test. Eighty-six urinalyses were nitrite positive: 67 (78%) contained TMP/SMX-sensitive isolates. Seventy-three urinalyses were nitrite negative; 60 (82%) contained sensitive isolates. There was no statistically significant difference in the proportion of isolates sensitive to TMP/SMX. Thus, we conclude that emergency physicians should not adjust antibiotic therapy for UTI based on nitrite results.

LaRue G.D. *Efficacy of ultrasonography in peripheral venous cannulation.* J Intraven Nurs. 2000; 23(1) : 29-34.p Abstract: A retrospective study of 431 patients who had peripherally inserted midclavicular or central catheters placed during a consecutive 13-month period using the conventional landmark method for placement was compared with a second group of 326 patients, who during a 12-month period had such catheters placed using ultrasonography. The data demonstrate a 42% decrease in the number of needle penetrations needed to successfully cannulate veins when ultrasound was used during placement. There is a 26% greater chance of successful cannulation of the vein on the first attempt with ultrasound-guided placements than with those using the traditional landmark method.

Latronico N. et al. *Limits of intermittent jugular bulb oxygen saturation monitoring in the management of severe head trauma patients.* Neurosurgery. 2000; 46(5) : 1131-8; discussion 1138-9.p Abstract: OBJECTIVE: To evaluate, in a prospective, observational study, whether bilateral monitoring of jugular bulb oxyhemoglobin saturation (SjO2), in addition to standard monitoring, results in modification of the management of severe head trauma. METHODS: The patients underwent bilateral jugular bulb cannulation and observation at 8-hour intervals, during which SjO2 was measured and the neurological condition and physiological variables were assessed. The study group was responsible for evaluating whether the physician's decision-making process was influenced by the detection of SjO2 abnormalities. The SjO2 discrepancy in simultaneous bilateral samples was also evaluated to determine whether it interfered with the interpretation of data and with clinical decision-making. The SjO2-related complications were monitored. RESULTS: Thirty patients underwent 319 observations. In 96% of patients, SjO2 was normal or high and had no influence on the diagnostic or therapeutic strategies. Treatment decisions were dictated by changes in clinical status and in intracranial and cerebral perfusion pressure. When these parameters were abnormal, treatment was administered, even if SjO2 was normal (101 observations). Conversely, when SjO2 was the only detected abnormality (34 observations), no treatment was administered. Abnormally low SjO2 values, caused by hypovolemia and hypocapnia, were detected in 3.4% of observations and actually modified the management. The discrepancies in simultaneous bilateral samples were substantial and gave rise to relevant interpretation problems. Fifteen percent of jugular catheters showed evidence of bacterial colonization. CONCLUSION: Intermittent SjO2 monitoring did not substantially influence the management of severe head trauma. Therefore, recommendation for its routine use in all patients seems inadvisable, and indications for this invasive method should no longer be defined on the basis of experts' opinions, but rather on randomized, prospective studies.

Laura R. et al. *Comparison of two different time interval protocols for central venous catheter dressing in bone marrow transplant patients: results of a randomized, multicenter study. The Italian Nurse Bone Marrow Transplant Group (GITMO).* Haematologica. 2000; 85(3) : 275-9.p Abstract: BACKGROUND AND OBJECTIVE: Care of central venous catheter (CVC) in patients undergoing bone marrow transplantation (BMT) raises significant problems related to the high risk of local infections due to the immunodeficient status, which in itself is a predisposing factor for systemic blood-stream infections. Although frequent changes of CVC dressing might theoretically reduce the incidence of infections, they are also accompanied by significant skin toxicity and patient discomfort. No study has yet addressed these

points. The objective of this study was to compare two different time interval protocols for CVC dressing in order to assess the effects on local infections and toxicity. DESIGN AND METHODS: In a multicenter study, 399 bone marrow transplant (BMT) patients with a tunneled CVC (Group A, 230 pts) or a non-tunneled one (Group B, 169 pts) were randomly allocated to receive CVC dressing changes every 5 or 10 days, if belonging to Group A, or 2 or 5 days, if in Group B. Transparent, impermeable polyurethane dressings were used for all patients. The rate of local infections at the site of CVC insertion was assessed by microbiological assays every 10 days, while the severity of skin toxicity was measured according to the ECOG scale. RESULTS: Sixty-five per cent of enrolled patients were finally evaluable. Patients (in both Groups) receiving CVC dressing changes at longer intervals did not show a significant increase in the rate of local infections, while those who received dressing every 2 days had a significant increase in local skin toxicity. Longer intervals were accompanied by a reduction in costs. INTERPRETATION AND CONCLUSIONS: The results of this study demonstrate that the increase in time interval between CVC dressing changes in BMT patients did not raise the risk of local infections, while significantly reducing patient discomfort and costs.

Lauterwein M. et al. *In vitro activities of the lichen secondary metabolites vulpinic acid, (+)-usnic acid, and (-)-usnic acid against aerobic and anaerobic microorganisms.* Antimicrob Agents Chemother. 1995; 39(11) : 2541-3.p Abstract: Secondary metabolites of different species of lichen were tested for their activities against a variety of microbial species. While gram-negative rods and fungi were not inhibited by these compounds, Staphylococcus aureus, Enterococcus faecalis, Enterococcus faecium, and some anaerobic species (Bacteroides and Clostridium species) were susceptible at the concentrations tested. Vulpinic acid generally was less active than usnic acid, regardless of its stereochemistry. The susceptibility to usnic acid was not impaired in clinical isolates of S. aureus resistant to methicillin and/or mupirocin.

Laverdiere M. et al. *Trends in antibiotic resistance of staphylococci over an eight-year period: differences in the emergence of resistance between coagulase positive and coagulase-negative staphylococci*. Microb Drug Resist. 1998; 4(2) : 119-22.p Abstract: The antimicrobial susceptibilities of 1058 Staphylococcus aureus and 2,163 coagulase-negative staphylococci (CNS) isolates obtained from clinical specimen between 1988 and 1995, were determined against 13 anti-staphylococcal antibiotics. During the study period the resistance of Staphylococcus aureus to ciprofloxacin, ceftazidime, and norfloxacin increased significantly by 7%, 4%, and 6%, respectively ($p < or = 0.001$). By comparison, the antibiotic resistance of CNS to ceftazidime, oxacillin, norfloxacin, ciprofloxacin, fusidic acid, and cefoxitin increased by 20%, 17%, 15%, 14%, 12% and 10%, respectively ($p < or = 0.001$). Invasive and non-invasive S. aureus had similar antibiotic resistance, whereas CNS invasive isolates were more resistant than noninvasive isolates to every antibiotics, except vancomycin and fusidic acid. These differences were significant ($p < 0.001$) for oxacillin, cefoxitin, and clindamycin. Our observations confirm that staphylococci and particularly CNS isolates show an important rate of increased resistance to the standard antimicrobials used for therapy, and that the rate of emergence of resistance differ considerably between coagulase-positive and coagulase-negative staphylococci.

Lavin B.S. *Antibiotic cycling and marketing into the 21st century: a perspective from the pharmaceutical industry.* Infect Control Hosp Epidemiol. 2000; 21(1 Suppl) : S32-5.p Abstract: Before the development of the first antimicrobial agents, bacteria already had demonstrated an ability to adapt to stress in the environment, resulting in the development of resistance that often makes the prevailing antibiotic treatment ineffective. The response to antimicrobial resistance in the medical community has been to use new or alternative antibiotics not previously used against the resistant bacteria. The pharmaceutical industry has responded to the resistance problem by producing newer antibiotics, either as modifications of currently existing compounds or as combinations of compounds that may inhibit or bypass the bacterial resistance mechanisms. The development of new antibiotics is a lengthy and costly process. To be successful, the pharmaceutical industry must anticipate the changing needs of the medical community, as well as the dynamic process of antimicrobial resistance. The marketing of new antimicrobial agents must be adaptable to the potential environmental pressures that induce bacterial resistance in order to ensure the longevity of the agents.

Lawrynowicz-Paciorek M. et al. *[Evaluation of the usefulness of selected commercial systems for identification of Staphylococcus species].* Med Dosw Mikrobiol. 1998; 50(3-4) : 161-9.p Abstract: The aim of the study was the assessment of the usefulness of commercially available systems for rapid identification of staphylococci. API STAPH (bioMerieux, France), ID 32 STAPH (bioMerieux, France), GPL (HTL, Poland) and Staph-Zym (Rosco, Denmark). The identifications were carried out according to producer's instruction. The material for the study comprised 76 staphylococcal strains, coagulase-positive and coagulase-negative. The strains were isolated from throat, nasal, wound, bone slivers, pus and blood of inpatients and from throat and nasal swabs of outpatients. Besides that, for the study staphylococcal strains were obtained from the American Collection of Typical Cultures (ATCC) and from the Polish Collection of Microorganisms (PCM). All tested strains were identified on the basis of classic biochemical tests. In the light of obtained results it is concluded that the commercial system most suitable for identification of staphylococci was ID 32 STAPH (bioMerieux), which has a wide spectrum of species identifiable with it and the highest percent (95%) of correctly identified species. The least suitable system was the GPL 15 (HTL, Poland).

Lawton R.M. et al. *Practices to improve antimicrobial use at 47 US hospitals: the status of the 1997 SHEA/IDSA position paper recommendations. Society for Healthcare Epidemiology of America/Infectious Diseases Society of America*. Infect Control Hosp Epidemiol. 2000; 21(4) : 256-9.p Abstract: OBJECTIVE: To determine the status of programs to improve antimicrobial prescribing at select US hospitals. DESIGN: Cross-sectional survey. PARTICIPANTS AND SETTING: Pharmacy and infection control staff at all 47 hospitals participating in phase 3 of Project Intensive Care Antimicrobial Resistance Epidemiology. RESULTS: All 47 hospitals had some programs to improve antimicrobial use, but the practices reported varied considerably. All used a formulary, and 43 (91%) used it in conjunction with at least one of the other three antimicrobial-use policies evaluated: stop orders, restriction, and criteria-based clinical practice guidelines (CPGs). CPGs were reported most commonly (70%), followed by stop orders (60%) and restriction policies (40%). Although consultation with an infectious disease physician (70%) or pharmacist (66%) was commonly used to influence initial antimicrobial choice, few (40%) reported a system to measure compliance with these consultations. CONCLUSIONS: In most hospitals surveyed, practices to improve antimicrobial use, although present, were inadequate based on recommendations in a Society for Healthcare Epidemiology of America and Infectious Disease Society of America joint position paper. There is room to improve antimicrobial-use stewardship at US hospitals.

Layton M.C. et al. *A mixed foodborne outbreak with Salmonella heidelberg and Campylobacter jejuni in a nursing home.* Infect Control Hosp Epidemiol. 1997; 18(2) : 115-21.p Abstract: OBJECTIVE: To investigate a mixed Salmonella heidelberg and Campylobacter jejuni foodborne outbreak in a nursing home. DESIGN: Retrospective cohort study with a nested case-control design. Cases were defined by positive stool-culture results. Controls needed to be both asymptomatic and culture-negative. SETTING AND PATIENTS: Residents of a 580-bed nursing home in Brooklyn, New York. RESULTS: Of the 580 residents, 119 (21%) developed illness. Of the 93 symptomatic patients who submitted specimens, cultures were

positive for S heidelberg in 24 (26%), C jejuni in 14 (15%), and both microorganisms in 25 (27%). Only the pureed diet was associated highly with infection by either Salmonella (odds ratio [OR], 17.6; 95% confidence interval [CI95], 4.8-68.7; P <.001), Campylobacter (OR, 13.3; CI95, 3.2-59.2; P <.001), or both organisms (OR, 8.9; CI95, 2.7-30.3; P <.001). Among the 42 pureed foods served during the 5 days before the outbreak, five meat or poultry items were associated most strongly with culture positivity. Of these five meat items, only a chopped-liver salad was implicated by the two employees reporting illness. A reported food-handling error occurred when ground, cooked chicken livers were placed in a bowl containing raw chicken-liver juices. INTERVENTION: Recommendations for proper cleaning and sanitizing of kitchen equipment to prevent cross-contamination between raw and cooked foods. CONCLUSIONS: Mixed foodborne outbreaks occur rarely. During this outbreak, contamination of a single food item with multiple bacterial pathogens was the likely source of transmission. Improper food-handling techniques that promote growth of one microorganism also allow growth of other pathogens that may be present. Because different sources and routes of transmission may be implicated for different pathogens, specific preventive measures may vary depending on the organisms involved.

Lazarevic G. et al. *[Antibiotic sensitivity of bacteria isolated from the urine of children with urinary tract infections from 1986 to 1995].* Srp Arh Celok Lek. 1998; 126(11-12) : 423-9.p Abstract: In adults and in children urinary system infections are mostly caused by gram-negative and rarely by gram-positive bacteria. Of gram-negative bacteria the most frequent cause of infections are Escherichia coli, Klebsiella species, Proteus mirabilis, Pseudomonas aeruginosa, Acinetobacter, Serratia etc., and of gram-positive bacteria Enterococcus, Staphylococcus, Streptococcus agalactiae. In rare cases the cause of infection may also be Pneumococcus and Haemophilus influenzae. AIM OF THE STUDY: The aim of the study was to investigate the sensitivity to antibiotics of gram-negative bacteria as the predominant cause of urinary infections. METHOD OF THE STUDY: We isolated 20,615 bacterium species from urine of children hospitalized or treated as outpatients at the University Children's Hospital in Belgrade. Urine was collected classically, i.e. by taking the second clean stream into a sterile test tube or by Uricult test. The samples were cultured on blood plates and endo-agar. Identification was done by standard bacteriologic methods and when findings were dubious API-20E (bioMerieux) was used. Bacterium sensitivity to nine antibiotics (ampicillin, cephalexin, cefotaxime, chloramphenicol, gentamicin, amikacin, co-trimoxazole, nalidixic acid and nitrofurantoin) was assessed with disc diffuse method on Muller-Hinton agars. RESULTS: Based on the obtained results, Escherichia coli species sensitivity to amikacin, gentamicin, cefotaxime, nalidixic acid and nitrofurantoin ranged from 90 to 100%; sensitivity to co-trimoxazole and chloramphenicol ranged from 70 to 80%, to cephalexin from 50 to 60%, while to ampicillin it was only 20%. Klebsiella species sensitivity to nalidixic acid and cefotaxime was 70-85%; to amikacin, cefotaxime, co-trimoxazole and gentamicin 60-80%; to cephalexin and chloramphenicol 40-50%, and to ampicillin only 5-15%. Proteus species showed sensitivity to amikacin, gentamicin, cefotaxime and nalidixic acid of 90-95%; to co-trimoxazole and chloramphenicol 70-80%; to cephalexin and ampicillin 40-50%, and to nitrofurantoin 10%. Pseudomonas aeruginosa species showed the highest level of sensitivity to amikacin (40-50%), and somewhat lower to gentamicin (10-40%), and a very low sensitivity to other antimicrobial drugs (10-25%). DISCUSSION: It may be noted from the above data that gram-negative bacteria are the cause of urinary infections in about 90% of cases, while gram-positive bacteria are the cause in only 10%, which is in accordance with data from literature. Of all antibiotic drugs ampicillin (a wide spectrum penicillin) had a very significant role in the therapy of urinary infections. However, the long-term usage of ampicillin led to increased resistance to the drug in infections caused by Escherichia coli. Natural resistance to ampicillin of Klebsiella species limited its usage when penicillin was first introduced. Proteus mirabilis species, especially those isolate in primary infection, are often sensitive to amino penicillin. Contrary to Proteus mirabilis, indole-positive Proteus and Providentie species show a high resistance to these antibiotics. Due to the crisis in our country and the lack of other antibiotics, ampicillin was widely used. The wide use of the drug caused evident resistance of Escherichia coli and Proteus mirabilis to this antibiotic. A fall in the sensitivity of Klebsiella to cephalexin, gentamicin, amikacin and co-timoxazole, which occurred in 1992, has been explained by intrahospital circulation of multiresistant Klebsiella species. The sensitivity of isolated gram-negative bacteria Escherichia coli, Klebsiella species, Proteus mirabilis and Pseudomonas aeruginosa was the most prominent to aminoglycosides (amikacin and gentamicin). The most frequent mechanism of enterobacterial resistance to trimethoprim and co-trimoxazole involves dihydrofolate reductase enzyme. Comparative studies related to the administration of co-trimoxazole have shown that the difference in the efficacy between thes.

Lazarus H.M. et al. *Multi-purpose silastic dual-lumen central venous catheters for both collection and transplantation of hematopoietic progenitor cells.* Bone Marrow Transplant. 2000; 25(7) : 779-85.p Abstract: Autologous peripheral blood progenitor cell (PBPC) transplantation frequently requires sequential placement and use of two separate central venous catheters: (1) a short-term, large-bore, stiff device inserted for leukapheresis, and after removal of that device, (2) a long-term, multilumen, flexible, Silastic catheter for administration of high-dose chemotherapy, re-infusion of hematopoietic cells, and intensive supportive care. We reviewed our recent experience with two dual-lumen, large-bore, Silastic multi-purpose ('hybrid') catheters, each of which can be used as a single device for both leukapheresis and long-term supportive care throughout the transplant process. Quinton-Raaf PermCath and Bard-Hickman hemodialysis/apheresis dual-lumen catheters were used as the sole venous access device in 112 consecutive patients who underwent autologous PBPC collection and transplantation. The catheter exit site was monitored three times a week, and lumen patency was assessed using clinical and radiologic techniques. Catheters were removed prematurely for persistent thrombus, positive blood cultures despite appropriate antibiotics, or mechanical dysfunction. There were no intra-operative or immediate post-operative complications relating to insertion. Thirty-two patients experienced catheter occlusion necessitating urokinase instillation. Persistent occlusive problems were noted in 16 patients, and in 10 patients the catheter had to be removed. Two exit site infections and 17 bacteremias occurred. Catheters had to be removed for persistent infection in two subjects and for mechanical problems in five others. Cost analysis comparing the hybrid catheters alone vs conventional devices revealed a charge of $4230 in patients with hybrid catheters vs. $7530 in those requiring a temporary non-Silastic dialysis catheter in addition to a flexible, long-term Silastic catheter. Hybrid, Silastic, dual-lumen, large-bore central venous catheters are safe, cost-effective and convenient multi-purpose venous access devices that may be used in the setting of autologous PBPC collection and transplantation. The rate of thrombotic, infectious and mechanical complications appears comparable to other central venous access devices.

Le Goff A. et al. *Evaluation of root canal bacteria and their antimicrobial susceptibility in teeth with necrotic pulp.* Oral Microbiol Immunol. 1997; 12(5) : 318-22.p Abstract: This study aimed to evaluate the microbiota of necrotic pulp in teeth without carious lesions where the crown and root were intact and to test the sensitivity of this microbiota to antibiotics in order to improve treatment. The necrotic pulp was sampled from 26 single-rooted teeth in intact pulp chambers. A total of 84 strains were isolated. The number of species isolated per tooth varied from 2 to 8, with a strong component (81%) of anaerobic bacteria. The most commonly represented species were Bacteroides gracilis, Propionibacterium acnes, Fusobacterium nucleatum, Prevotella buccae and Eubacterium lentum. The sensitivity of these organisms to amoxicillin, amoxicillin combined with

clavulanate and tetracycline was evaluated by Etest on 38 isolates. For all strains tested, the minimum inhibitory concentration values obtained were low and substantially below effective serum concentrations for these antibiotics. These data enable us to devise suitable treatments for acute development of apical lesions and to prevent dissemination of this source of infection to the rest of the host.

Le Gonidec P. et al. *[Impact of hospital infection on medical expenditures in a continuing care and rehabilitation service at a geriatric hospital].* Pathol Biol (Paris). 1998; 46(6) : 398-402.p Abstract: The costs of medical expenditures such as drugs, medical devices (MD), biological assays and nurses workload, were measured, before and after the onset of nosocomial infection (NI), in rehabilitation care departments of a 1000-beds geriatric teaching hospital. Data were collected retrospectively in medical records and nursing records. Nurse's workload was measured by the French indicator "Soins Infirmiers Personnalise a la Personne Soignee" (SIIPS). A week before and a week after the diagnosis of hospital-acquired infection, medical consumptions were compared. During the study 38 of the 206 patients admitted in rehabilitation care wards presented hospital-acquired infection. Data were collected for 31 of these 38 patients. Nosocomial infections are associated with an increased pharmaceutical dispensing: medication (mainly antibiotics) and medical device's cost; and an increased nurse's workload. This study suggests that infection surveillance may be helpful to a better understanding of pharmaceutical dispensing variation in geriatric rehabilitation care departments.

Le Moing V. et al. *Use of corticosteroids in glomerulonephritis related to infective endocarditis: three cases and review.* Clin Infect Dis. 1999; 28(5) : 1057-61.p Abstract: We report the cases of three patients treated for infective endocarditis (IE) for whom corticosteroids were added to the antibiotic treatment. They all had clinical and biological evidence of immune-mediated glomerulonephritis. The microorganisms responsible for IE were Coxiella burnetii, Streptococcus bovis, and Cardiobacterium hominis. Median duration of IE before antimicrobial therapy was 7 months. In all patients, renal function deteriorated despite appropriate antimicrobial treatment for a mean duration of 16 days, but it improved after addition of corticosteroid therapy. All patients were cured of IE. A literature review revealed four additional cases of IE-related glomerulonephritis in which adjunctive immunosuppressive therapy was considered to be effective. Although corticosteroid therapy is generally not recommended for IE, it should be considered for patients whose renal dysfunction secondary to glomerulonephritis does not improve with appropriate antimicrobial treatment, especially if the duration of the illness is long.

Le Saux N. et al. *Antimicrobial use in febrile children diagnosed with respiratory tract illness in an emergency department.* Pediatr Infect Dis J. 1999; 18(12) : 1078-80.p Abstract: BACKGROUND: In an era of increasing antibiotic resistance, the prevalence of antibiotic usage and associated factors should be ascertained to optimize their use. We set out to determine the prevalence of antibiotic use in febrile children diagnosed with respiratory tract illnesses at a children's hospital emergency department; to determine how often viral studies were conducted; and to identify patient characteristics associated with antibiotic use. METHODS: We conducted a retrospective study of antibiotic use in febrile children 3 months to 10 years old presenting with respiratory illnesses during two 1-month periods. Patient charts and laboratory tests were reviewed. Antibiotic use was related to diagnosis by logistic regression. RESULTS: A total of 836 patient visits were selected. Antibiotics were prescribed for otitis media in 96% of patients, for pneumonia in 100%, for pharyngitis in 66%, for bronchiolitis in 38%, for reactive airway disease in 24% and for viral or "upper respiratory tract illness" in 14%. For viral illness or upper respiratory tract infection, antibiotic use was associated with a fever duration of >48 h [odds ratio (OR), 3.2; 95% confidence interval (CI) 1.7, 5.9] and having a chest radiograph performed (OR 2.1; 95% CI 1.02, 4.37). Patients with pharyngitis who had a throat swab were less likely to receive an antibiotic (OR 0.08; 95% CI 0.02, 0.4) than those who did not have a swab. In this emergency department antibiotic use for these indications decreased by 11% during the 1997 to 1998 study interval ($P < 0.001$). CONCLUSION: Antibiotics were commonly prescribed for pharyngitis, bronchiolitis and reactive airway disease, which are conditions principally caused by viruses. Addressing reasons why there is a difference between guidelines and antibiotic use in these conditions may be important.

Le Saux N. et al. *Evaluating the benefits of antimicrobial prophylaxis to prevent urinary tract infections in children: a systematic review.* CMAJ. 2000; 163(5) : 523-9.p Abstract: BACKGROUND: The recurrence rate for urinary tract infections in children is estimated at between 30% and 40%. The use of low doses of antibiotics as prophylaxis for recurrent urinary tract infections is common clinical practice. However, prolonged antimicrobial therapy has the potential to contribute to problems of bacterial resistance and antimicrobial side effects. The aim of this review was to systematically examine the available evidence for the effectiveness of this intervention. METHODS: We conducted a literature search of 3 electronic databases for the period 1966 to 1999. We also searched bibliographies from conference proceedings and contacted content experts to ensure completeness of our database. Each trial was evaluated on the basis of the following inclusion criteria: target population (children), intervention (antibiotic v. no antibiotic), outcome (number of urinary tract infections) and study design (randomized controlled trial). Quality was assessed for the studies that met these criteria. RESULTS: Most of the studies identified were case series and cohort studies. Only 6 randomized trials fulfilled the inclusion criteria. All were of low quality (median 2, range 0 to 2 [maximum quality score 5]). Three trials dealt with children who had anatomically normal urinary tracts, and three included children with neurogenic bladder. The rate of infections for patients with normal urinary tracts ranged from 0 to 4.0 per 10 patient-years for the treatment groups and from 4.0 to 16.7 for the control groups. The recurrence rates for patients with neurogenic bladders in 2 trials were 2.9 and 17.1 per 10 patient-years for the treatment groups and 1.5 and 33.0 for the control groups. INTERPRETATION: The available evidence for using antimicrobial prophylaxis to prevent urinary tract infection in children with normal urinary tracts or neurogenic bladder is of low quality. This suggests that the magnitude of any benefit should at best be questioned. The surprising lack of data for children with reflux is of concern. Well-designed trials are needed to optimize the use of antimicrobials in children with recurrent urinary tract infection.

Leal A.L. et al. *[Susceptibility to antimicrobial agents in isolates from invasive Streptococcus pneumoniae in Colombia].* Rev Panam Salud Publica. 1999; 5(3) : 157-63.p Abstract: A study was done to determine the patterns of susceptibility to antimicrobial agents in isolates of Streptococcus pneumoniae that caused invasive disease diagnosed in children under the age of 5 in Colombia between 1994 and 1996, as well as to establish the distribution of the capsular types of the resistant isolates. The analysis was done using 324 isolates obtained during the performance of the National Serotyping Protocol for S. pneumoniae carried out in Bogota, Medellin, and Cali, Colombia, between July 1994 and March 1996. Of the 324 isolates, 119 (36.7%) showed diminished susceptibility to at least one antimicrobial agent, including 39 (12%) that showed diminished susceptibility to penicillin. Of these 39 resistant to penicillin, 29 showed intermediate resistance and 10 showed high resistance. Nine isolates (2.8%) showed resistance to ceftriaxone, 80 (24.7%) to the combination of trimethoprim and sulfamethoxazole (TMS), 49 (15.1%) to chloramphenicol, and 31 (9.6%) to erythromycin. Resistance to two antimicrobial agents was observed in 31 isolates (9.6%); multiple resistance was found in 22 (6.7%). These 22 multiresistant isolates all showed resistance to TMS. The most frequent associations were penicillin, TMS, and erythromycin (5 cases); penicillin, chloramphenicol, TMS, and erythromycin (4 cases); penicillin, ceftriaxone, chloramphenicol, and TMS (3 cases); and penicillin, ceftriaxone, chloramphenicol,

TMS, and erythromycin (3 cases). The most frequent serotypes in the penicillin-resistant isolates were: 23F (53.8%), 14 (25.6%), 6B (7.7%), 9V (5.1%), 19F (5.1%), and 34 (2.6%). The most frequent serotypes in the isolates resistant to antimicrobial agents other than penicillin were: 5 (37.5%), 23F (7.5%), 14 (18.8%), and 6B (13.8%). This difference in the distribution of the serotypes was statistically significant ($P < 0.0001$). The study results indicate the need to maintain active surveillance of antibiotic susceptibility patterns in order to avoid resistance in S. pneumoniae and to provide timely information to change practices regarding prescribing and consuming antimicrobial agents.

Leaños M.B. et al. *Identificación de especies y sensibilidad antimicrobiana de cepas de Enterococcus, aisladas en un hospital pediátrico.* Bol. méd. Hosp. Infant. Méx. 1997; 54(11) : 548-52.p Abstract: Introducción. El objetivo del estudio fue identificar las especies del género Enterococcus aisladas de pacientes pediátricos y conocer su sensibilidad antimicrobiana in vitro. Material y métodos. Las especies fueron identificadas mediante técnicas estándar. La sensibilidad antimicrobiana se efectuó por el método de dilución en agar, los antibióticos se probaron en concentraciones de 0.5 a 32 mg/L. Para gentamicina se incluyó una concentración de 2000 mg/L para detectar resistencia elevada. Resultados. De enero 1994 a junio 1995 se aislaron 289 cepas de Enterococcus: 111 de urocultivos, 89 puntas de catéter, 40 de secreciones, 34 de hemocultivos y 15 de otros líquidos corporales. Las especies identificadas fueron: 220 cepas (76.1 por ciento) de Enterococcus faecalis, 29 cepas (10 por ciento) Enterococcus avium, 16 cepas (5.5 por ciento) enterococcus raffinosus, 15 cepas (5.2 por ciento) Enterococcus faecium, 5 cepas (1.7 por ciento) Enterococcus hirae y 4 cepas (1.4 por ciento) Enterococcus malodoratus. La resistencia in vitro al grupo de aminoglucósidos (netilmicina, gentamicina y amikacina) varió de 70 a 90 por ciento, para los á-lactámicos (imipenem, penicilina y ampicilina) del 17 al 33 por ciento, para cloramfenicol 40 por ciento y para vancomicina 3.1 por ciento; 45 cepas mostraron alta resistencia a gentamicina. Conclusiones. La especie aislada con mayor frecuencia fue E. faecalis. La resistencia in vitro para aminoglucósidos fue elevada. La resistencia a vancomicina es baja. El 15.5 por ciento de las cepas tuvieron resistencia elevada a gentamicina(AU).

Leclercq R. *Enterococci acquire new kinds of resistance.* Clin Infect Dis. 1997; 24 Suppl 1 : S80-4.p Abstract: In recent years, enterococci have become increasingly resistant to a broad range of antimicrobial agents. The development of high-level resistance to aminoglycosides, penicillins, and glycopeptides singly and in combination has important clinical implications. Strains of Enterococcus faecium that are resistant to every useful available antibiotic have been described. Resistance to penicillin can be due to overproduction of penicillin-binding protein (which has low affinity for penicillins) or to production of beta-lactamase. High-level resistance of enterococci to gentamicin is due to the synthesis of a modifying enzyme. In this case, the synergistic activity of the combination of penicillin with any aminoglycoside (except for streptomycin) is totally abolished. Acquired resistance to glycopeptides is often plasmid-mediated and is associated with a major epidemic potential since certain plasmids are self-transferable from E. faecium to a variety of gram-positive organisms, including Staphylococcus aureus.

Lee A.Y. et al. *Management of venous thromboembolism in cancer patients.* Oncology (Huntingt). 2000; 14(3) : 409-17, 421; discussion 422, 425-6.p Abstract: Venous thromboembolism is a common complication in patients with cancer. The management of deep-vein thrombosis and pulmonary embolism can be a considerable challenge in these patients. Diagnosing venous thrombosis requires objective testing, and noninvasive investigations may be less accurate in patients who have cancer than in those who do not. Treatment of acute venous thrombosis at home with low-molecular-weight heparin is an attractive option in patients with malignant disease, in whom quality of life is especially important. Comorbid conditions, warfarin resistance, difficult venous access, and a potentially high bleeding risk are some of the factors that often complicate the prolonged course of anticoagulant therapy needed in this group. In addition, the use of central venous catheters is increasing, but the optimal treatment of catheter-related thrombosis remains controversial. This article reviews the current diagnostic and treatment approaches to venous thromboembolism in patients with cancer and provides several clinical scenarios to illustrate and discuss some common management problems.

Lee C.E. et al. *The incidence of antimicrobial allergies in hospitalized patients: implications regarding prescribing patterns and emerging bacterial resistance.* Arch Intern Med. 2000; 160(18) : 2819-22.p Abstract: BACKGROUND: The development of antimicrobial guidelines is one way in which institutions attempt to control emerging resistance, but the real challenge falls on promoting and ensuring adherence to these guidelines. Investigating reasons for the prescribing of alternative antimicrobial agents outside of these guidelines is crucial for modifying practices that may adversely impact institutional antimicrobial goals. METHODS: Retrospective cross-referencing of computerized pharmacy printouts and concurrent manual medical record review. RESULTS: Approximately 25% (470/1893) of the patients requiring antimicrobial therapy reported an allergy to at least 1 antimicrobial agent. The most commonly reported antimicrobial allergy was penicillin (295/1893 [15.6%]). Eighty-five patients (18.1%) reported having an allergy to 2 or more antimicrobial agents. Only 4% (27/601) of the reported antimicrobial allergies contained documentation as to the nature of the specific allergic reactions, while a manual medical record review revealed that 32% (23/73) of the antimicrobial allergies contained documentation of the specific allergic reaction. Ninety-eight (39. 7%) of 247 patients reporting an allergy only to penicillin and/or cephalosporin received vancomycin in comparison with 247 (17.4%) of 1423 patients without any antimicrobial allergies ($P<.001$). Similarly, 53 (21.5%) of 247 patients with reported penicillin and/or cephalosporin allergies received levofloxacin compared with 114 (8.0%) of 1423 patients without any antimicrobial allergy ($P<. 001$). CONCLUSION: The incidence of penicillin allergy at our institution exceeds population averages. This finding, in combination with limited documentation of drug allergies, appears to lead to the prescribing of alternative antimicrobial agents that do not fit into institutional antimicrobial guidelines and, in some instances, may put the patient at risk for infection and/or colonization with resistant organisms. Use of these alternative agents may adversely impact the ability to manage emerging antimicrobial resistance.

Lee C.H. et al. *Septic arthritis of the ankle joint*. Chang Keng I Hsueh Tsa Chih. 2000; 23(7) : 420-6.p Abstract: BACKGROUND: Septic arthritis of the ankle joint is a rare but serious disease. Very few reports in the literature have mentioned the method of care and treatment results of septic ankle. This study was designed to retrospectively review the treatment results and to analyze the prognostic factors of septic arthritis of the ankle inpatients at our hospital. We also formulated a protocol for the management of septic arthritis of the ankle joint. METHODS: All records of those patients with a diagnosis of septic ankle from 1985 to 1997 were retrospectively reviewed. There were 29 patients that met the diagnostic criteria of septic arthritis of the ankle joint (21 male and 8 female patients; 6 children and 23 adults). The average follow-up time was 5.5 years (ranging from 1.5 to 13.7 years). The patients' ages, associated diseases, single or multiple joint(s) involved, timing of treatment, and the final results of these cases were assessed. The infecting organism and drug sensitivity were discussed to determine the proper antibiotics regimen. RESULTS: Staphylococcus aureus was the most common infecting microorganism in the septic ankles. Combined therapy with oxacillin and gentamicine was effective against 88.1% of the infecting microorganisms. The poor prognostic factors for septic ankle included a positive bacterial culture, involvement of multiple joints simultaneously, a delay in treatment, and an increased number

of associated diseases. In addition, a high proportion of patients with septic ankle had gouty arthritis (43.5%). CONCLUSION: Early treatment (symptom duration of less than 5 days) significantly affected the final results. The early recognition and prompt treatment of this condition may reduce morbidity and mortality. Based on our results, oxacillin and gentamicine are recommended as the first-line antibiotics for the management of septic ankle.

Lee C.W. et al. *Pressure-derived fractional collateral blood flow: a primary determinant of left ventricular recovery after reperfused acute myocardial infarction*. J Am Coll Cardiol. 2000; 35(4) : 949-55.p Abstract: OBJECTIVES: We evaluated the relation between pressure-derived fractional collateral flow (PDCF) and left ventricular (LV) recovery after reperfused acute myocardial infarction (AMI). BACKGROUND: The functional significance of collateral flow remains uncertain in AMI. METHODS: The PDCF was measured in 70 patients with first AMI (pain onset <12 h) treated with primary angioplasty (PA), being determined by simultaneous measurement of mean aorta pressure (Pa), distal coronary pressure during the balloon occlusion (Poc), and central venous pressure (CVP): (Poc - CVP)/(Pa - CVP)*100. Sufficient collateral (group I) was defined as PDCF index >24% and insufficient collateral (group II) as PDCF index <24%. Echocardiography was performed before, and on day 3, day 7, and day 30 after PA. Wall-motion recovery index (RI) was obtained by dividing the number of improved wall-motion segments (>grade 1) at follow-up by the number of abnormal wall-motion segments within the infarct zone at baseline. RESULTS: Baseline characteristics were similar between both groups. Peak levels of creatine kinase were lower in group I than in group II (2,600+/-1,900 U/liter vs. 4,100+/-3,000, $p < 0.05$). At one month, infarct zone wall-motion score index (1.65+/-0.54 vs. 2.31+/-0.46, $p < 0.01$) and LV volume indexes were smaller in group I than in group II, whereas, LV ejection fraction was higher in group I than in group II (52.8+/-8.3 vs. 45.9+/-9.0, $p < 0.01$). The PDCF index was the strongest predictor of RI at one month ($r = 0.61$, $p < 0.01$). Time to reperfusion was not related to RI at one month. However, it was significantly related to RI in group II ($r = -0.34$, $p < 0.05$). CONCLUSIONS: The LV recovery after reperfused AMI is primarily determined by PDCF and is less dependent on time to reperfusion in patients with sufficient collaterals.

Lee H.J. et al. *High incidence of resistance to multiple antimicrobials in clinical isolates of Streptococcus pneumoniae from a university hospital in Korea*. Clin Infect Dis. 1995; 20(4) : 826-35.p Abstract: One hundred thirty-one strains of Streptococcus pneumoniae isolated from clinical specimens between January 1991 and April 1993 were serotyped and tested for susceptibility to 10 antimicrobials by the agar dilution method. Five serotypes (6A, 6B, 14, 19F, and 23F) accounted for 67% of all isolates. Seventy percent of isolates were not susceptible to penicillin, exhibiting either intermediate resistance (37%) or high-level resistance (33%); 82% of isolates from children and 59% of those from normally sterile body fluids were resistant to penicillin. A significantly increased rate of penicillin resistance (P <.01, Fisher's exact or chi 2 test) was associated with hospitalization, an age of < or = 15 years, ongoing antimicrobial therapy at the time of isolation of the organism, nosocomial acquisition, and several specific serotypes (6, 14, 19F, and 23F). No penicillin-resistant strain showed beta-lactamase activity. Various proportions of the penicillin-resistant strains also displayed resistance to cefaclor (89%), cefotaxime (82%), chloramphenicol (65%), erythromycin (52%), and ciprofloxacin (15%), but none was resistant to teicoplanin or vancomycin. The prevalence of pneumococcal resistance documented in Korea in this study is among the highest figures published to date.

Lee J. et al. *Methionyl adenylate analogues as inhibitors of methionyl-tRNA synthetase*. Bioorg Med Chem Lett. 1999; 9(10) : 1365-70.p Abstract: Four stable analogues of methionyl adenylate (3-6) were designed as inhibitors of methionyl-tRNA synthetase and synthesized from 2',3'-isopropylideneadenosine. They strongly inhibited aminoacylation activity of methionyl-tRNA synthetases isolated from Escherichia coli, Mycobacterium tuberculosis, Saccharomyces cerevisiae and human. Among the microorganisms tested, however, these chemicals showed the growth inhibition effect only on E. coli.

Lee K. et al. *Korean Nationwide Surveillance of Antimicrobial Resistance of Bacteria in 1998*. Yonsei Med J. 2000; 41(4) : 497-506.p Abstract: Antimicrobial resistance surveillance can provide information needed for empirical therapy of antimicrobial agents and for control of resistance. To determine the trend of antimicrobial resistance in Korea, in vitro susceptibility data in 1998 were collected from 25 hospitals participating to a program of Korean Nationwide Surveillance of Antimicrobial Resistance (KONSAR). The data were analyzed based upon hospital location and bed capacity. The results showed that cefoxitin-resistant E. coli and K. pneumoniae and 3rd-generation cephalosporin-resistant K. pneumoniae were prevalent, that 3rd-generation cephalosporin-resistant E. cloacae, S. marcesens and A. baumannii had increased, and ampicillin-resistant S. enterica were not rare. Oxacillin-resistant S. aureus, penicillin-non-susceptible pneumococci and beta-lactamase-producing H. influenzae were prevalent even smaller hospitals surveyed, and an increase of imipenem-resistant P. aeruginosa and vancomycin-resistant E. faecium is a new obvious threat. In general, resistance rates to some old antimicrobial agents, i.e., E. coli to ampicillin and S. aureus to oxacillin were high and did not vary greatly between the different levels of hospitals, while the rates to some of the newer ones, i.e., P. aeruginosa to imipenem, was quite variable and depended on the hospitals, probably reflecting difference in selective pressure.

Lee K. et al. *Emerging resistance of anaerobic bacteria to antimicrobial agents in South Korea*. Clin Infect Dis. 1996; 23 Suppl 1 : S73-7.p Abstract: In previous studies, Bacteroides fragilis group organisms isolated from Korean patients were more frequently resistant to various antimicrobial agents, including clindamycin, than were isolates in other countries. A recent report of increased resistance of Peptostreptococcus species prompted us to include such isolates in a study of antimicrobial susceptibility. anaerobes isolated in 1994 at a tertiary care hospital in Seoul were tested by agar dilution method. None of the B. fragilis group organisms were resistant to imipenem, cefoxitin, chloramphenicol, or metronidazole. However, 6.7% were resistant to ampicillin/sulbactam, 20.2% to cefotetan, 30.3% to piperacillin, 48.3% to cefotaxime, and 42.7% to clindamycin. Almost all of the Clostridium perfringens isolates were susceptible to all of the agents tested, except tetracycline. Peptostreptococcus isolates were susceptible to piperacillin, cefotaxime, and imipenem, while 7.4% were resistant to penicillin G, cefotetan, and metronidazole, and 25.9% were resistant to clindamycin. The isolates resistant to penicillin G, cefotetan, and metronidazole were identified as Peptostreptococcus anaerobius. In conclusion, besides the well-known high rate of resistance of B. fragilis group organisms to clindamycin, the emergence of resistance of Peptostreptococcus species isolates to beta-lactam drugs has become obvious in Korea.

Lee K. et al. *Antimicrobial resistance patterns of Bacteroides fragilis group organisms in Korea*. Yonsei Med J. 1998; 39(6) : 578-86.p Abstract: Antimicrobial resistance patterns of 913 clinical isolates of Bacteroides fragilis group organisms were monitored during an 8-year period in Korea. In general the resistance rates of the non-fragilis B. fragilis group species were higher than those of B. fragilis for all the drugs tested. The rate of resistance to clindamycin remarkably increased and those to some beta-lactam drugs such as piperacillin and cefotaxime also increased. No isolates were found to be resistant to imipenem, metronidazole, or chloramphenicol. beta-lactam and beta-lactamase inhibitor combinations and cefoxitin were more active than the other beta-lactams. Therefore, these agents may be considered when empirical selection of antimicrobial agents is required to treat severe anaerobic infections.

Lee M.S. et al. *Primary cutaneous nocardiosis.* Australas J Dermatol. 1999; 40(2) : 103-5.p Abstract: A case of primary cutaneous nocardiosis due to Nocardia asteroides occurring in a steroid-dependent asthmatic with no history of trauma is presented. He had a 5 month history of painful nodules on his right shin and calf. He was initially treated with a 6 week course of oral cephalexin 500 mg four times daily, followed by a 2 week course of minocycline 100 mg twice daily with worsening of the infection. A 12 week course of oral clarithromycin 500 mg twice daily led to complete resolution. A discussion of the problems associated with antimicrobial susceptibility testing and nocardia resistance is presented.

Lee P.Y. et al. *Endocarditis due to high-level gentamicin-resistant Enterococcus faecalis.* Postgrad Med J. 1995; 71(832) : 117-9.p Abstract: We report a case of aortic valve endocarditis caused by Enterococcus faecalis highly resistant to gentamicin, which failed to respond to conventional antibiotic combination therapy. Extensive in vitro testing was required to determine an appropriate antimicrobial regimen. Despite bacteriological resolution and cardiac surgery the patient died from complications of infective endocarditis.

Lee T.H. et al. *Low frequency of bacteremia after endoscopic mucosal resection.* Gastrointest Endosc. 2000; 52(2) : 223-5.p Abstract: BACKGROUND: Endoscopic mucosal resection has become a popular alternative for the treatment of early-stage neoplasia of the gastrointestinal tract. However, there are still no data on the frequency of bacteremia associated with this form of treatment. METHODS: We conducted a prospective study of 21 men and 17 women undergoing endoscopic mucosal resection with a cap-fitted panendoscope for upper gastrointestinal lesions. Blood cultures were performed before, 10 minutes after, and 4 hours after the procedure for both aerobic and anaerobic bacteria. RESULTS: Blood culture at baseline was negative in all the patients. Two of 38 patients (5.3 %) had positive blood culture at 10 minutes after the procedure. The isolated microorganisms were Streptococcus salivarius and Corynebacterium species. All patients had negative blood cultures 4 hours later. None of these 38 patients had any symptoms or signs associated with infection. CONCLUSIONS: Bacteremia associated with endoscopic mucosal resection is infrequent and transient.

Lee V.J. et al. *What's new in the antibiotic pipeline.* Curr Opin Microbiol. 1999; 2(5) : 475-82.p Abstract: Many advances have recently been made in the development of chemotherapeutic agents for bacterial infections. As a consequence of problematic antimicrobial-resistant bacteria, research is now directed towards narrow-spectrum agents rather than broad-spectrum agents. Further, orally active agents have always been desirable, but today's cost-saving environment, in line with a desire to minimize treatment costs, values reduced administration costs and keeping patients out of the hospital. There has been a recent increase in research into orally active antibacterial agents, such as carbapenems and cephalosporins, and non-glycopeptide natural products.

Lee Y.L. et al. *Low-level colonization and infection with ciprofloxacin-resistant gram-negative bacilli in a skilled nursing facility.* Am J Infect Control. 1998; 26(6) : 552-7.p Abstract: BACKGROUND: We report a 1-year surveillance study that evaluates colonization and infection with ciprofloxacin-resistant gram-negative bacilli (CR GNB) and the relation to quinolone use and other possible risk factors in a proprietary skilled nursing facility (SNF) with no history of outbreaks. METHODS: Rectal swabs obtained quarterly were streaked on MacConkey agar with ciprofloxacin discs (5 microg) to screen for CR GNB and later were speciated and the antimicrobial susceptibilities were confirmed by standardized disc-diffusion tests. RESULTS: The mean prevalence of CR GNB colonization was 2.6% (range 0.9% to 5.3%). The colonization frequency was higher in the last survey than it was in the first survey. CR GNB-colonized strains included Pseudomonas species (21%), but more than half were non-Pseudomonas enterics such as Acinetobacter baumannii (25%), Proteus mirabilis (17%), and Providencia stuartii (13%). None of the patients who had colonization with CR GNB had subsequent infections with the same species. Patients with colonization had more exposure to ciprofloxacin and they were more likely to have been recently admitted from an acute-care hospital and have decubitus ulcers. During the study period, of 336 patients surveyed, 98 (29%) patients developed suspected infections and cultures were done; the infection rate was 4.7 per 1000 patient days. Of these infected patients, 59 (60%) were infected by GNBs; the infection rate was 2.3 per 1000 patient days. Nineteen percent of the GNB infections were treated with a quinolone. (Overall, quinolones constituted about 17% of antibiotic usage in the SNF). Only 3 (5%) of the patients infected with GNB were infected with CR GNB, including Pseudomonas and Providenci a species. The CR GNB infections involved multiple sites, multiple organisms, and long length of stay in the SNF. CONCLUSIONS: The findings indicate that in this community SNF, a low frequency of colonization or infection with CR GNB existed. Whether continued moderate use of quinolones will lead to increasing levels of CR GNB will require further study.

Lee Y.L. et al. *Nasal colonization by methicillin-resistant coagulase-negative staphylococcus in community skilled nursing facility patients.* Am J Infect Control. 2000; 28(3) : 269-72.p Abstract: BACKGROUND: Methicillin-resistant coagulase-negative staphylococci (MRCNS) are increasing nosocomial pathogens in acute care hospital patients. However, there is little information on the epidemiology of MRCNS in skilled nursing facilities (SNFs). We report a pilot survey of the prevalence of MRCNS colonization in SNF patients. METHODS: Anterior nasal swabs were plated on oxacillin salt screening agar for selection of MRCNS. Suspected MRCNS were confirmed by coagulase and catalase tests and standard disc-diffusion antimicrobial susceptibility tests. RESULTS: The overall prevalence of MRCNS was 40% for in-house continuing SNF patients, 49% for newly admitted patients, and 60% for SNF nursing personnel. The prevalence was 13% in a "control" group of nonmedical personnel. Forty-six percent of MRCNS were resistant to ciprofloxacin. The frequency of colonization with MRCNS increased over time. After an average 17 months of facility stay, 32% of noncarriers acquired MRCNS. High frequency of colonization was associated with greater disability. CONCLUSION: Colonization with MRCNS is common among SNF patients, who can serve as a reservoir for transfer of such strains to acute care hospitals. Careful infection control practice, including judicious use of antibiotics with frequent handwashing, will remain critical policies for limiting spread of such strains.

Leebeek F.W. et al. *[Deep venous thrombosis of the arm: etiology, diagnosis and treatment (see comments)].* Ned Tijdschr Geneeskd. 2000; 144(8) : 361-4.p Abstract: Thrombosis of the upper extremity is frequently (30-52%) related to the use of an indwelling venous catheter, but it can also occur in healthy individuals after exercise. In the past it was considered a relatively benign thrombotic event, which was treated conservatively, sometimes even without anticoagulant therapy. Recent studies have shown that complications of deep venous thrombosis of the upper extremity occur frequently: pulmonary embolism (8-36%), recurrence thrombosis after cessation of anticoagulant treatment (2-15%) and post-thrombotic syndrome (up to 50%). Therefore when thrombosis of the upper extremity is clinically suspected, it should be objectively diagnosed by compression echography followed if negative by phlebography, with anticoagulant treatment directly afterward, preferably with low-molecular heparin and then acenocoumarol or phenprocoumon.

Leegaard T.M. et al. *Low occurrence of antibiotic resistance in Escherichia coli and staphylococci isolated from blood cultures in two Norwegian hospitals in 1991-92 and 1995-96.* APMIS. 1999; 107(12) : 1060-8.p Abstract: The aim of this study was to investigate the antibiotic resistance rates of major bacterial pathogens causing bloodstream infections in two very different types of hospital in Norway. We examined all

Escherichia coli and staphylococci (330 isolates) causing bloodstream infections from one general county hospital and one specialist national cancer hospital during the periods 1991-92 and 1995-96. Minimal inhibitory concentrations (MICs) were determined using the E-test. E. coli and staphylococci constituted 46.7% of all isolates from bloodstream infections in the two hospitals. Overall, E. coli isolates were resistant to amoxicillin (21%), trimethoprim (21%), doxycycline (20%) and trimethoprim-sulphamethoxazole (17%), while Staphylococcus aureus strains were resistant to benzylpenicillin (66%). No methicillin-resistant S. aureus was detected. Coagulase-negative staphylococci were often multiresistant, but remained fully sensitive to vancomycin. For a few antibiotics, significantly more resistance was found in the specialist hospital. In our material we found no significant increase in resistance between 1991-92 and 1995-96. In conclusion, antimicrobial resistance still remains low in important bacterial pathogens causing bloodstream infections in Norway.

Leeming J.P. *Treatment of ocular infections with topical antibacterials.* Clin Pharmacokinet. 1999; 37(5) : 351-60.p Abstract: Topically applied ophthalmic antibacterial preparations are widely used in the treatment of patients with superficial ocular infections. In addition, they are frequently used to augment treatment for intraocular infection administered systemically or via local instillation. Direct application delivers high concentrations of antimicrobial agents to the surface of the eye conveniently, quickly and with minimal systemic exposure to the agent. However, antibacterials are rapidly dissipated from the tear film and intraocular penetration of topical antibacterial agents is generally poor, necessitating intensive application for successful treatment of corneal infections. Therapeutic concentrations are rarely achieved at other sites in the eye. This article reviews what is known of the pharmacokinetics of topical ocular agents and how this information can be used to optimise ocular persistence and penetration and minimise systemic absorption of antibacterials. A review of the features of the most commonly employed topical antibacterials suggests that for the treatment of uncomplicated bacterial conjunctivitis there is little difference between the various agents in terms of clinical efficacy, although chloram-phenicol should be used with care because of its potential haematological toxicity. Carefully considered therapy is imperative for bacterial keratitis; fortified beta-lactam/aminoglycoside combinations are often used for these infections. The fluoroquinolones appear promising, but caution is necessary in treating keratitis of unknown aetiology with these agents alone because of inherent and emerging acquired resistance among Gram-positive bacteria.

Lefevre J.C. et al. *Comparative in vitro susceptibility of a tetracycline-resistant Chlamydia trachomatis strain isolated in Toulouse (France).* Sex Transm Dis. 1998; 25(7) : 350-2.p Abstract: BACKGROUND AND OBJECTIVES: We recently reported the first isolation of a tetracycline-resistant Chlamydia trachomatis strain in Toulouse from a woman treated with tetracycline. To characterize this isolate, its in vitro susceptibility was compared with those of 34 other C. trachomatis isolates recovered in Toulouse. STUDY DESIGN: The susceptibilities of C. trachomatis strains were determined in terms of minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) using McCoy cells in 96-well microdilution plates, with an inoculum of 5.10(3) to 1.10(4) inclusion-forming units/ml. The antimicrobial agents tested were tetracycline, azithromycin, erythromycin, ofloxacin, and pristinamycin. RESULTS: No difference was observed between the MICs and MBCs except for the tetracycline. Tetracycline-resistant strain MIC and MBC were > 64 micrograms/ml, although < 1% of the bacterial population showed resistance. For the other isolates, the MIC of tetracycline was < or = 0.25 microgram/ml. The antibiotics other than tetracycline were active in vitro against all strains. CONCLUSIONS: These results show that the tetracycline resistance observed in Toulouse differs from the "heterotypic resistance" described previously in the United States in multiresistant C. trachomatis isolates. They confirm that the resistance we observed may be a new phenomenon.

Lefkovits M. et al. *[An unusual presentation of tuberculosis].* Schweiz Med Wochenschr. 1996; 126(51-52) : 2241-3.p Abstract: A 67-year-old male was hospitalized because of nonspecific symptoms and bilateral pleural effusions. He gave no history of cough, dyspnea or thoracic pain. The blood counts showed moderate anemia and high-grade lymphopenia. The tuberculin test and the anergy-panel were both negative. Testing for HIV was negative. Analysis of pleural fluid showed an exudate with 47% lymphocytes and absence of acid-fast bacilli on Ziehl-Neelsen smear. On histologic examination, the pleural tissue showed no evidence of granuloma. However, cultures for mycobacteria of pleural tissue yielded M. tuberculosis. In this case of pleural tuberculosis, leading symptoms were absent and the tuberculin test was negative in the presence of active tuberculosis. In addition, the cells in the pleural effusion were not predominantly lymphocytic. Patients presenting with unclear effusion should undergo extensive investigations, including a tuberculin test, and anergy panel, pleural fluid cultures, and pleural biopsy with cultures for microorganisms, with the object of establishing or ruling out pleural tuberculosis.

Lehmann D. et al. *Susceptibility of pneumococcal carriage isolates to penicillin provides a conservative estimate of susceptibility of invasive pneumococci.* Pediatr Infect Dis J. 1997; 16(3) : 297-305.p Abstract: OBJECTIVE: Because of its practical importance for public health monitoring in developing countries, we aimed to determine whether susceptibility to penicillin of pneumococci isolated from the upper respiratory tract (URT) is representative of the susceptibility of pneumococci causing pneumonia in children. METHOD: The serogroup distribution and minimum inhibitory concentration of penicillin for 56 and 90 isolates from blood and cerebrospinal fluid, respectively, were compared with those of 833 pneumococcal carriage isolates from Papua New Guinean children. These included 154 and 98 strains from bacteremic and nonbacteremic hospitalized patients with pneumonia, respectively, 350 from outpatients with respiratory infections and 176 and 55, respectively, from children in a community-based study who were healthy or sick with pneumonia. RESULTS: Proportions of pneumococci intermediately resistant to penicillin were comparable in the URT and blood (60%) in 1985 through 1987 when serogroup distributions in the two sites were similar. However, penicillin resistance was higher in the URT (75%) than blood (44%) in 1980 through 1984 when the less frequently carried, less resistant serogroups (1 to 5, 7 to 12, 45 and 46) accounted for a high proportion of bacteremic strains. CONCLUSIONS: URT isolates from any group of sick or healthy children could provide a conservative estimate of antimicrobial susceptibility of invasive strains and is a practical way of monitoring susceptibility as well as evaluating the continued effectiveness of standard antibiotic therapy. If there was cause for concern, it would then be necessary to examine invasive isolates.

Leibovitz E. et al. *Nasopharyngeal carriage of multidrug-resistant Streptococcus pneumoniae in institutionalized HIV-infected and HIV-negative children in northeastern Romania.* Int J Infect Dis. 1999; 3(4) : 211-5.p Abstract: OBJECTIVES: The study compared nasopharyngeal carriage of resistant pneumoniae in human immunodeficiency virus (HIV)-seropositive and -seronegative children. METHODS: Nasopharyngeal colonization with Streptococcus pneumoniae was investigated during May 1996 in 162 HIV-negative infants and children (age range, 1-38 mo) and 40 HIV-infected children (age range, 39-106 mo) living in an orphanage in Iasi, northeastern Romania. The HIV-infected children lived separated from the other children and were cared for by a different staff. Streptococcus pneumoniae was isolated from 12 of 40 (30%) HIV-infected and from 81 of 160 (50%) HIV-negative children. Antimicrobial susceptibility to penicillin and ceftriaxone was determined by E-test, and to another five antibiotics by disk diffusion. Serotyping was performed by the Quellung method on 81 of 93 (87%) isolates. RESULTS: Serotypes 6A, 6B, 19A, and 23F together represented 98% of all isolates. Ninety-nine percent of S. pneumoniae isolates were resistant to

penicillin, and 74% were highly resistant to penicillin (minimum inhibitory concentration [MIC] > 1 mg/mL); MIC50 and MIC90 to penicillin of the isolates were 2 mg/mL and 8 mg/mL, respectively. Eighty-nine of ninety-one isolates were susceptible to ceftriaxone; 99%, 87%, 87%, 48%, and 21% of the isolates were resistant to trimethoprim-sulphamethoxazole, erythromycin, clindamycin, tetracycline, and chloramphenicol, respectively. Eighty-two (89%) isolates were multidrug resistant (resistant to =/>3 antibiotic classes); 37 of 92 (40%) isolates were resistant to 5 or more antibiotic classes, and 16 of these 37 (43%) belonged to serotype 19A. All serotype 19 isolates were highly resistant to penicillin. CONCLUSIONS: No significant differences were observed in the resistance rates of S. pneumoniae in HIV-infected children compared to HIV-negative children. Multidrug-resistant pneumococci were highly prevalent in this Romanian orphanage in both HIV-negative and older HIV-infected children. The observed high prevalence of multidrug-resistant pneumococci (coupled with high penicillin resistance) with a limited number of circulating serotypes emphasizes the need to further evaluate the conjugate vaccines in children at risk for invasive pneumococcal infection.

Leistevuo J. et al. *Resistance to mercury and antimicrobial agents in Streptococcus mutans isolates from human subjects in relation to exposure to dental amalgam fillings.* Antimicrob Agents Chemother. 2000; 44(2) : 456-7.p Abstract: Resistance to cefuroxime, penicillin, tetracycline, and mercury is reported for 839 Streptococcus mutans isolates from 209 human study subjects. The MICs of these drugs did not differ for isolates from one dental amalgam group and two nonamalgam subsets: a group with no known exposure to amalgam and a group whose members had their amalgam fillings removed.

Leistevuo T. et al. *Antimicrobial resistance of fecal aerobic gram-negative bacilli in different age groups in a community.* Antimicrob Agents Chemother. 1996; 40(8) : 1931-4.p Abstract: We measured the occurrence of antimicrobial resistance in fecal aerobic gram-negative bacilli by age in community subjects. For none of the eight antimicrobial agents studied were there any statistically significant differences in the carriage rates of resistance in different age groups. Bacterial resistance was common in all age groups, including the children, and occurred for all antimicrobial agents tested.

Leistevuo T. et al. *Colonization of resistant faecal aerobic gram-negative bacilli among geriatric patients in hospital and the community.* J Antimicrob Chemother. 1996; 37(1) : 169-73.p Abstract: Among the elderly most infections are caused by organisms of faecal origin. The study of the resistance of such Gram-negative bacilli should therefore be a priority. In this study, we determine the occurrence of resistance to five antimicrobials commonly used in geriatric outpatient care, and compare it with long-term and short-term hospitalized geriatric patients treated and not treated with antimicrobials.

Leistevuo T. et al. *Increase of antimicrobial resistance of faecal aerobic gram-negative bacteria in a geriatric hospital*. Age Ageing. 1996; 25(3) : 197-200.p Abstract: Antimicrobial resistance of faecal aerobic Gram-negative bacteria to eight different antimicrobials was determined by a velvet replica-plating method in 1988 and 1933. Faecal samples were taken from 131 geriatric inpatients in the Turku City Hospital with a hospitalization of more than 7 days. From 1987 to 1992 the use of first and second generation cephalosporins and ciprofloxacin increased from 3.32 defined daily doses (DDD) per bed to 24.25 DDD/bed and from 0.63 DDD/Bed to 28.11 DDD/bed, respectively. A statistically significant increase was observed in the frequency of samples resistant (with >= 1% of resistant colonies) to cefuroxime (p = 0.0004) and ceftazidime (p = 0.037) in patients who received antimicrobial therapy and to ampicillin (p = 0.046) in patients who had not received antimicrobial therapy. In addition, despite the decreased use of sulphonamides and trimethoprim (from 17.11 DDD/bed to 5.54 DDD/bed) no significant changes in the frequency of resistant faecal samples were observed. Use of ciprofloxacin has been found to cure resistance plasmids from bacteria in vitro. However, despite the increased use of ciprofloxacin, no decrease in faecal bacteria resistant to any of the other antimicrobials (i.e. trimethoprim) studied was observed.

Leistevuo T. et al. *Problem of antimicrobial resistance of fecal aerobic gram-negative bacilli in the elderly.* Antimicrob Agents Chemother. 1996; 40(10) : 2399-403.p Abstract: In this study, we assessed the magnitude of risk (odds ratio [OR]) of patients being colonized with fecal aerobic gram-negative bacilli in two geriatric hospitals compared with the community, and we associated the use of antimicrobial agents with bacterial resistance. One fecal sample was collected from each of 341 patients, aged 60 years or older, during the hospital stay or when visiting the outpatient service. Samples were collected in 1988 and 1993 to 1994. The aerobic gram-negative bacilli from all samples were examined for resistance to seven antimicrobials by a replica plating method. The long-term-hospitalized patients had a significantly higher risk of being colonized with bacilli resistant to ampicillin (OR, 14.3; 95% confidence interval [95% CI], 6.0 to 34.1), cefuroxime (OR, 7.5; 95% CI, 2.7 to 20.8), trimethoprim (ORs, 22.3; 95% CI, 8.6 to 57.8), and tetracycline (OR, 5.2; 95% CI, 2.4 to 10.9) than the outpatients. The respective ORs among the short-term-hospitalized patients compared with the outpatients were 4.0 (95% CI, 1.9 to 8.4), 7.5 (95% CI, 2.7 to 20.8), 5.5 (95% CI, 2 to 14), and 2.0 (95% CI, 1 to 4). In 1993 to 1994 compared with 1988, in both hospitals there was a significantly increased risk of colonization by bacilli resistant to ampicillin (OR, 3.1; 95% CI, 1.9 to 5.1), cefuroxime (OR, 3.8; 95% CI, 2.1 to 6.7), and tetracycline (OR, 1.6; 95% CI, 1.0 to 2.5). However, the total use of antimicrobial agents increased only among the patients of the short-term-care hospital.

Lejeune M. et al. *Defective functional activity and accelerated apoptosis in neutrophils from children with cancer are differentially corrected by granulocyte and granulocyte-macrophage colony stimulating factors in vitro.* Br J Haematol. 1999; 106(3) : 756-61.p Abstract: We have previously shown that polymorphonuclear leucocytes (PMN) harvested from children with cancer and exposed to chemotherapy exhibit defective bactericidal activities against both Gram-positive and Gram-negative microorganisms as well as accelerated apoptosis. In this study, PMN from children with cancer were evaluated to compare in vitro the corrective effects of the two myeloid colony stimulating factors G-CSF and GM-CSF on these defective pathways. Both G-CSF and GM-CSF were able to increase the defective bactericidal activities against S. aureus and E. coli. However, GM-CSF was consistently superior to G-CSF in correcting PMN microbicidal activity; this correction was incomplete since it did not reach the level observed in normal PMN exposed to GM-CSF. The accelerated apoptosis of PMN was not affected by G-CSF. In contrast, GM-CSF significantly prolonged the survival of the PMN although it did not reach the level of survival observed with normal PMN exposed to GM-CSF. These observations were consistent with other studies indicating that in PMN, microbicidal activities and apoptosis are differentially sensitive to the myeloid growth factors G-CSF and GM-CSF.

Lejeune M. et al. *Prolonged but reversible neutrophil dysfunctions differentially sensitive to granulocyte colony-stimulating factor in children with acute lymphoblastic leukaemia*. Br J Haematol. 1998; 102(5) : 1284-91.p Abstract: Treatment of average-risk acute lymphoblastic leukaemia (ALL) in children consists of 6 months of intensive chemotherapy followed by 18 months of maintenance therapy. Polymorphonuclear leucocyte (PMN) functions from children with ALL were studied in order to evaluate and compare the toxicity of the initial intensive treatment with the toxicity of the subsequent less intensive maintenance treatment. H2O2 and O2- production, evaluated by chemiluminescence, were significantly decreased during the intensive period but returned to normal values when maintenance therapy began. In contrast, bactericidal activity against Gram-positive and Gram-negative microorganisms remained at low levels throughout the treat-

ment but returned to normal values in patients off chemotherapy. PMN from patients on maintenance therapy exhibited an excess of morphological changes associated with apoptosis. This was confirmed by standard two-colour flow cytometry which revealed an increase in the number of hypodiploid cells, and increased expression of membrane phosphatidylserine together with a drastic reduction in the expression of the Fcgamma receptor IIIB (CD16). These defective PMN were differentially sensitive to the effects of granulocyte colony stimulating factor (G-CSF): G-CSF induced similar increase in chemiluminescence in control and patient PMN; GSF partially corrected the defective bactericidal activity; G-CSF did not affect the accelerated PMN apoptosis. These observations indicate that ALL children undergoing chemotherapy present PMN defective functions which are partially sensitive or even resistant to G-CSF.

Lejeune M. et al. *Defective polymorphonuclear leukocyte functions in children receiving chemotherapy for cancer are partially restored by recombinant human granulocyte colony-stimulating factor in vitro.* J Infect Dis. 1996; 174(4) : 800-5.p Abstract: Granulocyte colony-stimulating factor (G-CSF) has important direct and priming effects on different functions of normal mature polymorphonuclear leukocytes (PMNL). Previous study has shown an alteration in respiratory burst and bactericidal activities of PMNL harvested from children with cancer treated with chemotherapy. The present study evaluates the possibility that recombinant human (rh) G-CSF could correct these defective functions in vitro. Free radical formation in defective PMNL was enhanced by rhG-CSF to a level similar to that found in normal PMNL primed by rhG-CSF. The defective bactericidal activity against Escherichia coli and Staphylococcus aureus was also corrected. This bactericidal activity was not different from that observed in normal PMNL primed by rhG-CSF. In conclusion, correction of the altered free radical-formation pathway by rhG-CSF in these cells contributed to the restoration of normal bactericidal activity against both gram-positive and gram-negative microorganisms.

Lekowska-Kochaniak A. et al. *Antibiotic resistance of Campylobacter jejuni with reference to plasmid profiles of clinical and chicken isolates.* Acta Microbiol Pol. 1996; 45(3-4) : 249-59.p Abstract: A total of 47 clinical isolates and 52 poultry isolates of Campylobacter jejuni were characterized by their resistance to 16 antimicrobial agents and by plasmid profiles on agarose gel electrophoresis. Almost all isolates were susceptible to erythromycin, chloramphenicol, gentamycin and nitrofuratoin. Plasmids were detected in 19% of C. jejuni strains isolated from feces of children patients and in 36% of strains isolated from chicken. The presence of plasmid DNA was not found to be correlated with any definite resistance, despite of the number of resistant strains was also higher among poultry isolates. Plasmids, as well, does not seem to be essential for colonization of alimentary tract of pathogenic activity.

Lemann F. et al. *Arbitrary primed PCR rules out Clostridium difficile cross-infection among patients in a haematology unit.* J Hosp Infect. 1997; 35(2) : 107-15.p Abstract: Eight out of 20 (40%) patients with haematological malignancies hospitalized in the same unit of our hospital from 24 January to 24 April 1995, suffered from diarrhoea due to Clostridium difficile. The C. difficile isolates were characterized by serotyping and by arbitrary primed polymerase chain reaction (AP-PCR) using three different 10-mer oligonucleotides. It was found by serotyping that five patients had non-typeable isolates and three had serogroup H isolates. The AP-PCR typed all the isolates and yielded various patterns suggesting that there had been no cross-transmission between the patients. Control faecal sample cultures showed that two patients were still carrying the same isolates after specific treatment with vancomycin or metronidazole, and that one patient had acquired an isolate with a new AP-PCR type. AP-PCR was found to be a rapid, effective discriminative method for the immediate epidemiological tracking of hospital-acquired infections due to C difficile.

Leon M. et al. *[Diagnostic value of Gram staining of peri-catheter skin and the connection in the prediction of intravascular-catheter-related bacteremia].* Enferm Infecc Microbiol Clin. 1998; 16(5) : 214-8.p Abstract: BACKGROUND: To evaluate the diagnostic value of Gram stain of pericatheter skin swabs and the intravascular device hub in detecting catheter-related bacteremia (CRB) in critically-ill patients. METHODS: Over a 12-month period, 170 intravascular catheters (> 7 days in place) suspected as being the primary source of CRB were prospectively examined in adult patients admitted to 10 intensive care units of different hospitals in Spain. Blood cultures, Gram staining and culture of swabs obtained from skin entry side and catheter hub were performed before catheter removal. A semiquantitative culture of the catheter tip was carried out. Catheter-associated bacteremia was considered to be present if the same organism was isolated from the catheter tip, skin and/or hub, and blood cultures. RESULTS: The incidence rate of CRB was 15%. Staphylococcus epidermidis was the most frequently isolated microorganism. Considered together, the sensitivity, specificity, positive predictive value and negative predictive value for Gram staining of the skin and hub were 80, 81.9, 35.3 and 97.1%, respectively. CONCLUSIONS: The Gram stain of skin and hub swabs has a great utility in predicting CRB, specially in the absence of microorganisms. Gram stains of the above mentioned sites could be recommended as an easy and fast method to rule out the presence of CRB.

Leonardo M.R. et al. *In vivo antimicrobial activity of 2% chlorhexidine used as a root canal irrigating solution.* J Endod. 1999; 25(3) : 167-71.p Abstract: The aim of the present study was to evaluate the in vivo antimicrobial activity of 2% chlorhexidine gluconate (FCFRP-USP) used as a root canal irrigating solution in teeth with pulp necrosis and radiographically visible chronic periapical reactions. Culture techniques and measurement of the inhibition zone were used. Twenty-two root canals of incisors and molars of 12 patients were used. After accessing the canal, the first root canal sample was collected with two sterile paper points that were transferred to a tube containing reduced transport fluid. The root canal was instrumented using chlorhexidine solution. A small sterile cotton pellet was placed at the root canal entrance, and the cavity was sealed with zinc oxide-eugenol cement. The canals were maintained empty for 48 h. Three sterile paper points were then introduced to absorb the root canal fluid (second sample). One paper point was placed on an agar plate inoculated with Micrococcus luteus ATCC 9341 and incubated for 24 h at 37 degrees C, and the other two were submitted to microbiological evaluation. Present in 10 cases at baseline, mutans streptococci was reduced by 100% at the second assessment. Treatment showed an efficiency of 77.78% for anaerobic microorganisms at the second assessment. These data suggest that chlorhexidine prevents microbial activity in vivo with residual effects in the root canal system up to 48 h.

Leonas K.K. et al. *The relationship of selected fabric characteristics and the barrier effectiveness of surgical gown fabrics.* Am J Infect Control. 1997; 25(1) : 16-23.p Abstract: BACKGROUND: Relationships between selected fabric characteristics and the barrier effectiveness of surgical gown fabrics to liquid strike-through and bacterial transmission were examined. METHODS: Eight commercially available surgical gowns were evaluated in this study. Five of the gowns were disposable and were produced from nonwoven fabrics. Three of the gowns were reusable and were produced from woven fabrics. Standard test methods were used to evaluate the fabrics. Fabric characteristics evaluated included thickness, weight, pore size, and oil and water repellency. Yarn count was determined for the woven fabrics to establish the number of yarns per inch in both the warp (lengthwise) and fill (crosswise) fabric direction. Resistance of the fabrics to the penetration of microorganism suspensions under a hydrostatic pressure was determined. Microorganisms used in this study were ESCHERICHIA COLI AND STAPHYLOCOCCUS AUREUS: Scanning electron micrographs are presented to illustrate differences among fabrics. RESULTS: Results of this study showed that fabric

characteristics of construction, repellency, and pore size contributed to gown performance. Liquid strike-through was not always accompanied by bacterial transmission. CONCLUSIONS: Higher fabric repellency ratings and smaller pore size generally corresponded with higher barrier properties.

Leone M. et al. *[Catheter-related nosocomial urinary infections in intensive care: physiopathology, epidemiology and prevention (see comments)].* Ann Fr Anesth Reanim. 2000; 19(1) : 23-34.p Abstract: OBJECTIVES: Nosocomial urinary tract infections associated with bladders catheters are common and poorly understood. Data on the prevention of urinary tract infections are numerous and heterogenous. This update article aimed at analysing mechanisms, epidemiology and prevention of these infections. DATA SOURCES: We searched in the Medline database for articles in English or French, without limiting date of publication, using the following key words separely or in combination: urinary tract infection, nosocomial, catheter, infection urinaire, sonde urinaire. STUDY SELECTION: We considered all categories of articles. DATA EXTRACTION: Data on prevention of nosocomial urinary tract infections were analysed in depth. DATA SYNTHESIS: The data on pathogenesis of nosocomial urinary tract infections are still controversial. Various means for preventing urinary tract infections have been recommended: addition of antibacterial agents to urinary drainage system, inclusion of antimicrobial components into the catheter itself, antibiotic prophylaxis or closed sterile drainage system. Their efficiency in intensive therapy unit has not yet been fully assessed. The therapy of these infections is still under debate and requires additional prospective studies to establish the optimal management. CONCLUSION: Catheter-associated urinary tract infections reflect the general hygiene policy, starting with nurse practice patterns at catheter insertion, and ending with antibio-therapy prescriptions by medical staff.

Leonhardt A. et al. *Microbial findings at failing implants.* Clin Oral Implants Res. 1999; 10(5) : 339-45.p Abstract: The aim of this study was to evaluate qualitative differences in the subgingival microbiota at titanium implants, ad modum Branemark, demonstrating clinical and radiographic signs of loss of supporting tissues (peri-implantitis) as compared to implants surrounded by healthy tissues. A total of 37 patients demonstrating 1 or more implants with bone loss > or = 3 threads, bleeding on probing and/or suppuration and 51 patients with clinically healthy mucosa and no bone loss were recruited for the study. In each patient subgingival bacterial samples were obtained using paper-points, and subjected to microbiological analysis by culture. The two types of clinical conditions showed distinct bacterial profiles. For implants with peri-implantitis putative periodontal pathogens, such as Porphyromonas gingivalis, Prevotella intermedia/Prevotella nigrescens and Actinobacillus actinomycetemcomitans, were found in 60% of the cases and microorganisms primarily not associated with periodontitis, such as Staphylococcus spp., enterics and Candida spp., were found in 55% of the peri-imaplant lesions. In contrast, implants surrounded by healthy tissue demonstrated a microbiota associated with periodontal health. The results indicate that the microbiota of the healthy peri-implant sulci is similar to that from corresponding conditions around teeth. However, in peri-implant areas staphylococci, enterics and yeasts were found almost as frequently as periopathogens indicating differences as compared to the microbiota around periodontitis affected teeth. A microbiological diagnosis may therefore be of guidance for the choice of antimicrobial treatment in patients with peri-implant infection.

Leow Y.H. et al. *Comparing the efficacy of pefloxacin and ciprofloxacin in the treatment of acute uncomplicated gonococcal urethritis in males.* Ann Acad Med Singapore. 1995; 24(4) : 515-8.p Abstract: The aim of this study was to compare the efficacy of single-dose pefloxacin 400 mg and ciprofloxacin 250 mg in the treatment of acute uncomplicated gonococcal urethritis in males. One hundred and twenty male patients with uncomplicated gonococcal urethritis were assigned alternately to receive single oral doses of either pefloxacin 400 mg or ciprofloxacin 250 mg. Forty-one out of 43 patients (95.3%) of the pefloxacin group and 46 of 47 (97.9%) of the ciprofloxacin group were cured of gonorrhoeae. The rates of post-gonococcal urethritis were 57.7% and 53.3% in the pefloxacin and ciprofloxacin groups respectively. There was a high incidence of penicillinase-producing gonococci (34.2%). High level resistance to pefloxacin (minimum inhibitory concentration [MIC] >1.0 mg/l) resulting in clinical failure on 400 mg stat dose was noted in 1 isolate. It also showed decreased susceptibility to ciprofloxacin (MIC 0.25 mg/l). Another isolate showed high-level resistance (MIC 0.06 mg/l) to ciprofloxacin 250 mg stat dose with concomitant decreased susceptibility to pefloxacin (MIC >1.0 mg/l). Ciprofloxacin 250 mg stat dose is still useful for the treatment of uncomplicated gonococcal urethritis in males. The cure rate of 95.3% with pefloxacin at 400 mg stat dose is acceptable, but needs to be monitored with caution. The emergence of a more resistant strain of Neisseria gonorrhoeae to fluoroquinolones calls for vigilance in the monitoring of antimicrobial susceptibility.

Lepelletier D. et al. *Escherichia coli: epidemiology and analysis of risk factors for infections caused by resistant strains.* Clin Infect Dis. 1999; 29(3) : 548-52.p Abstract: This study analyzes the epidemiology of hospital and community-acquired infections caused by Escherichia coli. The antimicrobial resistance pattern was used to characterize the isolates, and a prospective observational study was performed to assess the relationship between antimicrobial use and bacterial resistance. The study was conducted during a 3-month period in a 1,200-bed tertiary care hospital in Nantes, France. An E. coli infection was diagnosed in 3.8% of the patients (507 of 13,384) admitted to the hospital between 1 January and 31 March 1996. Of the 507 isolates, 205 (40.4%) were resistant to at least one antimicrobial; 40% were resistant to amoxicillin, 30% to amoxicillin/clavulanate, 38% to ticarcillin, and 16% to trimethoprim-sulfamethoxazole, while resistance to other antimicrobials was low. Prior receipt of antimicrobial and/or immunosuppressive therapy was significantly associated with infection caused by a resistant organism.

Leroy O. et al. *Community-acquired pneumonia in the intensive care unit: epidemiological and prognosis data in older people.* J Am Geriatr Soc. 1999; 47(5) : 539-46.p Abstract: OBJECTIVES: To compare epidemiological data, etiology, and prognosis of severe community-acquired pneumonia (CAP) in the intensive care unit (ICU) according to age (< or > or = 65 years) and to determine prognostic factors of CAP in older people. DESIGN: A retrospective (1987-1992) and prospective (1993-95) multicenter study. SETTING: Six ICUs in the north of France. PATIENTS: Five hundred five patients admitted to an ICU for severe CAP. MEASUREMENTS: Patient characteristics were compared with regard to age. Prognosis of CAP in older patients was studied by stepwise discriminant analysis. RESULTS: Two hundred seventy-eight patients (55%) were aged 65 years or older. Comparison of epidemiological data between older and younger patients revealed a higher prevalence of women (38% vs 29%), more severe underlying comorbidities (anticipated death within 5 years: 59% vs 26%), and more frequent chronic respiratory insufficiency (48% vs 33%) in the older patients. In this study group, 224 organisms were isolated from 172 patients (62%); those identified most frequently were Gram-negative bacilli (34%), S. pneumoniae (32%), and Staphylococcus sp. (19%). Compared with younger patients, no significant differences in bacteriological data were observed. However, crude and attributable mortality rates were significantly higher in the older patients (33% vs 21% and 30% vs 19%, respectively). Prognosis analysis identified four independent predictors of mortality in the older patients: initial septic shock (relative risk (RR) = 3), sepsis-related complications (RR = 4.3), hospital-acquired lower respiratory tract superinfections (RR = 2), and nonspecific pneumonia-related complications (RR = 2.8). CONCLUSION: The bacterial etiology provides some approaches to empirical therapy for older patients with severe community-acquired

pneumonia. In addition, the inappropriateness of withholding intensive care for reasons of age alone is emphasized.

Leroy O. et al. *Simplified prediction rule for prognosis of patients with severe community-acquired pneumonia in ICUs.* Chest. 1999; 116(1) : 157-65.p Abstract: STUDY OBJECTIVES: To develop a simplified prognostic prediction rule for patients admitted to ICUs for severe community-acquired pneumonia (CAP). SETTING: Six ICUs in the north of France. PATIENTS: Five hundred five patients admitted to ICUs over a 9-year period (from 1987 to 1995) for severe CAP. INTERVENTIONS: Retrospective prognosis analysis and multivariate analysis using a credit scoring technique. MEASUREMENTS: The primary outcome measure was ICU mortality. RESULTS: Among the 505 patients, 472 were eligible for the prognosis study. The ICU mortality rate was 22.9%. Multivariate analysis identified, on the basis of the patient's medical history and initial examination on ICU admission, six independent predictors of mortality: age > or = 40 years, anticipated death within 5 years, nonaspiration pneumonia, chest radiograph involvement > 1 lobe, acute respiratory failure requiring mechanical ventilation, and septic shock. An initial risk score based on these factors classified patients into three risk classes of increasing mortality: 4% in class I, 25% in class II, and 60% in class III. Multivariate analysis of events occurring during ICU stay identified three independent predictors of mortality: hospital-acquired lower respiratory tract superinfections, nonspecific CAP-related complications, and sepsis-related complications. An adjustment risk score based on these factors was essential to accurately predict the final outcome of patients in the initial risk class II. CONCLUSIONS: As an aid to clinicians in stratifying the prognosis of patients with severe CAP, the simplified prediction rule used in this study could be useful for therapeutic decisions and appropriate care.

Leroy O. et al. *Effect of hospital-acquired ventilator-associated pneumonia on mortality of severe community-acquired pneumonia.* J Crit Care. 1999; 14(1) : 12-9.p Abstract: PURPOSE: The purpose of this article is to evaluate, using two pairwise case-control studies, attributable mortality linked to hospital-acquired ventilator-associated pneumonia (HA-VAP) complicating the intensive care unit (ICU) stay of patients exhibiting severe community-acquired pneumonia (CAP). MATERIALS AND METHODS: Over an 11-year period, 498 patients with severe CAP were collected. Among them, 43 exhibited HA-VAP. In a first case-control study, these patients were matched with control on the basis of six confounding variables known to be general ICU prognosis factors. In a second case-control study, six variables specifically linked to CAP prognosis were used for matching. RESULTS: In the two case-control studies, each case patient was matched with one control patient. In the first analysis, success of matching was achieved in 198 of 258 (77%) variables used for matching. In the second analysis, matching was successful for 242 of 258 (94%) confounding variables used. Eighteen patients died, compared with, respectively, 6 (P =.003) and 7 (P =.01) controls. Attributable mortality of HA-VAP was similar in the two pairwise analyses, respectively, 28% (risk ratio = 3.0; 95% confidence interval, 1.32 to 6.82) and 26% (risk ratio = 2.57; 95% confidence interval, 1.2 to 5.52). CONCLUSION: When confounding factors were controlled, HA-VAP appeared to increase mortality of severe CAP requiring ICU admission.

Leroyer A. et al. *Prolongation of hospital stay and extra costs due to hospital-acquired infection in a neonatal unit.* J Hosp Infect. 1997; 35(1) : 37-45.p Abstract: A case-control study to evaluate the mean extra stay and corresponding cost of neonates acquiring a hospital-acquired infection (HAI) was performed on all patients admitted to a neonatology unit and discharged alive in 1994. Cases were identified from medical records. Controls were matched to cases for birthweight, gestational age, mode of admission to the unit, previous stay in an intensive care unit and presence of a central venous catheter. Costs were taken as those of the extra days attributable to HAI, i.e. the mean difference in the length of stay between cases and controls. Among a cohort of 616 neonates, 34 (5.5%) had one or more HAIs (average = 1.1). The mean extra cost per infected case was 52,192 FF (US$10,440), corresponding to 5.2 extra days in hospital.

Lesens O. et al. *Bacteremia and endocarditis caused by a Gordonia species in a patient with a central venous catheter.* Emerg Infect Dis. 2000; 6(4) : 382-5.p Abstract : We report the first case of endocarditis caused by a Gordonia species genetically related to G. sputi but exhibiting some atypical biochemical features in a 31-year-old woman with a central venous catheter. This unusual pathogen may be a new cause of opportunistic infections in patients with severe underlying diseases.

Leung W.K. et al. *Subgingival microbiota of shallow periodontal pockets in individuals after head and neck irradiation.* Oral Microbiol Immunol. 1998; 13(1) : 1-10.p Abstract: This study aimed at investigating the subgingival plaque microorganisms of shallow pockets (< or = 5 mm) in subjects who previously received irradiation in the head and neck region for treatment of nasopharyngeal carcinoma. Direct microscopy and anaerobic culture were used. Subgingival paper point samples were taken from 6 tooth-sites (one/sextant) per subject for direct microscopy (n = 108). Another set of paper points was taken from the deepest of the previously selected sites (one per subject) with: group A) no bleeding on probing to the sulcus depth (n = 9) and group B) bleeding on probing to the sulcus depth (n = 6) for microscopic and anaerobic culture study. Under the microscope, the microflora was found to be a complex mixture comprising gram-positive and gram-negative cocci, rods and filaments, fusiforms, curved rods and spirochetes. Low level of fungi were observed and mycelia were occasionally detected. There was no significant variation in the plaque bacterial morphotypes observable according to sites of isolation and no significant difference between group A and group B in morphotypes of the different microflora. The predominant cultivable microflora comprised several species of facultative and obligate anaerobic bacteria: Gemella, Peptostreptococcus, Staphylococcus, Stomatococcus, Streptococcus, Actinomyces, Eubacterium, Lactobacillus, Propionibacterium, Neisseria, Veillonella, Bacteroides, Campylobacter, Capnocytophaga, Fusobacterium, Kingella, Porphyromonas and Prevotella species. There was no difference between the two groups except the significantly higher proportion of Kingella dentrificans isolated from group B sites. However, colonization of the gingival sulcus in these individuals by microbes that are normal flora of: skin (Peptostreptococcus prevotii and Propionibacterium granulosum) and gut (Eubacterium aerofaciens, Fusobacterium mortiferum and Fusobacterium varium) was detected. These findings appear to suggest that the major components of the subgingival microflora of shallow sites in previously head- and neck-irradiated individuals are similar to that of gingivitis sites in the normal population although they may contain bacterial or fungal species uncommon in normal subjects.

Leuschner R.G. et al. *Histamine and tyramine degradation by food fermenting microorganisms.* Int J Food Microbiol. 1998; 39(1-2) : 1-10.p Abstract: Microorganisms suitable for food fermentation were examined with regard to their potential to degrade histamine and tyramine. Out of 64 lactic acid bacteria evaluated in this study, 27 degraded histamine and one tyramine, respectively, with low activity. Among 32 strains of Brevibacterium linens and coryneform bacteria, 21 exhibited histamine and tyramine oxidase activity. None of 20 strains of Staphylococcus carnosus tested degraded histamine or tyramine. One strain out of nine strains of Geotrichum candidum degraded tyramine slightly. Among 44 strains of Micrococcus sp. examined, 17 degraded either one or two biogenic amines. In this study Micrococcus varians (M. varians) LTH 1540 exhibited the highest tyramine oxidase activity of all strains tested and was therefore investigated in detail. The enzyme was found to be located in the cytoplasm and was not membrane bound. The reaction end

product p-hydroxyphenyl acetic acid was detected by HPLC analysis. An activity staining for the amine oxidase in a native polyacrylamide gel based on the formation of H2O2 during amine oxidation was developed. Resting cells of the strain exhibited optimal tyramine oxidase activity at a pH of 7 at 37-40 degrees C. The enzyme in the cell free extract had a pH optimum between 7-8. The enzyme activity was decreased by NaCl, glucose and hydralazine. Phenylethylamine and tryptamine were oxidized at lower concentrations than tyramine. The potential for amine degradation was not found to be associated with that of formation of biogenic amines, as 23 microorganisms with the ability to metabolise biogenic amines exhibited no decarboxylase activity toward histidine, tyrosine, phenylalanine, lysine or ornithine.

Leuschner R.G. et al. *Method for the rapid quantitative detection of lipolytic activity among food fermenting microorganisms.* Int J Food Microbiol. 1997; 37(2-3) : 237-40.p Abstract: A standard method for the detection of free fatty acids (FFAs) in milk was modified and applied to the measurement of the lipolytic activity of microorganisms in a model system containing either homogenised pork or beef fat tissue. The increase in FFAs was measured colorimetrically using palmitic acid as a standard. Among the strains tested, two strains of Staphylococcus xylosus and one strain of Staphylococcus carnosus were found to display lipolytic activity. For all strains, a higher increase in FFA was observed in broth supplemented with pork fat than with beef fat. All three strains displayed lipolytic activity when tested on tributyrin agar plates.

Lever A.M. et al. *Comparative antimicrobial efficacy of multi-purpose lens care solutions using the FDA's revised guidance document for industry: stand-alone primary criteria*. CLAO J. 1999; 25(1) : 52-6.p Abstract: PURPOSE: We evaluated six single-bottle, multi-purpose lens care solutions and a two component lens care system for disinfection efficacy according to the stand-alone primary criteria within the recently published U.S. Food and Drug Administration (FDA) Guidelines. METHODS: One-tenth mL of 1 x 10(8) colony forming units (CFU)/mL of bacterial and fungal challenge organisms was added to each test solution. Following a specified period (e.g., each manufacturer's labeled minimum disinfection time), aliquots of inoculated test solution were neutralized and plated on validated recovery media. After incubation the number of viable microorganisms were enumerated and mean log reductions determined. RESULTS: ReNu and ReNu MultiPlus met the FDA's acceptance criteria for stand-alone disinfectants against all challenge organisms: Staphylococcus aureus, Serratia marcescens, Pseudomonas aeruginosa, Candida albicans, and Fusarium solani. Opti-Free Express failed to meet the FDA's stand-alone disinfectant acceptance criteria for S. aureus, S. marcescens and C. albicans and Opti-Free Express with Opti-Free Supraclens failed to meet the acceptance criteria for either S. aureus and C. albicans. Opti-One failed to meet the FDA's stand-alone disinfectant acceptance criteria for C. albicans and F. solani. Both Complete and Solo-Care failed to meet the FDA's acceptance criteria for C. albicans. CONCLUSIONS: This evaluation provides a direct comparison of antimicrobial activity (based on stand-alone criteria) for commercially available multi-purpose lens care solutions at their labeled minimum disinfection times. The results of this study should be considered when selecting appropriate lens care systems for patients.

Levett P.N. *Antibiotic sensitivity of neisseria gonorrhoeae isolates in Barbados; longitudinal surveillance 1990-1994.* West Indian med. j. 1995; 44(4) : 130-2.p Abstract: The antimicrobial susceptibility of 775 isolates of Neisseria gonorrhoeae, recovered in Barbados over a five-year period, was studied by disc diffusion. Sensitivity to penicillin declined from 56 percent in 1990 to 38 percent in 1994. The prevalence of á-lactamase production rose from 30 percent to 50 percent during this period and sensitivity to tetracycline declined from 96 percent to 46 percent, while co-trimoxazole and spectinomycin sensitivities varied. Ceftriaxone, norfloxacin and erythromycin were the only compounds tested to which sensitivity remained uniform. The results confirm the current recommendations by several agencies that ceftriaxone or an oral fluoroquinolone should be considered the drug of choice for the empirical treatment of gonorrhoea (AU).

Levett P.N. et al. *Genital tract infections in sexually active women in Barbados.* West Indian med. j. 1995; 44(4) : 128-32.p Abstract: Ninety-eight women attending three different clinics were prospectively studied for the presence of genital tract infections, including Chlamydia trachomatis. Of these 98 women, 35 were presenting to a polyclinic with symptoms of genital tract infection, 55 were attending an antenatal clinic for their first visit, and 8 referred to a colposcopy clinic because of an abnormal Papanicolaou smear were included. Gonorrhoea was detected in one patient, syphilis in two, and Trichomonas vaginalis in six. Candida albicans and Chlamydia trachomatis were each detected in 18 patients, while the most common condition was bacterial vaginosis, detected in 35 patients. The prevalence of these infections was lowest in patients referred for colposcopy and highest in the women attending the antenatal clinic, Chlamydia trachomatis was the most common sexually-transmitted pathogen detected in this population. These data emphasise the need for an aggressive approach to the diagnosis and treatment of chlamydial infection in females (AU).

Levin A.S. et al. *Intravenous colistin as therapy for nosocomial infections caused by multidrug-resistant Pseudomonas aeruginosa and Acinetobacter baumannii*. Clin Infect Dis. 1999; 28(5) : 1008-11.p Abstract: Sixty nosocomial infections caused by Pseudomonas aeruginosa and Acinetobacter baumannii resistant to aminoglycosides, cephalosporins, quinolones, penicillins, monobactams, and imipenem were treated with colistin (one patient had two infections that are included as two different cases). The infections were pneumonia (33% of patients), urinary tract infection (20%), primary bloodstream infection (15%), central nervous system infection (8%), peritonitis (7%), catheter-related infection (7%), and otitis media (2%). A good outcome occurred for 35 patients (58%), and three patients died within the first 48 hours of treatment. The poorest results were observed in cases of pneumonia: only five (25%) of 20 had a good outcome. A good outcome occurred for four of five patients with central nervous system infections, although no intrathecal treatment was given. The main adverse effect of treatment was renal failure; 27% of patients with initially normal renal function had renal failure, and renal function worsened in 58% of patients with abnormal baseline creatinine levels. Colistin may be a good therapeutic option for the treatment of severe infections caused by multidrug-resistant P. aeruginosa and A. baumannii.

Levin B.R. et al. *Compensatory mutations, antibiotic resistance and the population genetics of adaptive evolution in bacteria.* Genetics. 2000; 154(3) : 985-97.p Abstract: In the absence of the selecting drugs, chromosomal mutations for resistance to antibiotics and other chemotheraputic agents commonly engender a cost in the fitness of microorganisms. Recent in vivo and in vitro experimental studies of the adaptation to these "costs of resistance" in Escherichia coli, HIV, and Salmonella typhimurium found that evolution in the absence of these drugs commonly results in the ascent of mutations that ameliorate these costs, rather than higher-fitness, drug-sensitive revertants. To ascertain the conditions under which this compensatory evolution, rather than reversion, will occur, we did computer simulations, in vitro experiments, and DNA sequencing studies with low-fitness rpsL (streptomycin-resistant) mutants of E. coli with and without mutations that compensate for the fitness costs of these ribosomal protein mutations. The results of our investigation support the hypothesis that in these experiments, the ascent of intermediate-fitness compensatory mutants, rather than high-fitness revertants, can be attributed to higher rates of compensatory mutations relative to that of reversion and to the numerical bottlenecks associated with serial passage. We argue that these bottlenecks are intrinsic to the population dynamics of parasitic and commensal microbes and dis-

cuss the implications of these results to the problem of drug resistance and adaptive evolution in parasitic and commmensal microorganisms in general.

Levy J. *The effects of antibiotic use on gastrointestinal function*. Am J Gastroenterol. 2000; 95(1 Suppl) : S8-10.p Abstract: The bacterial flora of the gastrointestinal (GI) tract plays an important role in maintaining the integrity of the enterocyte, modulating metabolic and immunologic processes, and protecting against colonization by invasive pathogens. Disruption of this finely tuned and stable gut flora by antibiotics, infection, chemotherapy, or radiation has profound effects on the protective barrier and results in overgrowth by pathogens, invasion and translocation of toxins, and life-threatening infections. Use of antibiotics promotes the emergence of resistant organisms, and multiple-antibiotic resistance has become a major public health issue. Preservation of protective species or recolonization with nonpathogenic yeasts or lactobacilli during periods of stress (infections, drugs) has begun to show promise in the management of patients receiving multiple antibiotics, particularly in hospital-acquired infections.

Lewis M.T. et al. *In vitro evaluation of broad-spectrum beta-lactams tested in medical centers in Korea: role of fourth-generation cephalosporins. The Korean Antimicrobial Resistance Study Group.* Diagn Microbiol Infect Dis. 1999; 35(4) : 317-23.p Abstract: Levels of resistance to the "third-generation" cephalosporins among isolates of clinical bacteria in Korea have been increasing at a rapid rate. This study evaluated the activity of cefepime, a "fourth-generation" cephalosporin, and six other broad-spectrum beta-lactam antimicrobials (cefpirome, ceftazidime, ceftriaxone, imipenem, piperacillin/tazobactam 4 micrograms/mL fixed concentration[, oxacillin) against 404 isolates of clinical bacteria from Korea. Susceptibility profiles of each isolate were established using the Etest (AB BIODISK, Solna, Sweden) method of susceptibility testing. Only the carbapenem imipenem was > 90% effective in inhibiting each of the species tested (Escherichia coli, Klebsiella, spp., Citrobacter spp., Enterobacter spp., indole-positive Proteae, Serratia spp., Acinetobacter spp., Pseudomonas aeruginosa, and oxacillin-susceptible staphylococci). Imipenem was followed by cefepime > cefpirome > piperacillin/tazobactam > ceftazidime > ceftriaxone in overall rank order of usable spectrum against the isolates tested. Extended spectrum beta-lactamase producing phenotypes were much more prevalent among the Klebsiella spp. (48.8%) than the E. coli (5.0%) isolates. Cefepime was much more active than cefpirome, 95.1% susceptible as compared with 70.7% susceptible, against the 41 isolates of Klebsiella spp. The results of this study corroborates findings from earlier studies with levels of resistance to the broad-spectrum beta-lactams in Korea continuing to rise indicating the need for intervention strategies.

Lewis M.T. et al. *In vitro evaluation of cefepime and other broad-spectrum beta-lactams against bacteria from Indonesian medical centers. The Indonesia Antimicrobial Resistance Study Group.* Diagn Microbiol Infect Dis. 1999; 35(4) : 285-90.p Abstract: The in vitro activity of cefepime and six other broad-spectrum beta-lactams (cefpirome, ceftazidime, ceftriaxone, imipenem, piperacillin/tazobactam (4 micrograms/mL fixed concentration), and oxacillin was evaluated against 191 isolates of clinical bacteria from Indonesia. Susceptibility testing was performed using Etest (AB BIODISK, Solna, Sweden) methodology. Isolates from 10 species groups were selected for analysis: Escherichia coli, Klebsiella spp., Enterobacter spp., indole-positive Proteae, Serratia spp., Acinetobacter spp., Pseudomonas aeruginosa, and oxacillin-susceptible staphylococci. The overall rank order of spectrum of activity was (% resistant): imipenem (2.2%) > cefepime (7.3%) > piperacillin/tazobactam > cefpirome > ceftazidime > ceftriaxone (16.2%). The "fourth-generation" cephalosporins, cefepime and cefpirome, displayed greater activity compared with the "third-generation" cephalosporins, ceftazidime, and ceftriaxone, against the 60 E. coli and Klebsiella spp. (30 each) isolates. Phenotypic extended spectrum beta-lactamase occurrence rates among the E. coli and Klebsiella spp. were 23.3 and 33.3%, respectively. Imipenem, cefepime, and cefpirome inhibited 95.7% of the 46 isolates of inducible Amp C cephalosporinase producing Enterobacteriaceae. The majority of the resistance observed to imipenem and cefepime among tested Indoneisian strains was attributable to the nonfermentative Gram-negative bacilli, P. aeruginosa and Acinetobacter spp. These results indicate the presence of beta-lactam resistance in Indonesia and the need for continued antimicrobial surveillance in this nation and region of the world, preferably using accurate quantitative methods.

Lewis M.T. et al. *Frequency of occurrence and antimicrobial susceptibility patterns for pathogens isolated from latin american patients with a diagnosis of pneumonia: results from the SENTRY antimicrobial surveillance program (1998).* Diagn Microbiol Infect Dis. 2000; 37(1) : 63-74.p Abstract: The correct empiric choice of antimicrobial therapy in the treatment of pneumonia in hospitalized patients has established itself as a major therapeutic challenge to clinicians. Selection of an inappropriate antimicrobial agent could lead to increased rates of mortality and morbidity. Characteristics of pathogens responsible for this infection such as species prevalence, overall antimicrobial resistance rates, and mechanisms of detected resistance could serve as an invaluable resource to clinicians in making such therapeutic selections. This report addresses the aforementioned problems/needs by analysis of 712 strains isolated from the lower respiratory tract of patients hospitalized with a diagnosis of pneumonia in 10 Latin American medical centers in the SENTRY Antimicrobial Surveillance Program (1998). The four most frequently isolated pathogens (no/% of total) were: Pseudomonas aeruginosa (191/26.8%), Staphylococcus aureus (171/24.0%), Klebsiella spp. (86/12.1%), and Acinetobacter spp. (75/10.5%); representing nearly 75.0% of all isolates. More than 40 antimicrobial agents (23 reported) were tested against these isolates by reference broth microdilution methodology, and susceptibility profiles were established. The nonfermentative Gram-negative bacteria (P. aeruginosa and Acinetobacter spp.) exhibited high levels of resistance to the agents tested. Amikacin (77.5% susceptible) was the most active drug tested against P. aeruginosa 50.0% against the Acinetobacter spp. isolates. Based on published interpretive criteria, over 22.0% of the Klebsiella spp. and 12.5% of the Escherichia coli were classified as extended spectrum beta-lactamase (ESBL) producers. Of the cephalosporin class compounds tested against the Klebsiella spp. and E. coli isolates, cefepime demonstrated the highest rates of susceptibility (84.9% and 91.7%, respectively). This compound also fared well against the Enterobacter spp. isolates, inhibiting 88.2% of the isolates tested, many of which were resistant to ceftazidime and ceftriaxone. Resistance to oxacillin among the S. aureus isolates was nearly 50. 0%, with vancomycin, teicoplanin, and the streptogramin combination quinupristin/dalfopristin inhibiting all isolates. Several clusters of multiply resistant organisms were also observed, and further characterization by ribotyping and pulsed-field gel electrophoresis established possible patient-to-patient spread. The results of this study indicate that rates of resistance among respiratory tract pathogens continue to rise in Latin America, with specific concerns for the high prevalence of nonfermentative Gram-negative bacteria isolated, oxacillin resistance rates in S. aureus, and the epidemic dissemination of multiply-resistant strains in several medical centers. International surveillance programs (SENTRY) should assist in the control of escalating antimicrobial resistance in this geographic area.

Lewis M.T. et al. *In vitro evaluation of cefepime and other broad-spectrum beta-lactams in 22 medical centers in Japan: a phase II trial comparing two annual organism samples. The Japan Antimicrobial Resistance Study Group.* Diagn Microbiol Infect Dis. 1999; 35(4) : 307-15.p Abstract: An antimicrobial resistance surveillance study in Japan is presented representing the second year (Phase II) results from 22 medical centers. Each participant laboratory tested (Etest, AB BIODISK, Solna, Sweden) 100 organisms, 10 strains each from 10 species groups

including Escherichia coli, Klebsiella spp., Enterobacter spp., Citrobacter spp., indole-positive Proteae, Serratia spp., Acinetobacter spp., Pseudomonas aeruginosa, and oxacillin-susceptible Staphylococcus aureus and coagulase-negative staphylococci. Generally only modest variations in the activity of the studied broad-spectrum beta-lactams was observed compared to the study a year before. Specifically, extended spectrum beta-lactamase (ESBL) rates in E. coli increased (2.9 to 8.1%), but the ESBL rate in Klebsiella spp. fell (8.6 to 5.0%). Overall the resistance to the beta-lactams varied from a 4.7% decrease (ceftazidime as a consequence of a modified staphylococcal breakpoint criteria) to a 1.0% increase (cefepime, not significant). The rank order of spectrums in 1998 only changed for cefoperazone-sulbactam (6.1% resistance) that was active against more strains than cefpirome (6.8% resistance). The overall spectrum rank order for the 1998 Japan sample (% resistance) was: cefepime (3.2%) > imipenem (4.1%) > cefoperazone-sulbactam (6.1%) > cefpirome (6.8%) > ceftazidime (8.4%) > piperacillin (19.9%). As with a similar study in 1997, imipenem-resistant isolates of P. aeruginosa and Serratia spp. were discovered with metalloenzymes, usually found in the same medical centers. These results demonstrate the continued in vitro activity and potential sustained clinical efficacy of several broad-spectrum beta-lactams in Japan. Rapid emergence of new or novel resistance were not wide spread using a precise quantitative MIC system. Continued surveillance in this nation would be prudent to document the activity of this clinically valuable class of safe, antimicrobial agents.

Li C.C. et al. *Antimicrobial susceptibilities of Campylobacter jejuni and coli by using E-test in Taiwan*. Scand J Infect Dis. 1998; 30(1) : 39-42.p Abstract: To report the in vitro antibiotic susceptibility of Campylobacter species, we determined the MICs of 6 antibiotics by E-test for 93 human clinical strains and 35 chicken strains. The 6 antimicrobial agents tested were gentamicin, erythromycin, clindamycin, tetracycline, ciprofloxacin, and nalidixic acid. Isolates from humans were significantly more susceptible than chicken strains to erythromycin, clindamycin and ciprofloxacin. Nearly all of the human and chicken strains were susceptible to gentamicin. Among human isolates of C. jejuni, cross-resistance between nalidixic acid and ciprofloxacin was found in 66% of the strains, but none of the nalidixic acid-susceptible strains was resistant to ciprofloxacin. The higher prevalence of ciprofloxacin resistance in this area may be attributable to the large amount use of quinolones in poultry. Because of the high resistance rates of chicken isolates to the commonly used antimicrobial agents, it is necessary to create innovative methods to limit the inappropriate use of antibiotics in poultry in order to prevent the spread of the drug-resistant strains to humans.

Li C.H. et al. *Septic arthritis in hemophilia with central venous catheter: a case report*. Pediatr Hematol Oncol. 2000; 17(2) : 187-9.p Abstract: A case is reported of septic arthritis in a child with human immunodeficiency virus-negative hemophilia A associated with a Staphylococcus aureus catheter-associated septicemia. The infection occurred in relation to the use of a totally implantable central venous catheter. The organism was eventually eradicated with antibiotics injected via the catheter. With increasing use of such catheters in the hemophilic population, clinicians should be alerted to the possibility of septic arthritis for prompt diagnosis and treatment.

Li F. et al. *Molecular detection of bacterial DNA in venereal-associated arthritis.* Arthritis Rheum. 1996; 39(6) : 950-8.p Abstract: OBJECTIVE: To evaluate the utility of polymerase chain reaction (PCR) amplification in detecting DNA from venereal-associated microorganisms in the synovial fluid of patients with inflammatory arthritis. METHODS: Oligonucleotide primers were developed for nested PCR based on Chlamydia, Ureaplasma, and Neisseria DNA sequences. PCR products were detected by gel electrophoresis and dot-blot hybridization. Primers specific for the target bacterial DNA were used to search for bacterial DNA in 61 synovial fluid specimens from patients with inflammatory arthritis, including several clinically associated with venereal infection. RESULTS: Five of the 61 synovial fluid specimens were positive for Neisseria gonorrhoeae DNA. Four of the 5 patients had clinical diagnoses of gonococcal arthritis; the other patient had an unexplained monarthritis. One specimen from a patient with a clinical diagnosis of gonococcal arthritis was negative for N gonorrhoeae. Three of the 61 specimens were positive for Chlamydia DNA. Two were derived from patients with clinical diagnoses of reactive arthritis or Reiter's syndrome, and 1 was from a patient with unexplained monarthritis. One of the 61 specimens was positive from Ureaplasma DNA; this sample was from a patient with a clinical diagnosis of Reiter's syndrome. In an additional patient with Reiter's syndrome, Ureaplasma DNA was also found in prostate biopsy tissue and a urine sample obtained after prostate massage (synovial fluid not available). CONCLUSION: These data support the classification of these 3 venereal-associated arthritides as infectious processes, and suggest that PCR for bacterial DNA is a useful method for detecting infectious agents in synovial fluid.

Liao W.Y. et al. *Bacteriology of infected cavitating lung tumor.* Am J Respir Crit Care Med. 2000; 161(5) : 1750-3.p Abstract: Differentiation between in situ infection and simple tumor necrosis in cavitating lung tumors by means of imaging studies is difficult. In this study, we prospectively investigated the role of ultrasound (US)-guided transthoracic aspiration for bacteriologic examination of infected cavitating lung tumors, and the influence of the culture results on the treatment of patients. Twenty-two patients (18 men and four women) with cavitating lung tumors treated from January 1996 to October 1998 were included. All patients underwent US-guided transthoracic aspiration for bacterial, fungal, and mycobacterial cultures. Microorganisms were isolated from six of seven febrile patients and one of 15 nonfebrile patients. A total of nine pathogens were isolated from seven patients: Klebsiella pneumoniae (n = 3); Haemophilus influenzae (n = 2); Enterococcus faecium (n = 1); Bifidobacterium (n = 1); Shewanella putrefaciens (n = 1); and Mycobacterium tuberculosis (n = 1). Two pathogens were isolated from the aspirate cultures in two patients, while the others had monomicrobial infection. The six febrile patients who had positive lung aspirate cultures were treated with empiric antimicrobial agents before the culture results were available, and the culture results led to adjustment of the antibiotic regimen in five of these. The clinical conditions of the six patients with infected cavitating lung tumors improved after the initiation of individualized antimicrobial treatment. Pneumothorax occurred in one patient, and was the sole procedure-related complication. In conclusion, US-guided transthoracic aspiration is helpful for differentiating infected cavitating lung tumors from simple tumor necrosis. Infection in cavitating lung tumors is common among febrile patients, and the culture results can guide modification of the antimicrobial therapy.

Liassine N. et al. *In vitro activity of cefpirome against microorganisms isolated in haematology, oncology and intensive care units in Switzerland*. Scand J Infect Dis. 1997; 29(6) : 615-21.p Abstract: The in vitro activity of cefpirome, a new parenteral fourth-generation cephalosporin, was investigated in the 5 university hospitals of Switzerland, and compared to 9 other antibiotics mainly used in hospitals, such as ceftazidime, ceftriaxone, cefotaxime, piperacillin, imipenem, gentamicin, vancomycin, ciprofloxacin and ofloxacin. A total number of 992 strains collected only from intensive care units and haematology-oncology units were tested by microdilution according to NCCLS. Cefpirome showed an excellent activity against all Enterobacteriaceae (MIC90 = 4 mg/l), methicillin-susceptible staphylococci (MIC90 = 1 mg/l), Streptococcus pneumoniae (MIC90 = 0.25 mg/l) and Haemophilus influenzae (MIC90 = 0.12 mg/l) isolates. Its activity was superior to that of third-generation cephalosporins against cephalosporinase-depressed mutants of Enterobacter cloacae and Citrobacter freundii isolates (MIC90 > 32 mg/l for third-generation cephalosporins vs 4 mg/l for cefpirome). The MICs of cefpirome of 3 strains of Klebsiella spp. with an

extended-spectrum-beta-lactamase were lower (MIC90 = 2 mg/l) than those of third-generation cephalosporins (MICs90 > 32 mg/l). Against Pseudomonas aeruginosa cefpirome was as active as ceftazidime. The activity of cefpirome was poor against methicillin-resistant staphylococci, enterococci and nosocomial Gram-negative bacteria such as Stenotrophomonas maltophilia.

Liassine N. et al. *Antimicrobial susceptibility of bacterial pathogens in the oropharynx of healthy children.* Eur J Clin Microbiol Infect Dis. 1999; 18(3) : 217-20.p Abstract: In a study to determine the prevalence and antimicrobial susceptibility of bacterial pathogens in the oropharynx of healthy children, throat swabs obtained from 1765 children were cultured and the organisms recovered tested by the disk diffusion method and the E test. Six hundred ninety-one children (39.1%) harbored Haemophilus influenzae, 112 (6.3%) Streptococcus pyogenes, 73 (4.1%) Moraxella catarrhalis, 52 (2.9%) Streptococcus pneumoniae, and 50 (2.8%) Neisseria meningitidis in their oropharynx. The rate of penicillin resistance was 2%, 0%, and 12%, respectively, for Streptococcus pneumoniae, Streptococcus pyogenes, and Neisseria meningitidis. Ampicillin resistance was observed in 8.6% of Haemophilus influenzae strains and 78% of Moraxella catarrhalis strains and was associated with the presence of beta-lactamase, except in one strain of Haemophilus influenzae. Five (4.4%) isolates of Streptococcus pyogenes were resistant to macrolides. The low level of resistance observed in this area contrasts with the high rates reported in the literature.

Liberati A. et al. *Antibiotic prophylaxis in intensive care units: meta-analyses versus clinical practice.* Intensive Care Med. 2000; 26 Suppl 1 : S38-44.p Abstract: OBJECTIVE: At least 7 meta-analyses (MA) have been published since 1991 on the effectiveness of antibiotic prophylaxis in Intensive care units (ICU) patients, but controversy still remains about the overall effectiveness and risk-benefits profile of the treatment. This paper aims to summarise available data on effectiveness and discuss reasons why the controversy is still open and possible directions for future research. DESIGN: Review of available published MA on the effectiveness of various regimens of antibiotic prophylaxis with particular emphasis on the results of the individual patient data analysis published in 1998. SETTING: MA or randomised control trials (RCTs), published and unpublished, conducted anywhere in the world. PATIENTS AND PARTICIPANTS: Unselected adult ICU populations included in studies, published and unpublished, comparing different forms of antibiotic prophylaxis. MAIN OUTCOME MEASURE: Respiratory tract infections (RTIs) - however defined in individual studies - and total mortality. DATA SOURCES: General information from the 7 MAs published between 1991 and 1999 and detailed information from the MA published in the British Medical Journal in 1998 that reported data on 5727 patients enrolled in 33 RCTs; access to individual patients data could be obtained from 25 of 33 RCTs and allowed a confirmatory individual patient MA on 4343 patients. RESULTS: Pooled estimates from 16 RCTs (including 3361 patients) testing the effect of the topical and systemic antibiotic combination indicates a significant reduction of both RTIs (OR=0.35, 95% CI=0.29-0.41) and total mortality (OR=0.80, 95% CI=0.69-0.93). Five and 23 patients need to be treated to prevent one infection and one death, respectively, using this treatment. Pooled data from the 17 RCTs (including 2366 patients) testing the effect of a regimen based on topical antimicrobials indicated a statistically significant reduction in RTIs (OR=0.57, 95% CI=0.46-0.69) but not in total mortality (OR=1.01; 95% CI=0.84-1.22). Individual patient data analyses confirmed these results. CONCLUSIONS: After over 30 RCTs and seven MAs, there is strong evidence that antibiotic prophylaxis can reduce both RTIs and total mortality in ICUs patients in a statistically and clinically significant way. Concerns about the possible occurrence of antimicrobial resistance are not supported by available data but cannot, at the same time, be ruled out due to methodologic inadequacies of the studies carried out so far. Whether new trials are needed, and how they should be designed to answer the question of the potential for antibiotic resistance following widespread use of the treatment, are now the main issues to be settled. Convening an international panel of clinical experts and methodologists could be appropriate, in order to explore the best way to resolve the controversy that seems to be preventing the widespread use of a treatment that the best analysis of available data now indicates is effective.

Liberra K. et al. *Corollosporine, a new phthalide derivative from the marine fungus Corollospora maritima Werderm. 1069.* Pharmazie. 1998; 53(8) : 578-81.p Abstract: Extracts of the culture medium from the marine fungus Corollospora maritima exhibited concentration dependent antibacterial activity against Staphylococcus aureus and other microorganisms. Bioactivity-guided fractionation and purification afforded the new isobenzofuranone or phthalid type compound corollosporine.

Lieberman D. et al. *Etiology of respiratory tract infection in adults in a general practice setting.* Eur J Clin Microbiol Infect Dis. 1998; 17(10) : 685-9.p Abstract: A prospective study was conducted over a 3-month winter period in three general practice clinics in an urban population in southern Israel to identify the etiological agents of respiratory tract infections (RTI) in adults. RTI was defined as an acute febrile illness with cough, coryza, sore throat or hoarseness. Serum samples were taken from all patients in both the acute and convalescent phases of their illness. Tests were conducted for detection of 17 microorganisms known to cause RTI, including serological tests for 16 known pathogens. An etiological diagnosis was established in 80 (66%) of the 122 patients who participated in the study. The distribution of the etiological agents was as follows: influenza B virus in 27 (22%) patients. Chlamydia pneumoniae in 22 (18%), Legionella spp. in 15 (12%), Mycoplasma pneumoniae in 13 (11%), influenza A virus in 11 (9%), Bordetella pertussis in 9 (7%), adenovirus in 4, Epstein Barr virus in 4, Haemophilus influenzae in 3, beta-hemolytic streptococci in 3, Streptococcus pneumoniae in 2, respiratory syncytial virus in 2, parainfluenza 1 virus in 2 and parainfluenza 2 virus in 1. No patients were found to be infected with Coxiella burnetii, Moraxella catarrhalis or parainfluenza 3 virus. More than one pathogen was identified in 27 (34%) patients in whom an etiological diagnosis was established. It is concluded that RTI is caused by a broad spectrum of etiological agents, a considerable number of patients having evidence of infection with more than one pathogen. The therapeutic significance of these findings should be elucidated in further studies.

Liese J. et al. *Long-term follow-up and outcome of 39 patients with chronic granulomatous disease.* J Pediatr. 2000; 137(5) : 687-693.p Abstract: OBJECTIVES: To evaluate the clinical long-term course in patients with chronic granulomatous disease (CGD) with respect to different CGD subtypes and currently used antimicrobial prophylactic measures. Study design: The records of 39 patients with CGD who were monitored during a period of 22 years were reviewed. All infections, infectious complications, and clinical outcomes were documented for a total observation period of 610 patient-years and were stratified with respect to different CGD subtypes. RESULTS: Lymphadenitis, skin abscesses, and pneumonia occurred in 87%, 72%, and 59% of the patients, respectively. In 151 microbiologic isolates Staphylococcus aureus, Aspergillus species, Candida species, Pseudomonas species, and Salmonella species were the most frequently detected microorganisms. There were 167 severe infections requiring hospitalization and intravenous antimicrobial treatment, resulting in an incidence of 3.7 severe infections per 100 patient months (SI/100 PM). Long-term antibiotic prophylaxis significantly reduced the incidence of severe bacterial infections from 4.8 SI/100 PM to 1.6 SI/100 PM (P =.0035). In contrast, fungal infections increased under antibiotic prophylaxis from a mean incidence of 0.2 SI/100 PM to 1.9 SI/100 PM (P =.04). We found a 50% survival rate through the fourth decade of life, with a plateau after the third decade of life. Patients with a complete absence of cytochrome

b(558) showed an earlier manifestation of their disease and a higher incidence of infections and had significant lower survival than patients with only diminished cytochrome b(558) or autosomal recessive CGD. CONCLUSIONS: Infections with Aspergillus species have become the major cause of infectious complications and death in patients with CGD. Prophylactic and therapeutic measures are needed to further increase life expectancy and quality for patients with CGD.

Lilja M. et al. *Selective attachment of beta-haemolytic streptococci group A to oropharyngeal epithelium in health and disease.* Acta Otolaryngol. 1997; 117(5) : 744-9.p Abstract: Localization and semiquantification of beta-haemolytic streptococci, Group A (GABHS), GABHS attachment and general bacterial attachment to epithelial cells (bacterial number and morphology) were studied during GABHS-positive acute tonsillitis and pharyngitis infections and among healthy GABHS carriers. Samples were collected from various areas of the oropharynx (palatine tonsils, posterior oropharyngeal wall, palatoglossal arch and buccal mucosa). During acute tonsillitis and pharyngitis, GABHS grew in samples obtained from the palatine tonsils and posterior oropharyngeal wall. The ratio of GABHS colonies to other aerobic colonies increased, and GABHS became attached to epithelial cells of both palatine tonsils and posterior oropharyngeal wall. In GABHS carriers, GABHS were found mainly on the palatine tonsils, but these microorganisms were not attached to the epithelium. Overall bacterial attachment to tonsillar and oropharyngeal epithelial cells increased during active tonsillitis and pharyngitis.

Lim T.K. *Emerging pathogens for pneumonia in Singapore.* Ann Acad Med Singapore. 1997; 26(5) : 651-8.p Abstract: The death rate from pneumonia in Singapore has increased steadily over the past decade. The emerging respiratory pathogens may have contributed to this increased mortality. New challenges have arisen from changes in the characteristics of the host and the susceptibilities of the various pathogens to antibiotics. There has been a 60-fold increase in the incidence of penicillin resistance in Streptococcus pneumoniae, the major pathogen for community-acquired pneumonia (CAP). Gram-negative bacilli are the major pathogens in severe CAP with Klebsiella pneumonia being the most frequently isolated organism. There has been a small increase in the number of cases of Legionnaire's disease and a marked increase in the incidence of melioidosis. While the overall incidence of tuberculosis has been unchanged, the number of non-residents with tuberculosis has doubled in the past 5 years. The rising prevalence of human immunodeficiency Virus infection is reflected in an increasing number of apparently healthy young men who present with CAP caused by Pneumocystis carinii. There is increasing resistance to antibiotics among gram-negative bacilli and Staphylococcus aureus, the dominant pathogens in hospital-acquired pneumonia. New strategies are urgently needed to prevent the emergence of pathogens in the hospital environment which may be resistant to all known antibiotics.

Lima A.A. et al. *High frequency of strains multiply resistant to ampicillin, trimethoprim-sulfamethoxazole, streptomycin, chloramphenicol, and tetracycline isolated from patients with shigellosis in northeastern Brazil during the period 1988 to 1993.* Antimicrob Agents Chemother. 1995; 39(1) : 256-9.p Abstract: The occurrence and antimicrobial resistance pattern of Shigella isolates obtained from persons in community and hospital-based studies of diarrhea and matched controls in northeastern Brazil were studied. The isolation rate of Shigella spp. from patients with diarrhea during 1988 to 1993 varied from 4.5% (26 of 575) for the urban community of Goncalves Dias to 6.7% (12 of 179) and 5.9% (7 of 119) for Hospital Infantil and Hospital Universitario, respectively. Of the 55 Shigella isolates (45 from patients with diarrhea, 8 from controls, and 2 undetermined) 73% (40 of 55) were Shigella flexneri, 16% (9 of 55) were S. sonnei, 7% (4 of 55) were S. boydii, and 4% (2 of 55) were S. dysenteriae. Of 39 S. flexneri strains, over half were resistant to ampicillin, trimethoprim-sulfamethoxazole, or both. Over 64% were resistant to streptomycin, chloramphenicol, and tetracycline. Overall, 82% of all S. flexneri isolates were resistant to four or more antimicrobial agents tested. As elsewhere, in the northeast of Brazil, ampicillin and trimethoprim-sulfamethoxazole are no longer reliable for treatment of S. flexneri infection. Most Shigella strains were resistant to four or more antimicrobial agents. Nalidixic acid was still useful for treatment of infections due to S. flexneri.

Limia A. et al. *Five-year analysis of antimicrobial susceptibility of the Streptococcus milleri group.* Eur J Clin Microbiol Infect Dis. 1999; 18(6) : 440-4.p Abstract: Susceptibility to 17 antibiotics was studied in 180 strains of the Streptococcus milleri group (88 Streptococcus anginosus, 63 Streptococcus constellatus, and 29 Streptococcus intermedius) isolated over a 5-year period. Minimum inhibitory concentrations of penicillin were in the intermediate range for 5.6% of the strains. Resistance to erythromycin and clindamycin was found in 17.1% and 16.6% of the isolates, respectively. A steady increase in the susceptibility to ciprofloxacin was observed over the study period. Imipenem was the most active beta-lactam agent tested. Glycopeptide antibiotics showed excellent activity. Only slight differences between the three species were found in terms of antibiotic susceptibility. Intermediate resistance to penicillin is appearing among the Streptococcus milleri group in our area; consequently, care must be taken when choosing a macrolide for the management of infections caused by these microorganisms.

Limyati D.A. et al. *Jamu Gendong, a kind of traditional medicine in Indonesia: the microbial contamination of its raw materials and endproduct.* J Ethnopharmacol. 1998; 63(3) : 201-8.p Abstract: An examination on the microbiological quality of seven kinds of Jamu Gendong (JG) and their raw materials has been conducted according to the requirements of microbial contamination in traditional medicine, issued by the Department of Health of Indonesia in 1986. Samples of JG and their raw materials were taken from producers in three districts of Surabaya. The samples were subject to the following examinations: total plate count (TPC), MPN coliform, the enumeration of molds and yeasts, the presence or absence of Staphylococcus aureus, Salmonella and Vibrio. Each time the JG samples were taken from different producers together with their raw materials. The results of this investigation showed that most of the JG samples were heavily contaminated with bacteria, yeasts and molds. For bacteria, taken from the TPC results, their numbers were ranging from 7.7 x 10(2) microorganisms/ml to too many to count (TMTC). For yeasts and molds the numbers showed variations from 0 microorganisms/ml to TMTC. Contamination with Coliform in 1 ml of JG were ranged from 0 to > 2.4 x 10(6) microorganisms. In most of the samples pathogenic Staphylococci, Salmonella sp. and Vibrio sp. were not detected, so that a conclusion can be drawn that most of the contamination in JG are saprophytic, only a few pathogenic. The results also show that it is possible to have JG which fulfill the government's requirements. Similar results were obtained with the plant material constituents of JG such as rhizomes, leaves, herbs and fruits of Piper nigrum and Piper retrofractum, with the exception of Piper betle leaves and P. retrofractum fruits, both showing low contamination of Coliform bacteria. However, the fruits of Citrus aurantifolia and Morinda citrifolia were less contaminated, just like seeds of Oryza sativa, Parkia roxburghii, bulbs of Allium sativum and the pulp of Tamarindus indica. With these plant constituents of JG, it might be of interest to screen their antibacterial and antifungal activities.

Lin H.C. et al. *Prevalence of antimicrobial resistance among clinical isolates of Haemophilus influenzae in Taiwan.* J Formos Med Assoc. 1999; 98(5) : 319-25.p Abstract: The purpose of this study was to determine the prevalence of resistance to various antimicrobial drugs among Haemophilus influenzae isolates in Taiwan. Two hundred and ninety-six clinical isolates of H. influenzae were prospectively obtained from nine teaching hospitals throughout Taiwan, from June 1994 to April 1995. All isolates were examined for the presence of type b

encapsulation and beta-lactamase production. Antibiotic susceptibility was determined by means of standard broth microdilution procedures. Twenty-three isolates (7.8%) were type b, and the overall rate of beta-lactamase production was 58.1% (172/296). The rates of resistance to antibiotics were 58.1% for ampicillin, 33.8% for trimethoprim-sulfamethoxazole, 20.6% for chloramphenicol, 27% for tetracycline, 6.7% for azithromycin, 3.4% for cefaclor, and 0.3% for cefuroxime. Cefixime, ceftriaxone, and ciprofloxacin were active against all H. influenzae isolates. Thirty (10.1%) of the 296 isolates were resistant to three drugs (ampicillin, chloramphenicol, and tetracycline), 16 of which (5.4%) were resistant to four drugs (ampicillin, chloramphenicol, tetracycline, and trimethoprim-sulfamethoxazole). There was a marked increase in the rates of ampicillin resistance and beta-lactamase production among H. influenzae isolates compared with a previous survey in Taiwan conducted 9 years ago. In addition, isolates with multiple drug resistance were also identified. Continued efforts are needed to monitor antibiotic resistance patterns of H. influenzae in the region.

Lin J.C. et al. *Phlebotomy overdraw in the neonatal intensive care nursery.* Pediatrics. 2000; 106(2) : E19.p Abstract: OBJECTIVE: Because blood loss attributable to laboratory testing is the primary cause of anemia among preterm infants during the first weeks of life, we quantified blood lost attributable to phlebotomy overdraw, ie, excess that might be avoided. We hypothesized that phlebotomy overdraw in excess of that requested by the hospital laboratory was a common occurrence, that clinical factors associated with excessive phlebotomy loss would be identified, and that some of these factors are potentially correctable. DESIGN, OUTCOME MEASURES, AND ANALYSIS: Blood samples drawn for clinical purposes from neonates cared for in our 2 neonatal special care units were weighed, and selected clinical data were recorded. The latter included the test performed; the blood collection container used; the infant's location (ie, neonatal intensive care unit [NICU] and intermediate intensive care unit); the infant's weight at sampling; and the phlebotomist's level of experience, work shift, and clinical role. Data were analyzed by univariate and multivariate procedures. Phlebotomists included laboratory technicians stationed in the neonatal satellite laboratory, phlebotomists assigned to the hospital's central laboratory, and neonatal staff nurses. Phlebotomists were considered experienced if they had worked in the nursery setting for >1 year. Blood was sampled from a venous or arterial catheter or by capillary stick from a finger or heel. Blood collection containers were classified as tubes with marked fill-lines imprinted on the outside wall, tubes without fill-lines, and syringes. Infants were classified by weight into 3 groups: <1 kg, 1 to 2 kg, and >2 kg. The volume of blood removed was calculated by subtracting the weight of the empty collection container from that of the container filled with blood and dividing by the specific gravity of blood, ie, 1.050 g/mL. The volume of blood withdrawn for individual laboratory tests was expressed as a percentage of the volume requested by the hospital laboratory. RESULTS: The mean (+/- standard error of the mean) volume of blood drawn for the 578 tests drawn exceeded that requested by the hospital laboratory by 19.0% +/- 1.8% per test. The clinical factors identified as being significantly associated with greater phlebotomy overdraw in the multiple regression model included: 1) collection in blood containers without fill-lines; 2) lighter weight infants; and 3) critically ill infants being cared for in the NICU. Because the overall R(2) of the multiple regression for these 3 clinical factors was only.24, the random factor of individual phlebotomist was added to the model. This model showed that there was a significant variation in blood overdraw among individual phlebotomists, and as a result, the overall R(2) increased to.52. An additional subset analysis involving 2 of the 3 groups of blood drawers (ie, hospital and neonatal laboratory phlebotomists) examining the effect of work shift, demonstrated that there was significantly greater overdraw for blood samples obtained during the evening shift, compared with the day shift when drawn using unmarked tubes for the group of heavier infants cared for in the NICU. CONCLUSION: Significant volumes of blood loss are attributable to overdraw for laboratory testing. This occurrence likely exacerbates the anemia of prematurity and may increase the need for transfusions in some infants. Attempts should be made to correct the factors involved. Common sense suggests that blood samples drawn in tubes with fill-lines marked on the outside would more closely approximate the volumes requested than those without. Conversely, the use of unmarked tubes could lead to phlebotomy overdraw because phlebotomists may overcompensate to avoid having to redraw the sample because of an insufficient volume for analysis. We were surprised to observe that the lightest and most critically ill infants experienced the greatest blood overdraw. (ABSTRACT TRUNCATED).

Lin J.H. et al. *Right lung agenesis with left pulmonary artery sling.* Pediatr Pulmonol. 2000; 29(3) : 239-41.p Abstract: We report on a 2-month-old infant girl who had right pulmonary agenesis and an unusual course of the left pulmonary artery. Computed tomography and cardiac catheterization showed that the left pulmonary artery arose from the main pulmonary artery, crossing the midline, and reaching the left lung via an aberrant course between the esophagus and trachea. The coexistence of right pulmonary agenesis and left pulmonary sling is extremely rare. Unlike in other reports, our patient remained symptom-free and in good health, with normal growth and development until age 2 years, when she died from complications during an attack of bronchiolitis caused by respiratory syncytial virus. Copyright 2000 Wiley-Liss, Inc.

Lin J.J. et al. *Disinfection of denture base acrylic resin.* J Prosthet Dent. 1999; 81(2) : 202-6.p Abstract: STATEMENT OF PROBLEM: During repair or adjustments of acrylic resin removable complete and partial dentures, particles of the acrylic resin from the interior of the prosthesis may expose dental personnel to microbial health hazards if the prosthesis has not been thoroughly disinfected. PURPOSE: This study investigates the efficacy of a commercially prepared microbial disinfectant (Alcide) on the external and internal surfaces of acrylic resins. MATERIAL AND METHODS: Four groups of acrylic resin were incubated in an experimental model to simulate the oral environment over time. Specimens were treated in 2 groups, disinfected and not disinfected, and then further grouped by breaking and not breaking. Analysis was performed with microbial colony counts, SEM, and statistical analyses. RESULTS: Viable microorganisms still remain on the internal and external surfaces of treated resins. CONCLUSION: Chlorine dioxide reduces, but does not eliminate, viable microorganisms on these dental prostheses.

Lin R.D. et al. *Capnocytophaga bacteremia: clinical features of patients and antimicrobial susceptibility of isolates.* J Formos Med Assoc. 1998; 97(1) : 44-8.p Abstract : Capnocytophaga has been recognized as an opportunistic pathogen causing systemic infections in immunocompromised individuals with granulocytopenia and oral ulceration. Treatment of Capnocytophaga infection is often empiric. We retrospectively analyzed the clinical features of all patients with Capnocytophaga bacteremia seen at the National Taiwan University Hospital between January 1981 and December 1996 and the antimicrobial susceptibility of the isolates recovered from these patients. All the patients had underlying diseases, namely neoplastic disease (9 patients), hyperthyroidism (1), and bronchiectasis and tetralogy of Fallot (1). The clinical features of these patients were primary bacteremia (10) and pneumonia (1). Nine patients had nosocomial bacteremia and 10 patients had monomicrobial bacteremia. None had septic shock. All the patients responded well to appropriate antimicrobial therapy and survived. All isolates were susceptible to amoxicillin-clavulanate, imipenem, ciprofloxacin, erythromycin, clindamycin, tetracycline, and chloramphenicol but resistant to aminoglycosides and sulfamethoxazole-trimethoprim. The susceptibilities to penicillin, ampicillin, piperacillin, cephalosporins, and aztreonam were variable. Capnocytophaga bacteremia should be included in the differential diagnosis of febrile neutropenia in immunocompromised patients, especially in the presence of oral mucositis and ulceration.

Lin S.Y. et al. *Acinetobacter calcoaceticus-baumannii complex bacteremia: analysis of 82 cases.* J Microbiol Immunol Infect. 1998; 31(2) : 119-24.p Abstract: Eighty-two cases of Acinetobacter calcoaceticus-baumannii complex bacteremia were identified during a 33-month period, from November 1993 to July 1996, at the Veterans General Hospital, Taipei. All cases were due to hospital-acquired infections, with 28 cases of polymicrobial bacteremia. Most patients had severe debilitating conditions: 26 had malignancies, 40 required stay in Intensive Care Unit and 17 had undergone major operations. The main predisposing factors included central venous catheterization, endotracheal intubation or tracheostomy, prior antibiotic therapy and prolonged hospitalization. Amikacin, tobramycin, and ceftazidime were the most effective agents in vitro against A. calcoaceticus-baumannii complex. 32 patients (39 %) died during hospitalization, 19 of the cases (23 %) directly attributed to septicemia. Factors that adversely influenced mortality included polymicrobial bacteremia, inappropriate antimicrobial therapy and prior antibiotic treatment. Of particular interest is the fact that none of the patients who did not receive appropriate antimicrobial therapy survived. Early diagnosis and appropriate antibiotic therapy are critical for improving the prognosis of A. calcoaceticus-baumannii complex bacteremia.

Lin Y.S. et al. *Disinfection of water distribution systems for Legionella.* Semin Respir Infect. 1998; 13(2) : 147-59.p Abstract: Hospital-acquired legionnaires' disease arises from the presence of Legionella in hospital water systems. Legionella not only persists in hot water tanks but is also found in the biofilm throughout the entire water distribution system. Conditions within water systems that promote Legionella colonization include water temperature, configuration and age of the hot water tank, physicochemical constituents of the water, plumbing materials, and commensal microflora. Hospital-acquired legionnaires' disease has been prevented by instituting control measures directed at the water distribution system. These include superheat-and-flush, copper/silver ionization, ultraviolet light, instantaneous heating systems, and hyperchlorination. Each of the above disinfection methods has been proven to be effective in the short-term, but long-term efficacy has been difficult due to limitations associated with each method. The complexities of Legionella disinfection, including advantages and disadvantages of each method, are reviewed. A successful Legionella prevention program requires cooperation and communication among hospital administrative personnel, engineers, and infection control staff. Routine environmental surveillance cultures for Legionella are the critical component for successful long-term disinfection. Culture results document the efficacy of the disinfection method and alert the hospital staff to consider Legionella in hospitalized patients with pneumonia.

Lina B. et al. *Chronic bacteraemia due to Staphylococcus epidermidis after bone marrow transplantation.* J Med Microbiol. 1995; 42(3): 156-60.p Abstract: A chronic bacteraemia due to Staphylococcus epidermidis occurred in a patient undergoing allogeneic bone marrow transplantation. Forty-two S. epidermidis isolates were obtained from blood cultures over a period of 5 months. Isolates were separated into three groups by SmaI macrorestriction characterisation with pulsed-field gel electrophoresis (PFE-1, one isolate; PFE-2, 32 isolates; PFE-3, nine isolates). Differences were detected in antimicrobial susceptibility patterns among isolates belonging to group PFE-2. The two strains, PFE-2 and PFE-3, were both responsible for the chronic bacteraemia and were isolated during different admissions to the hospital. A central venous catheter was the portal of entry for PFE-2. DNA macro-restriction analysis with pulsed-field gel electrophoresis was helpful in the epidemiological investigation of this S. epidermidis chronic bacteraemia.

Lina G. et al. *Involvement of Panton-Valentine leukocidin-producing Staphylococcus aureus in primary skin infections and pneumonia.* Clin Infect Dis. 1999; 29(5) : 1128-32.p Abstract: Panton-Valentine leukocidin (PVL) is a cytotoxin that causes leukocyte destruction and tissue necrosis. It is produced by fewer than 5% of Staphylococcus aureus strains. A collection of 172 S. aureus strains were screened for PVL genes by polymerase chain reaction amplification. PVL genes were detected in 93% of strains associated with furunculosis and in 85% of those associated with severe necrotic hemorrhagic pneumonia (all community-acquired). They were detected in 55% of cellulitis strains, 50% of cutaneous abscess strains, 23% of osteomyelitis strains, and 13% of finger-pulp-infection strains. PVL genes were not detected in strains responsible for other infections, such as infective endocarditis, mediastinitis, hospital-acquired pneumonia, urinary tract infection, and enterocolitis, or in those associated with toxic-shock syndrome. It thus appears that PVL is mainly associated with necrotic lesions involving the skin or mucosa.

Linares J. *Community-acquired antimicrobial resistance: is it controllable?* Int J Clin Pract Suppl. 1998; 95 : 23-6.p Abstract: Antimicrobial agents were introduced into medical use about 50 years ago. Since then, the prevalence of antimicrobial resistance in community-acquired pathogens has increased rapidly worldwide. The relationship between antibiotic use and resistance is strongly supported by data from several studies. In Spain, the resistance rates for community-acquired pathogens are among the highest in Europe and coincide with a high consumption of antimicrobial agents. In contrast, in Finland, after a nationwide reduction in the use of macrolides for outpatient therapy, there has been a significant decline in the frequency of erythromycin resistance among group A streptococcal isolates. The control of community-acquired antimicrobial resistance is a challenge for the future and will require the early detection of resistance genes through global and local surveillance, prompt containment of resistant pathogens, and judicious use of antimicrobials.

Lind I. *Antimicrobial resistance in Neisseria gonorrhoeae.* Clin Infect Dis. 1997; 24 Suppl 1 : S93-7.p Abstract: The changing patterns of antimicrobial resistance in Neisseria gonorrhoeae have been reviewed regularly since the introduction of antimicrobial therapy in the 1930s. At present, ceftriaxone, fluoroquinolones, and spectinomycin have remained efficient as single-dose treatment of gonorrhea worldwide. To ensure that limited resources can be used in the best possible way, continuous surveillance of gonococcal resistance to antimicrobials is needed.

Linden P.K. *Clinical implications of nosocomial gram-positive bacteremia and superimposed antimicrobial resistance.* Am J Med. 1998; 104(5A) : 24S-33S.p Abstract: The coexistence of a pathogen population with an ever-increasing resistance to many antibiotics and a patient population characterized by increasingly complex clinical problems has contributed to an increase in the bloodstream infections associated with gram-positive bacteria. This serious therapeutic challenge has already been associated with an increase in infection-related morbidity and mortality, a prolongation of hospital stays, and an escalation of healthcare costs. Vancomycin resistance, long prevalent among the enterococci, has emerged in strains of Staphylococcus aureus. Several cases of infection caused by S. aureus strains with intermediate-level resistance to vancomycin (MIC=8 microg/mL) have recently been reported. As glycopeptide resistance accelerates among the gram-positive bacteria, so does the potential for adverse clinical consequences associated with bloodstream infections caused by these pathogens. The patients least able to tolerate the effects of uncontrolled bloodstream infections are also those at the highest risk for the development of infections caused by glycopeptide-resistant pathogens. In this at-risk population, a poor outcome may be anticipated if effective antibiotic therapy is unavailable. Appropriate rationing of vancomycin and other antimicrobial agents that increase the selection of antibiotic-resistant strains of gram-positive bacteria and the rapid development of novel antimicrobial agents with reliable gram-positive activity must be immediate priorities if the threat posed by glycopeptide-resistant gram-positive pathogens is to be countered.

Linden P.K. et al. *Vancomycin-resistant enterococci: the clinical effect of a common nosocomial pathogen*. Diagn Microbiol Infect Dis. 1999; 33(2) : 113-20.p Abstract: Enterococcus spp. is now the third most common pathogen among hospitalized patients, accounting for nearly 12% of nosocomial infections. Enterococcus faecalis is the most prevalent enterococcal species (85%-89%), whereas Enterococcus faecium accounts for 10%-15% of enterococcal isolates. Only 5% of E. faecalis isolates are resistant to glycopeptides. E. faecium has also been shown to be resistant to nonglycopeptide compounds, such as penicillins (97%), high-level gentamicin (52.1%), and high-level streptomycin (58.3%). Numerous risk factors for vancomycin-resistant enterococci (VRE) have been identified, including as length of hospital- or ICU-stay, proximity to a hospitalized, colonized VRE, patient severity of illness, renal failure, recent surgery, immunosuppression, and organ recipient status. An important risk factor is prior exposure to antibiotics such as vancomycin, ceftazidime, ciprofloxacin, and metronidazole, as well as the number and duration of recent antibiotics. Interventions to reduce nosocomial VRE cross-transmission have also been studied. Using gowns in addition to gloves diminished the incidence of VRE in one study, but had a negligible effect in a second study. Studies have shown that in many cases (> 60%) vancomycin usage is inappropriate. While controlling the use of vancomycin alone has only variably diminished VRE colonization, other efforts such as narrowing the spectrum of antibiotics, antiseptics, and reducing immunosuppression may be salutary. Attempts to eradicate VRE intestinal carriage with enteral agents (bacitracin, tetracycline + rifampin, novobiocin) have been reported but seem to have only a transient effect. Non-antimicrobial interventions such as removal of intravenous or bladder catheters and/or surgical or percutaneous drainage may be beneficial. In addition, the development of new antimicrobial agents such as streptogramins, glycopeptides, everninomicins, and oxazalididones will hopefully play an important role in reducing morbidity from these pathogens.

Linden P.K. et al. *Differences in outcomes for patients with bacteremia due to vancomycin-resistant Enterococcus faecium or vancomycin-susceptible E. faecium*. Clin Infect Dis. 1996; 22(4) : 663-70.p Abstract: To determine the differences in outcome in cases of enterococcal bacteremia due to vancomycin-resistant organisms, we compared consecutive patients on a liver transplant service who had clinically significant bacteremia due to vancomycin-resistant Enterococcus faecium (VREF) (n = 54) with a contemporaneous cohort of patients who had vancomycin-susceptible E. faecium (VSEF) bacteremia (n = 48). VREF bacteremia occurred significantly later in the hospitalization than did VSEF bacteremia (43 days vs. 24 days, respectively; P <.01); in addition, VREF was more frequently the sole blood pathogen isolated (91% of patients) than was VSEF (56% of patients) (P =.0002). Invasive interventions for intraabdominal and intrathoracic infection were required more often in the VREF cohort than in the VSEF cohort (34 of 45 patients vs. 20 of 41 patients, respectively; P =.01). Vancomycin resistance more frequently resulted in recurrent bacteremia (22 of 54 patients infected with VREF vs. 7 of 48 patients infected with VSEF; P =.006), persistent isolation of Enterococcus species at the primary site (27 of 33 patients infected with VREF vs. 7 of 18 patients infected with VSEF; P =.005), and endovascular infection (4 patients infected with VREF vs. none infected with VSEF). The decrement in patient survival, as measured from the last bacteremic episode, was greater in the VREF cohort (P =.02). Vancomycin resistance, shock, and liver failure were independent risk factors for Enterococcus-associated mortality. Higher rates of refractory infection, serious morbidity, and attributable death occurred in the VREF cohort and were partially mediated by the lack of effective antimicrobial therapy.

Linden P.K. et al. *Effect of quinupristin/dalfopristin on the outcome of vancomycin-resistant Enterococcus faecium bacteraemia: comparison with a control cohort*. J Antimicrob Chemother. 1997; 39 Suppl A : 145-51.p Abstract: Serious infection with vancomycin-resistant Enterococcus faecium (VREF) strains has no proven effective antimicrobial therapy. We compared the clinical and bacteriological outcomes of 20 patients with VREF bacteraemia treated with quinupristin/dalfopristin (RP 59500), an investigational streptogramin, with a historical cohort of 42 patients with VREF bacteraemia treated with other agents. Quinupristin/dalfopristin demonstrated in-vitro bacteriostatic activity against all 20 initial VREF blood isolates (MIC range 0.03-0.50 mg/L) by macrobroth dilution. The clinical characteristics of both groups were comparable for major outcome-dependent variables. There were five cases of recurrent VREF bacteraemia in the quinupristin/dalfopristin-treated cohort and 21 in the controls (P = 0.11); persistence of VREF at the primary site was found in six and 18 of the evaluable patients with follow-up cultures in these two cohorts (P = 0.06). In-hospital mortality was high in both groups: 65% in the quinupristin/dalfopristin group and 52% in the control group; however, VREF-associated mortality was significantly lower in the quinupristin/dalfopristin group (five and 17 respectively; P = 0.05). Follow-up susceptibility testing of five VREF isolates in the quinupristin/ dalfopristin group did not demonstrate resistance to quinupristin/dalfopristin. Quinupristin/ dalfopristin may be a useful agent for the therapy of serious VREF infection. Further clinical investigations are warranted to confirm or refute its clinical efficacy.

Lindmark A. et al. *Characterization of the biosynthesis, processing, and sorting of human HBP/CAP37/azurocidin*. J Leukoc Biol. 1999; 66(4) : 634-43.p Abstract: Azurocidin is a multifunctional endotoxin-binding serine protease homolog synthesized during the promyelocytic stage of neutrophil development. To characterize the biosynthesis and processing of azurocidin, cDNA encoding human preproazurocidin was stably transfected to the rat basophilic leukemia cell line RBL-1 and the murine myeloblast-like cell line 32D cl3; cell lines previously utilized to study the related proteins cathepsin G and proteinase 3. After 30 min of pulse radiolabeling, two forms of newly synthesized proazurocidin (34.5 and 37 kDa), differing in carbohydrate content but with protein cores of identical sizes, were recognized. With time, the 34.5-kDa form disappeared, while the 37-kDa form was further processed proteolytically, as judged by digestion with N-glycosidase F. Conversion of high-mannose oligosaccharides into complex forms was shown by acquisition of complete resistance to endoglycosidase H. Radiosequence analysis demonstrated that the amino-terminal seven amino acid propeptide of proazurocidin was removed in a stepwise manner during processing; initial removal of five amino acids was followed by cleavage of a dipeptide. Presence of the protease inhibitors Gly-Phe-diazomethyl ketone, bestatin, or leupeptin inhibited only the cleavage of the dipeptide, thus indicating the involvement of at least two amino-terminal processing enzymes. Translocation of azurocidin to granules was shown by subcellular fractionation. Similar results, with efficient biosynthesis, processing, and targeting to granules in both cell lines, were obtained with a mutant form of human preproazurocidin lacking the amino-terminal heptapropeptide. In conclusion, this investigation is an important addition to our previous studies on related azurophil granule proteins, and provides novel information concerning the biosynthesis and distinctive amino-terminal processing of human azurocidin.

Ling J.M. et al. *Antimicrobial susceptibilities and molecular epidemiology of Salmonella enterica serotype enteritidis strains isolated in Hong Kong from 1986 to 1996*. J Clin Microbiol. 1998; 36(6) : 1693-9.p Abstract: The incidence of salmonellosis has been increasing in Hong Kong since 1989. The most common Salmonella enterica serotype isolated in 1994 was S. enteritidis. The antimicrobial susceptibilities and molecular epidemiology of 275 S. enteritidis strains isolated in this locality between 1986 and 1996 were studied. Over 99% of the isolates were susceptible to 17 of the 19 antimicrobial agents tested. One isolate harbored an autotransferring plasmid that confers resistance to tetracycline and trimethoprim-sulfamethoxazole. Another isolate harbored a mobilizable plasmid that confers resistance to ampicillin and cephalothin. This isolate was found to produce a beta-lactamase with a pI of 5.2. A total of 264 isolates (96%) were found

to harbor one to five plasmids, and the majority (254) harbored a 60-kb plasmid. Of these isolates, 94% contained identical 60-kb plasmids. Based on plasmid profiles, plasmid and chromosomal fingerprints, ribotypes, and randomly amplified polymorphic DNA (RAPD) patterns, 170 (62%) isolates were allocated to group 1b. About 90% of isolates had identical or similar DNA fingerprints, ribotypes, and RAPD patterns, suggesting that a predominant clone of S. enteritidis was circulating in Hong Kong during the period being studied.

Ling T.K. et al. *An increase in Helicobacter pylori strains resistant to metronidazole: a five-year study.* Helicobacter. 1996; 1(1) : 57-61.p Abstract: BACKGROUND: Metronidazole is one of the most commonly used antimicrobial agents for the treatment of Helicobacter pylori infection. Resistance to metronidazole has been reported worldwide but with a wide range of prevalence. We started using the classical triple therapy (bismuth, tetracycline, and metronidazole) for H. pylori infection in 1991 but recently have experienced a decline in its efficacy in curing the infection. Thus our aim was to investigate in a single center the prevalence of metronidazole-resistant H. pylori over a period of 5 years. MATERIALS AND METHODS: A total of 1,015 different H. pylori strains collected over a period of 5 years were tested for sensitivity against metronidazole, ampicillin, tetracycline, and imipenem. Antibiotic sensitivity was tested by the disk diffusion and agar dilution methods. To elucidate further the possible relationship between these metronidazole-resistant strains, genomic DNA digestion by the Hae III endonuclease and ribotyping were undertaken in a selected group of isolates. RESULTS: In 1991, 29 of 132 (22.0%) tested strains of H. pylori were found to be resistant to metronidazole. Since our initiation at that time of a triple therapy of bismuth, metronidazole, and tetracycline, the prevalence of metronidazole-resistant strains rose rapidly to 73.2% in 1995. All H. pylori isolates were sensitive to ampicillin, tetracycline, and imipenem. A high degree of genomic heterogeneity was found among these isolates. Thus it is unlikely that the resistant strains of H. pylori were originated from a single clone. CONCLUSIONS: This study shows a rapid increase in metronidazole-resistant H. pylori with the use of an anti-Helicobacter regimen that contains metronidazole. We anticipate that the efficacy of metronidazole-containing anti-Helicobacter regimens will decline with the rapid rise in resistant strains of H. pylori.

Lingstrom P. et al. *Effects of frequent mouthrinses with palatinose and xylitol on dental plaque.* Eur J Oral Sci. 1997; 105(2) : 162-9.p Abstract: The aim was to evaluate the effects of frequent mouthrinses with palatinose, xylitol and a mixture of palatinose and xylitol on plaque pH, plaque formation and cariogenic microorganisms. 15 subjects refrained from toothbrushing during 3 test periods and rinsed 15 x daily for 4 d with 10 ml of: (1) 50% palatinose, (2) 37.5% palatinose + 12.5% xylitol, or (3) 50% xylitol. A contrast period with no mouthrinses was also carried out. The 4 periods were carried out in a randomized order with a cross-over design. After the 4-day periods, 3 parameters were measured: (1) plaque pH during the first 30 min after a mouthrinse with palatinose, a mixture of palatinose and xylitol or xylitol alone, directly followed by a 2nd rinse with 10% sucrose; (2) number of mutans streptococci and lactobacilli in plaque and saliva; (3) plaque index. The most pronounced pH drop for the sugar substitutes was found when rinsing with 50% palatinose after the palatinose period, and the least pH drop with 50% xylitol after the xylitol period. The sucrose rinse gave similar pH fall after all 4 periods. The microbial data showed no differences between the 4 periods, but the mutans streptococcus counts in saliva decreased after the xylitol period in contrast to the 3 other periods. Regarding the plaque index, xylitol gave lower scores compared to the other 3 periods.

Lipsitch M. et al. *From the cover: the epidemiology of antibiotic resistance in hospitals: paradoxes and prescriptions.* Proc Natl Acad Sci U S A. 2000; 97(4) : 1938-43.p Abstract: A simple mathematical model of bacterial transmission within a hospital was used to study the effects of measures to control nosocomial transmission of bacteria and reduce antimicrobial resistance in nosocomial pathogens. The model predicts that: (i) Use of an antibiotic for which resistance is not yet present in a hospital will be positively associated at the individual level (odds ratio) with carriage of bacteria resistant to other antibiotics, but negatively associated at the population level (prevalence). Thus inferences from individual risk factors can yield misleading conclusions about the effect of antibiotic use on resistance to another antibiotic. (ii) Nonspecific interventions that reduce transmission of all bacteria within a hospital will disproportionately reduce the prevalence of colonization with resistant bacteria. (iii) Changes in the prevalence of resistance after a successful intervention will occur on a time scale of weeks to months, considerably faster than in community-acquired infections. Moreover, resistance can decline rapidly in a hospital even if it does not carry a fitness cost. The predictions of the model are compared with those of other models and published data. The implications for resistance control and study design are discussed, along with the limitations and assumptions of the model.

Lipsitch M. et al. *Population dynamics of tuberculosis treatment: mathematical models of the roles of non-compliance and bacterial heterogeneity in the evolution of drug resistance.* Int J Tuberc Lung Dis. 1998; 2(3) : 187-99.p Abstract: SETTING: Patient non-compliance and/or spatial heterogeneity in drug concentration or effectiveness may contribute to the emergence of drug resistance during multiple-drug chemotherapy of tuberculosis. OBJECTIVE: Using mathematical models of mycobacterial population dynamics under antimicrobial treatment, to assess the effects of non-compliance, heterogeneity and other factors on the success of treatment. DESIGN: A mathematical model is used to generate predictions about the ascent of drug resistance in treated hosts with non-compliance and/or a 'protected compartment' of bacteria where only one drug is active; simulations of a more realistic version of this model take into account random mutation, and different assumptions about the size of, and growth rate of bacteria in, the protected compartment. RESULTS: The existence of a protected compartment can increase the likelihood of resistance to the single drug active in that compartment, but only if bacteria resistant to that drug can grow in the protected compartment or if the host is non-adherent to the treatment regimen. However, the protected compartment may also slow the ascent of bacteria resistant to drugs not active in it (e.g. isoniazid) by providing a reservoir of non-selected mycobacteria. The model predicts that relative rates of killing are more important than mutation rates in determining the order in which resistant mutants ascend. Model predictions, in combination with data about drug resistance patterns, suggest that non-compliance, but not heterogeneity, is an important cause of treatment failure. CONCLUSION: Patterns of acquired drug resistance may be used to infer processes of selection during treatment; mathematical models can aid in generating predictions about the relative impacts of treatment parameters in the evolution of resistance, and eventually in suggesting improved treatment protocols.

Lister P.D. *Emerging resistance problems among respiratory tract pathogens.* Am J Manag Care. 2000; 6(8 Suppl) : S409-18.p Abstract: The number-1 indication for antibiotic prescriptions in the United States is a respiratory tract infection. The changing spectrum of pathogens and emerging bacterial resistance are changing the way these infections are managed. The epidemiology of community-acquired pneumonia has changed significantly in the past 20 years, with increased diversity of pathogens and mortality. Emerging resistance in respiratory tract pathogens, particularly to beta-lactams, is an increasing concern. Of the important gram-negative pathogens, more than a third of Haemophilus influenzae isolates are now resistant to beta-lactam antibiotics, as well as virtually all isolates of Moraxella catarrhalis. Of the gram-positive organisms, more than 40% of Streptococcus pneumoniae isolates are no longer susceptible to penicillin, and methicillin resistance has been reported in up to half of Staphylococcus

aureus isolates in some institutions. Among staphylococci, resistance to the beta-lactam methicillin is often accompanied by resistance to multiple classes of antibiotics, particularly the macrolides. Little resistance to fluoroquinolones has been reported among gram-negative respiratory tract pathogens and S pneumoniae, although increasing resistance may be seen as these drugs are used with increasing frequency. In contrast, fluoroquinolone resistance can develop rapidly in S aureus and appears to be associated with methicillin resistance. Fortunately, many of the newer fluoroquinolones appear to offer significant activity against methicillin-resistant S aureus isolates and are active against ciprofloxacin-resistant strains of S pneumoniae. Today, to combat respiratory tract infections, a broad-based empiric therapy needs to be used and bacterial resistance must be taken into account. New antimicrobial options must be considered, with an emphasis on effective drug use and optimal dosing. Even if a direct relationship between antibiotic resistance and clinical outcomes in the treatment of pneumonia in adults has not been extensively demonstrated, the increasing problem of resistance has changed treatment approaches for respiratory tract infections as a whole.

Lister P.D. *Multiply-resistant pneumococcus: therapeutic problems in the management of serious infections.* Eur J Clin Microbiol Infect Dis. 1995; 14 Suppl 1 : S18-25.p Abstract: The control of penicillin-resistant pneumococci has become one of the more serious therapeutic challenges facing clinicians today. The occurrence and geographical coverage of these microorganisms have increased rapidly since they were first recognized in the late 1960s. They have now been reported from every continent, and in some regions can account for over 60% of the pneumococci isolated. An even greater concern is the propensity of penicillin-resistant pneumococci towards resistance to multiple antibiotics, including the cephalosporins and non-beta-lactam drugs. In areas where multiply-resistant strains are common, the therapeutic choices for the treatment of life-threatening infections may be limited to drugs which are either toxic for the patient or for which we are only beginning to gain clinical experience. As the importance of Streptococcus pneumoniae in meningitis continues to increase and multiply-resistant strains become more widespread and entrenched, it is essential that the search for more well-tolerated and effective treatment regimens continues. However, unless the effect of antibiotics on the selection of these resistant pathogens is addressed and a more judicious approach towards drug use is taken; this resistance problem will continue well into the future.

Listgarten M.A. et al. *Comparative microbiological characteristics of failing implants and periodontally diseased teeth.* J Periodontol. 1999; 70(4) : 431-7.p Abstract: BACKGROUND: The purpose of this report was to compare the distribution of periodontal pathogens recovered from failing implants and teeth with adult and recurrent forms of periodontitis. METHODS: A total of 41 consecutive microbial samples from patients with failing implants (IMP) were received at the Microbiology Testing Laboratory (MTL) of the University of Pennsylvania over a 2-year period. Paired control samples were selected from samples received concurrently by MTL from 41 patients with a diagnosis of adult periodontitis (AP) and 41 with a diagnosis of recurrent or refractory periodontitis (RP). Patients' mean ages for the 3 categories were 59, 47, and 53 years, respectively. Samples were collected with paper points or scalers and shipped in prereduced medium by express mail to the laboratory where they were processed within 48 hours from the time of collection. Culture was used for detection of A. actinomycetemcomitans, C. rectus, P. intermedia/nigrescens, E. corrodens, P. micros, Capnocytophaga and Fusobacterium sp., enteric Gram-negative rods, Enterococcus and Staphylococcus sp., and yeast. P. gingivalis and B. forsythus were detected by indirect immunofluorescence. Morphotypes were enumerated by dark-field microscopy. RESULTS: The most frequently detected microorganisms from IMP were B. forsythus (59%), spirochetes (54%), Fusobacterium (41%), P. micros (39%), and P. gingivalis (27%). Recovery levels (mean +/- SD) were 1+/-1, 4+/-5, 4+/-5, 9+/-11, 1+/-2, respectively. The most frequently detected organisms for AP were B. forsythus (83%), Fusobacterium (80%), spirochetes (79%), P. gingivalis (59%), P. micros (51%), and E. corrodens (37%), at levels 2+/-2, 5+/-4, 9+/-6, 4+/-5, and 6+/-7, respectively. Corresponding data for RP were B. forsythus (85%), Fusobacterium (83%), P. gingivalis (60%), spirochetes (59%), C. rectus (56%), and P. micros (56%), at levels of 3+/-2, 8+/-8, 4+/-4, 2+/-2, 1+/-1, and 9+/-10, respectively. CONCLUSIONS: These results indicate that the detection frequency and levels of recovery of some periodontal pathogens in failing implants are significantly different from that of teeth with periodontitis; however, the detection frequency and levels of recovery are similar in teeth affected by adult and refractory (recurrent) forms of periodontitis.

Liu H.H. *Antibiotic resistance in bacteria. A current and future problem.* Adv Exp Med Biol. 1999; 455 : 387-96.p Abstract: Bacterial pathogens have become increasingly resistant to commonly used antibiotics. In some cases, there are no remaining first-line options for therapy. Problem pathogens which may cause dermatologic and rheumatologic infections will be discussed, including vancomycin-resistant staphylococci and enterococci as well as the multiply-resistant Gram-negative bacilli. Risk factors for acquisition of these organisms and diagnostic studies available for their detection will be reviewed. The underlying mechanisms of resistance, geographic prevalence, potential for continued spread, and proposed strategies for prevention and control are examined. Finally, information on the newer topical and systemic antimicrobial agents, including investigational therapies, will be presented.

Liu I.X. et al. *Baicalin synergy with beta-lactam antibiotics against methicillin-resistant Staphylococcus aureus and other beta-lactam-resistant strains of S. aureus.* J Pharm Pharmacol. 2000; 52(3) : 361-6.p Abstract: Bacterial resistance to antibiotics is a serious global problem and includes strains of beta-lactam-resistant Staphylococcus aureus and methicillin-resistant S. aureus (MRSA). Novel antimicrobials and/or new approaches to combat the problem are urgently needed. The Chinese herb Xi-nan Huangqin (Scutellaria amoena C.H. Wright) has been used in traditional Chinese medicine to treat a wide range of infectious diseases. In this study we have examined the antibacterial action of baicalin, a flavone isolated from the herb. When combined with 16 microg mL(-1) baicalin, minimum inhibitory concentrations (MICs) of benzylpenicillin against MRSA and penicillin-resistant S. aureus were reduced from 125 and 250 microg mL(-1) to 4 and 16 microg mL(-1), respectively. This activity of baicalin was dose-dependent. Viable counts showed that the killing of MRSA and beta-lactam-resistant S. aureus cells by 10 to 50 microg mL(-1) ampicillin, amoxycillin, benzylpenicillin, methicillin and cefotaxime was potentiated by 25 microg mL(-1) baicalin. From the study it was concluded that baicalin has the potential to restore the effectiveness of beta-lactam antibiotics against MRSA and other strains of beta-lactam-resistant S. aureus. In view of its limited toxicity baicalin offers potential for the development of a valuable adjunct to beta-lactam treatments against otherwise resistant strains of microorganisms.

Liu J.D. et al. *The isolation results and the antimicrobial agents susceptibility analysis of Haemophilus from the sputum of the elderly suffering from respiratory tract disease.* Rinsho Biseibutshu Jinsoku Shindan Kenkyukai Shi. 1999; 10(2) : 71-5.p Abstract: OBJECTIVE: To inform the isolation and antibiotics susceptibility results of Haemophilus in the sputum of old men suffering from respiratory tract disease so that the epidemiological information and treatment can be available to physicians. METHODS: Two groups-group A, patients=562, group B, healthy volunteers=57 expectorated specimens of sputum were cultured with a special medium for Haemophilus. The isolates were then identified with API NH Identification plates and detected with ATB NH antibiotics susceptibility cards, finally, we got the statistics data of Haemophilus species and antibiotics susceptibility rates from Datatrac statistic system of VITEK 32. RESULTS: Haemophilus

were detected in 132 specimens out of 562 (23.5%), which includes 6 strains of H. influenzae (4.5%). 122 strains of H. parainfluenzae, 4 strains of H. aphrophilus (3.1%). At the same time, 3 strains of Haemophilus were isolated from group B. Following are the susceptibility rates of sixteen antibiotics of 132 strains of Haemophilus, 73.4% to amoxicillin, 92.4% to amoxicillin and clavulanic acid, 83.3% to cefactor, 90.9% to cefotaxime, 79.5% to cefuroxime-axetil, 52.3% to kanamycin, 25.0% to gentamycin, 72.0% to spectinomycin, 79.5% to chloramphenicol, 50.0% to tetracycline, 9.1% to erythromycin, 42.4% to pristhomycin, 49.2% to rosoxacin, 62.96% to pefloxacin, 97.7% to rifampin, 33.3% to sulfonamides. CONCLUSION: There is a high isolation rate of Haemophilus in the sputum of the elderly suffering from respiratory tract diseases, The H. parainfluenzae is the main Haemophilus in our area of study, which it deserves good attention by clinical microbiological laboratory. In addition, the antibiotics susceptibility results indicate that this species is more susceptible to beta-lactams antibiotics and is less susceptible to some others such as macrolides and aminoglycosides, etc. So, the drug treatment should be based on these antibiotics susceptibility results in order to guide the specific therapy.

Liu W.Z. et al. *Furazolidone-containing short-term triple therapies are effective in the treatment of Helicobacter pylori infection*. Aliment Pharmacol Ther. 1999; 13(3) : 317-22.p Abstract: BACKGROUND: A furazolidone-containing therapeutic regimen for Helicobacter pylori infection has attracted special interest in the face of a rising world-wide metronidazole resistant H. pylori, and the expense of currently used antimicrobial regimens. AIM: To evaluate the efficacy of furazolidone-containing regimens in eradicating H. pylori. METHODS: One-hundred and forty H. pylori positive patients with endoscopically confirmed duodenal ulcer or functional dyspepsia received one of four different regimens to eradicate H. pylori. In the first trial, the patients were randomly assigned to receive a 1-week course of furazolidone 100 mg b.d. and clarithromycin 250 mg b.d., with either tripotassium dicitrato bismuthate (TDB) 240 mg b.d. (FCB group) or lansoprazole 30 mg daily (FCL group). In the second trial, the patients were randomly assigned to receive a 1-week course of clarithromycin 250 mg b.d. and omeprazole 20 mg daily, with either furazolidone 100 mg b.d. (FCO group) or metronidazole 400 mg b.d. (MCO group). Endoscopy was repeated 4 weeks following completion of therapy with re-assessment of H. pylori status on gastric biopsies by histology and culture. RESULTS: Four patients (1 in FCB, 1 in FCO and 2 in MCO groups) dropped out because they refused a follow-up endoscopy. Eradication rates of H. pylori on an intention-to-treat basis in the FCB, FCL, FCO and MCO groups were 91% (32/35, 95% CI: 82-99%), 91% (32/35, CI: 82-99%), 86% (30/35, CI: 74-97%) and 74% (26/35, CI: 60-89%) (all $P > 0.05$), respectively. Mild side-effects occurred in 15% of the 140 patients. In MCO group, the eradication rate in the patients infected with metronidazole-sensitive isolates of H. pylori was 86%, but dropped to 67% in those with metronidazole-resistance strains ($P = 0.198$). CONCLUSION: One-week regimens containing furazolidone and clarithromycin in combination with TDB or a proton pump inhibitor fulfil the criteria for successful H. pylori therapy.

Liu Y.C. et al. *Detection of antimicrobial activity in urine for epidemiologic studies of antibiotic use.* J Clin Epidemiol. 1999; 52(6) : 539-45.p Abstract: Antibiotic resistance is the inevitable consequence of the selective pressure of antimicrobial drug use and the adaptive plasticity of the microorganisms. Excessive and irrational use of antimicrobial drugs is a problem in all countries. It is particularly troublesome in developing countries where there is a heavy burden of infectious diseases. This study was designed to determine whether detection of antimicrobial activity in the urine might be a useful tool for epidemiologic studies of the interaction between antibiotic use and resistance in developing countries. A laboratory marker is necessary because the history of antimicrobial drug use may be unreliable. Serial specimens or spontaneously voided urine were obtained from healthy volunteers given a single oral dose of commonly used antimicrobial drugs. Urine was also obtained from hospitalized patients the morning after the last dose of an antimicrobial drug and from untreated controls. Assays were performed with standard American Type Culture Collection (Rockville, MD) stains of Bacillus stearothermophilus, Escherichia coli, and Streptococcus pyogenes. Antimicrobial activity could not be detected in pretreatment urine. After a single oral dose, the beta lactam antibiotics and erythromycin could be detected for about 12 to 24 hours, whereas clindamycin, tetracycline, trimethoprim/sulfamethoxazole, and ciprofloxacin could be detected for 48 or more hours. In hospitalized patients, receiving multiple drugs, the following were the sensitivity and specificity for detection of antimicrobial activity: for B. stearothermophilus, 100.0% and 85.9%, respectively; for S. pyogenes, 94.9% and 94.9%, respectively; and for E. coli, 71.8% and 98.7%, respectively. The combination of E. coli and Streptococcus pyogenes exhibited a sensitivity of 97.4% and specificity of 94.9%. Detection of antimicrobial activity in urine is a promising method to determine antimicrobial drug use in epidemiologic studies, particularly in populations in which drug use history is unreliable.

Liu Y.C. et al. *Extent of antibiotic use in Taiwan shown by antimicrobial activity in urine*. Lancet. 1999; 354(9187) : 1360.p Abstract: Taiwan has high prevalence of antibiotic resistant, community-acquired respiratory pathogens. We investigated whether there was a high frequency of antibiotic use in the community. Antimicrobial activity in urine was detected in 55.2% of 1182 patients on arrival at an emergency department, 25.1% of 203 internal medicine out-patients, 7.6% of 471 high school students, and 7.4% of 202 people at a centre for senior citizens.

Livermore D.M. et al. *Quality of antimicrobial susceptibility testing in the UK: a Pseudomonas aeruginosa survey revisited*. J Antimicrob Chemother. 1999; 43(4) : 517-22.p Abstract: As part of a programme to assess the usefulness of routine antimicrobial susceptibility data as a surveillance tool, we reviewed the results of a national survey of resistance in Pseudomonas aeruginosa, undertaken in 1993. Twenty-four UK laboratories contributed isolates for centralized MIC testing, indicating also their own susceptibility test data. As reported previously (Chen et al. (1995) Journal of Antimicrobial Chemotherapy 35, 521-34), the rate of false resistance (isolates reported susceptible, but found resistant on MIC testing/all isolates reported susceptible) was 0.6-8%, according to the antimicrobial and breakpoint. Review showed that this favourable position reflected the fact that >88% of isolates were susceptible to any given antimicrobial and—in most cases—were correctly reported as such. Reporting was more erratic for resistant isolates: for beta-lactams and amikacin, isolates resistant at the highest MIC breakpoints were equally likely to be reported as 'susceptible' or 'resistant'; such misreporting was less common with ciprofloxacin and gentamicin but still occurred in 9-20% of cases. Conversely, up to 73% of the isolates reported as resistant proved to be susceptible at high breakpoints, and up to 44% were susceptible at low breakpoints. Miscategorizations did not reflect failure to detect particular mechanisms but, rather, the fact that MIC and zone breakpoints for P. aeruginosa serve to cut 'tails' of resistant organisms from continuous distributions, not to distinguish discrete populations. In this situation, some disagreement between routine tests and MICs is inevitable, but the frequency at which highly resistant isolates were reported as sensitive is disturbing. For surveillance, we conclude that resistance rates based on routine tests are unreliable for P. aeruginosa. This situation may improve with greater standardization of routine testing, but the continuous susceptibility distributions without discrete resistant and susceptible populations militate against perfect agreement. Despite these deficiencies, routine data should allow trend analysis.

Ljungman G. et al. *Midazolam nasal spray reduces procedural anxiety in children*. Pediatrics. 2000; 105(1 Pt 1) : 73-8.p Abstract: OBJECTIVE: Anxiety and pain even in minor procedures are still great problems in pediatrics, not least in pediatric oncology. Conscious

sedation is indicated when other means to overcome a child's fear fail. The aim of this study was to investigate whether intranasal administration of midazolam given before insertion of a needle in a subcutaneously implanted central venous port could reduce anxiety, discomfort, pain, and procedure problems. METHOD: Forty-three children with cancer participated in this randomized, double-blind, placebo-controlled, crossover study in which nasal administration of midazolam spray,.2 mg/kg body weight, was compared with placebo. Children, parents, and nurses completed a visual analog scale questionnaire to evaluate efficacy. RESULTS: Parents and nurses reported reduced anxiety, discomfort, and procedure problems for children in the midazolam group and would prefer the same medication at next procedure. They also reported pain reduction. Children reported reduced anxiety and procedure problems but reduction of pain and discomfort was not significant. No serious or unexpected side effects occurred. Nasal discomfort was the most common side effect (17/38 approximately 45%) and the primary reason for dropouts (8/43 approximately 19%). Anxiety varied with age but not with gender. When anxiety increased, the differences between midazolam and placebo increased. CONCLUSION: Nasal midazolam spray offers relief to children anxious about procedures, such as insertion of a needle in a subcutaneously implanted intravenous port, venous blood sampling, venous cannulation, etc. Its use, however, may be limited by nasal discomfort in some patients for whom rectal and oral routes might be alternatives.

Llanes Gonzalez L. et al. *[Antimicrobial prophylaxis in urology].* Actas Urol Esp. 1997; 21(6) : 540-8.p Abstract: Antimicrobial prophylaxis in surgery has proven to be effective in controlled randomized trials. Usage in Urology is known at least since the '30s although its effectiveness has only become known since 1979. METHODS: Review of literature related to surgical antibiotic prophylaxis, more specifically urological surgery, basically from 1991 to 1995, but without overlooking those papers that have become classics due to their impact. RESULTS AND CONCLUSIONS: Efficacy of antimicrobial prophylaxis in urological surgery is nowadays beyond all doubt. Usage is indicated in the presence of sterile urine and dosage must be short, in single dosis in the immediate pre-operative or within 24 hours after the procedure. However, there is a number of issues that deserve to be treated in more detail for better understanding. Those are the establishment of adequate prophylactic regimes in renal transplantation and the use of antimicrobials based on their pharmacokinetic characteristics to optimize the prophylactic purpose.

Llanes R. et al. *[Antimicrobial resistance in Haemophilus influenzae in the city of Havana, Cuba].* Rev Argent Microbiol. 1996; 28(1) : 17-21.p Abstract: Fifty five Haemophilus influenzae strains were studied to determine their resistance to different antimicrobial drugs. They were isolated in Habana City, Cuba, during June 1992 to May 1993, from invasive and non invasive infections. An agar dilution method, according to NCCLS guidelines, was employed. We observed that 49%, 47.3% and 27.3% were resistant to ampicillin, tetracycline and chloramphenicol, respectively. beta-lactamase production was demonstrated in 22 strains (40%). There was neither resistance to ceftriaxone, cefotaxime nor rifampicin. 36.4% of the strains were multiresistant, being described 7 different resistance patterns. The rate of resistance to the drugs was substantially higher among serotype b than among non type b strains.

Llanes R. et al. *Resistencia antimicrobiana en Haemophilus influenzae en la ciudad de La Habana, Cuba.* Rev. argent. microbiol. 1996; 28. (1) : 17-21.p Abstract: Se realizó un estudio de la resistencia a los antimicrobianos en 55 cepas de Haemophilus influenzae, aisladas en el período comprendido entre junio de 1992 y mayo de 1993 de igual número de pacientes pediátricos con infecciones invasivas y no invasivas; se utilizó el método de dilución de placas de agar, según las recomendaciones del NCCLS. De las cepas estudiadas, 49 por ciento, 47,3 por ciento y 27,3 por ciento fueron resistentes a la ampicilina, tetraciclina y cloranfenicol, respectivamente. No se detectó resistencia a la ceftriaxona, cefotaxima ni rifampicina. El 36,4 por ciento de las cepas fueron multiresistentes, presentándose una distribución heterogénea en 7 patrones de resistencia. Se demostró la producción de á-lactamasa en 22 cepas (40 por ciento). La tasa de resistencia a las diferentes drogas fue mayor en cepas del serotipo b que en aquellas no b (AU).

Lloyd-Still J.D. et al. *Essential fatty acid deficiency and predisposition to lung disease in cystic fibrosis.* Acta Paediatr. 1996; 85(12) : 1426-32.p Abstract: Essential fatty acid (EFA) deficiency is a predisposing factor for pulmonary infection with Staphylococcus aureus and Pseudomonas aeruginosa, the two major pathogenic microorganisms in cystic fibrosis (CF). OBJECTIVE: The goal of this study was to investigate the essential fatty acid status of CF patients from infancy to 20 years old. MATERIALS AND METHODS: Plasma fatty acid profiles for phospholipid (PL) were determined for cord (n = 6), 4 months (n = 40), 16 months (n = 25), 3 y (n = 8), 5-10 y (n = 10), and 10-20 y (n = 10) aged CF patients and compared to their respective control; cord (n = 22), 1-36 months (n = 38) and adult (n = 100). Significance was established by Student's t-test ($p < 0.05$). RESULTS: The plasma PL fatty acid profile for all CF patients, except cord, revealed consistent deficiency in omega 3 and omega 6 EFAs. These deficiencies were most marked at infancy and more pronounced for patients with meconium ileus. CONCLUSIONS AND RELEVANCE: EFA deficiency may contribute to the predisposition of CF infants to develop respiratory disease and to the excess cytotoxic activity found in bronchoalveolar lavage fluid at 2 months of age in the majority of screened infants.

Locker G.J. et al. *Lethal Waterhouse-Friderichsen syndrome in posttraumatic asplenia.* J Trauma. 1995; 39(4) : 784-6.p Abstract: We herein report a case of fulminant lethal Waterhouse-Friderichsen syndrome in an elderly female patient seven years after posttraumatic splenectomy. In contrast to various reports, this patient had not been vaccinated against Streptococcus pneumoniae, Neisseria meningitidis, or Haemophilus influenzae, respectively, although infections with these microorganisms are known to cause the main lethal diseases in asplenic patients. Again, we recommend obligatory vaccinations against the mentioned bacteria for it is known that this decreases the risk of fatal septic events in these patients. To optimize prevention, it is imperative to vaccinate patients undergoing splenectomy before discharge from hospital.

Lode H. *Potential interactions of the extended-spectrum fluoroquinolones with the CNS.* Drug Saf. 1999; 21(2) : 123-35.p Abstract: The new generation fluoroquinolones — sparfloxacin, levofloxacin, grepafloxacin and trovafloxacin — have been designed to respond to the clinical need for extended antimicrobial cover in the face of increasing global microbial resistance. Their main focus is in the treatment of respiratory infections, particularly those acquired in the community. CNS adverse effects, such as dizziness and headache, are known to occur relatively commonly with some fluoroquinolones and are not, in general, well tolerated by patients. The structural component of the fluoroquinolone molecule believed to be responsible for improved gram-positive activity is also believed to be implicated in the production of CNS adverse effects, including those arising from drug interactions with theophylline and NSAIDs. Inhibition of brain gamma-aminobutyric acid (GABA) receptor binding appears to be a strong indicator of CNS activity, though N-methyl-D-aspartate receptor binding has also been implicated. In accordance with the results of these predictive studies, clinical trials have found sparfloxacin, levofloxacin and grepafloxacin to be associated with a low incidence of CNS events. Trovafloxacin has been found to be associated with a higher incidence of CNS events (particularly lightheadedness and dizziness) than the other 3 agents. Ongoing and future clinical studies will help to define the usefulness of the predictive models, as well as reveal the full CNS adverse event profile of these and other investigational fluoroquinolones.

Lode H. et al. *Treatment of community-acquired pneumonia: a randomized comparison of sparfloxacin, amoxycillin-clavulanic acid and erythromycin.* Eur Respir J. 1995; 8(12) : 1999-2007.p Abstract: The treatment of community-acquired pneumonia is empirical in most cases and must cover a wide range of potential pathogens, such as Streptococcus pneumoniae, including penicillin-resistant strains, Haemophilus influenzae and intracellular microorganisms. The objective of this double-blind, randomized, parallel group study was to compare the efficacy and safety of sparfloxacin (400 mg loading dose, followed by 200 mg o.d.) with that of oral amoxycillin-clavulanic acid (500/125 mg t.i.d.) or oral erythromycin (1 g b.i.d.), during 7-14 days in 808 patients with confirmed community-acquired pneumonia. The overall success rates for sparfloxacin (87%), amoxycillin-clavulanic acid (80%) and erythromycin (85%) were similar in evaluable patients, and the equivalence hypothesis used for the statistical analysis showed at least an equivalent efficacy for the three antibiotics tested. The analysis of microbiologically documented infections (40% of the patients) showed that overall success rates were similar for S. pneumoniae and H. influenzae infections. Treatment withdrawal was necessary in 3.5, 2.5 and 7.7% of the patients treated with sparfloxacin, amoxycillin-clavulanic acid and erythromycin, respectively. This study indicates that sparfloxacin was at least as effective as amoxycillin-clavulanic acid or erythromycin in the treatment of mild-to-moderate community-acquired pneumonia and that the adverse effects were similar in the three groups.

Lodinova-Zadnikova R. et al. *Effect of preventive administration of a nonpathogenic Escherichia coli strain on the colonization of the intestine with microbial pathogens in newborn infants.* Biol Neonate. 1997; 71(4) : 224-32.p Abstract: In a randomized, double-blind study, 27 healthy newborn infants were colonized with the nonpathogenic Escherichia coli strain Nissle 1917 (E. coli DSM 6601, Mutaflor) during the first 5 days of life by daily oral inoculation of 1 ml of a suspension with 10(8) living cells. A second group of 27 newborns, used as controls, received a placebo suspension (1 ml of phosphate-buffered saline) instead. Stool samples were taken on days 1, 2, 3, 5, and 21, and 6 months after birth. All samples were examined for the presence of the nonpathogenic E. coli strain and of pathogenic and potentially pathogenic microorganisms. The administered E: coli strain was detected in the stools of the colonized newborns from day 2 and remained present throughout the study in more than 90% of these infants. Colonization with true and potential bacterial pathogens was significantly reduced in infants receiving E. coli strain Nissle 1917 compared to the placebo group—both with respect to numbers of pathogens and to the spectrum of species.

Loebstein R. et al. *Pregnancy outcome following gestational exposure to fluoroquinolones: a multicenter prospective controlled study.* Antimicrob Agents Chemother. 1998; 42(6) : 1336-9.p Abstract: Concerns regarding the teratogenicity of fluoroquinolones have resulted in their restricted use during gestation. This is despite an increasing need for their use due to emerging bacterial resistance. The objectives of the present investigation were to evaluate pregnancy and fetal outcomes following maternal exposure to fluoroquinolones and to examine whether in utero exposure to quinolones is associated with clinically significant musculoskeletal dysfunctions. We prospectively enrolled and followed up 200 women exposed to fluoroquinolones (norfloxacin, ciprofloxacin, ofloxacin) during gestation. Pregnancy outcome was compared with that for 200 controls matched for age and for smoking and alcohol consumption habits. Controls were exposed to nonteratogenic, nonembryotoxic antimicrobial agents matched by indication, duration of therapy (+/- 3 days), and trimester of exposure. Rates of major congenital malformations did not differ between the group exposed to quinolones in the first trimester (2.2%) and the control group (2.6%) (relative risk, 0.85; 95% confidence interval, 0.21 to 3.49). Women treated with quinolones had a tendency for an increased rate of therapeutic abortions compared with the rate among women exposed to nonteratogens (relative risk, 4.50; 95% confidence interval, 0.98 to 20.57), resulting in lower live-birth rates (86 versus 94%; P = 0.02). The rates of spontaneous abortions, fetal distress, and prematurity and the birth weight did not differ between the groups. Gross motor developmental milestone achievements did not differ between the children of the mothers in the two groups. We concluded that the use of fluoroquinolones during embryogenesis is not associated with an increased risk of major malformations. There were no clinically significant musculoskeletal dysfunctions in children exposed to fluoroquinolones in utero. The higher rate of therapeutic abortions observed in quinolone-exposed women compared to that for their controls may be secondary to the misperception of a major risk related to quinolone use during pregnancy.

Lohner K. et al. *Differential scanning calorimetry and X-ray diffraction studies of the specificity of the interaction of antimicrobial peptides with membrane-mimetic systems.* Biochim Biophys Acta. 1999; 1462(1-2) : 141-56.p Abstract: Interest in biophysical studies on the interaction of antimicrobial peptides and lipids has strongly increased because of the rapid emergence of antibiotic-resistant bacterial strains. An understanding of the molecular mechanism(s) of membrane perturbation by these peptides will allow a design of novel peptide antibiotics as an alternative to conventional antibiotics. Differential scanning calorimetry and X-ray diffraction studies have yielded a wealth of quantitative information on the effects of antimicrobial peptides on membrane structure as well as on peptide location. These studies clearly demonstrated that antimicrobial peptides show preferential interaction with specific phospholipid classes. Furthermore, they revealed that in addition to charge-charge interactions, membrane curvature strain and hydrophobic mismatch between peptides and lipids are important parameters in determining the mechanism of membrane perturbation. Hence, depending on the molecular properties of both lipid and peptide, creation of bilayer defects such as phase separation or membrane thinning, pore formation, promotion of nonlamellar lipid structures or bilayer disruption by the carpet model or detergent-like action, may occur. Moreover, these studies suggest that these different processes may represent gradual steps of membrane perturbation. A better understanding of the mutual dependence of these parameters will help to elucidate the molecular mechanism of membrane damage by antimicrobial peptides and their target membrane specificity, keys for the rationale design of novel types of peptide antibiotics.

Loiez-Durocher C. et al. *[Drug resistance in Mycobacterium tuberculosis: diagnostic methods].* Ann Biol Clin (Paris). 2000; 58(3) : 291-7.p Abstract: The increasing frequency of multidrug-resistant strains of M. tuberculosis becomes dramatic in industrialized countries as well as in developing countries, particularly among patients infected with human immunodeficiency virus. It needs to formulate rapid strategies for diagnosing multidrug-resistant tuberculosis. For these new drug resistance, novel detection methods are developed in order to identify the resistant strains and to undertake efficacious antituberculosis therapies more rapidly. The phenotypic methods are based on the measurement of the microbial growth on nutritional supplement with antimicrobial agents; however, these proportional methods, such as the method in solid medium, the Bactec radiometric method or the MGIT method (mycobacterial growth indicator tube), are time consuming and give results in 5 to 21 days. In contrast, the genotypic tests, using knowledge of the genes involved in the resistance, reduce the time to detection of resistance from weeks to days. After amplification of the segment of the gene encoding the drug target by PCR, these methods are based on the identification of the different mutations conferring the antimicrobial resistance in M. tuberculosis. These methods are applied with success for detection of rifampicin resistance, conferring by mutations in a defined region of the rpoB gene for 99% of cases; on the contrary, results are less for other antituberculous drugs because of the insufficiency of knowledge of the molecular basis of drug resistance.

Loo V.G. et al. *In-vitro susceptibility of Helicobacter pylori to ampicillin, clar-*

ithromycin, metronidazole and omeprazole. J Antimicrob Chemother. 1997; 40(6) : 881-3.p Abstract: The in-vitro activities of omeprazole and three antimicrobial agents against 89 clinical isolates of Helicobacter pylori from a population with duodenal ulcer disease were determined by an agar dilution method. Resistance rates were 20% for metronidazole (MIC > 8 mg/L), 1% for clarithromycin (MIC > 2 mg/L) and zero for ampicillin (MIC > 8 mg/L). Omeprazole was relatively active against H. pylori in vitro (MIC < or = 8 mg/L).

Lopaciuk U. et al. *[Analysis of blood of children hospitalized in the Children Memorial Health Institute between July 1992 and November 1995].* Pediatr Pol. 1996; 71(6) : 523-7.p Abstract: A total number of 6840 blood cultures were taken from 1753 patients hospitalized in the Children's Memorial Health Institute since 07.1992 to 11.1995. Among 6840 blood samples 679 (10.2%) were culture positive and 745 microorganisms were detected; 83.5% Gram(+) bacteria, 9.1% Enterobacteriaceae rods, 1.6% nonfermenters, anaerobes - 3.1% and yeast 2.1%. Fifty two percent of all isolated strains were represented by CoNS. These bacteria were isolated mainly from children hospitalized in cardiology, cardiosurgery, neurosurgery, gastroenterology departments and dialysis unit. We found 68% methicillin resistant strains of CoNS. S. aureus was isolated from blood of children on parenteral nutrition, peritoneal fluid from patients on CAPD, and from blood of children with osteomyelitis/arthritis. Fourty percent of the S. aureus strains were methicillin resistant. Nonfermenters and Enterobacteriaceae rods were isolated predominantly from ICU and gastroenterology department. High percentage of these strains were multiresistant to various antibiotics: penicillins, I and II generations cephalosporins, aminoglycosides and others.

Lopardo H. et al. *Streptococcus pyogenes: vigilancia de su resistencia a los antibióticos en un hospital pediátrico.* Infectol. microbiol. clin. 1995; 7(3) : 53-6.p Abstract: En varios países del mundo comenzaron a aislarse en forma creciente cepas de Streptococcus pyogenes resistentes a eritromicina. Este trabajo tuvo por objeto verificar la sensibilidad a penicilina, lincosamidas y macrólidos de los estreptococos del grupo A aislados en nuestro hospital entre 1989 y 1994. Se estudió un total de 373 cepas aisladas principalmente de exudados faríngeos por el método de dilución en medio sólido. Ninguna cepa resultó resistente a penicilina y sólo en 1989 se aislaron cepas resistentes a eritromicina (1,6 por ciento para ese año). Las dos cepas resistentes presentaron un patrón de sensibilidad compatible con el mecanismo MLS inducible. En conclusión, S. pyogenes continúa siendo uniformemente sensible a penicilina mientras que tanto la eritromicina como los nuevos macrólidos y las lincosamidas mantienen su efectividad in vitro como para seguir siendo considerados como alternativas para el tratamiento de infecciones estreptocócicas en nuestro medio (AU).

Lopes M.F. et al. *Partial characterization of the cohemolytic factor produced by Streptococcus uberis and comparison with the CAMP-factor.* FEMS Immunol Med Microbiol. 1995; 12(3-4) : 205-12.p Abstract: Exosubstances (cohemolysins) produced by Streptococcus agalactiae (CAMP-factor) and Streptococcus uberis (Uberis-factor) showing hemolytic synergism with beta-lysin produced by Staphylococcus aureus were compared. Cohemolytic activity was evaluated in the supernatants of bacterial cultures, before and after ammonium sulfate precipitation. Sheep erythrocytes sensitized with beta-lysin were used as substrate. The assays were performed in microtiter plates and results were expressed as cohemolytic units/ml. Maximum cohemolytic activity was detected, respectively, after 8 h and 14 h of growth in Columbia broth in S. uberis and S. agalactiae cultures. Cohemolytic activities of both microorganisms showed similarities when submitted to various physical and chemical treatments. They were significantly decreased by heating at 60 degrees C and 100 degrees C, or in presence of trypsin, and were abolished in the presence of Tween 20. Activities were found to be stable in crude supernatants and concentrated preparations maintained at -20 degrees C for 3 months. Differences were related to levels of activity and kinetics of detection during the growth cycle. The results indicate the proteic nature, at least in part, of the Uberis factor. Analysis by PAGE in the presence or absence of SDS allowed us to correlate Uberis activity with a protein band with apparent molecular mass of 42 kDa, while CAMP activity was associated with a protein band of 27 kDa.

López Antuñon F.J. et al. *Bacterial resistance to antibiotics in acute respiratory infections (ARIs).* Arch. med. Res. 1997; 28(2) : 195-203.p Abstract: In this review article, we make suggestions on how to approach the increasing problem worlwide of bacterial acute respiratory infections resistant to antibiotics. After a brief description of the main mechanisms of bacterial resistance, i.e., enzymatic inactivation by á-lactamases, reduction in the permeability of the outer membrane and the developlment of PBPs that have decreased affinity for the antibiotic, we analyze documented experiences on the response to different groups of antibiotics (á- lactam antibiotics, cephalosporins, carbapenems and quinolones), of the most commonly isolated bacteria from invasive respiratory infections (Haemophilus influenzae, Streptococcus pneumoniae and Moraxela (Branhamella) catarrhañis). Antimicrobial agent susceptibility in vivo and in vitro testing and the corelation of their results provide the basic information for the adoption of adequate policies and strategies for better use of antibioticas in bacterial respiratory infections; proper surveillance would allow to make intelligent changes in such a policy. Standardized recommendations for clinical practice on the use of antibiotics could be misleading, iatrogenic, and could complicate the resistance problem. To prevent and control. the rise and spread of bacterial resistance, an interdisciplinary approach is needed(AU).

Lopez Bartolome O. et al. *[Microbiologic diagnosis of Helicobacter pylori and its resistance to antibiotics].* Rev Clin Esp. 1998; 198(7) : 420-3.p Abstract: From March 1995 to February 1996 a total of 386 gastroduodenal biopsies were processed for microbiological diagnosis of Helicobacter pylori which included culture, Gram staining and urease test. For susceptibility studies to five antimicrobial agents, 35 additional gastroduodenal biopsies (n = 421) were added. There were 272 (70.4%) positive cultures, 220 (56.9%) samples with positive urase test and 244 (63.2%) with positive result in Gram-staining; both tests were statistically significant compared with culture ($p < 0.05$). Considering culture as the reference method, sensitivity and specificity values for the urease test were 77.0% and 92.1% and for Gram staining 86.7% and 92.9%, respectively. A total of 11 isolates were recovered from the 35 biopsies processed only for culture. Susceptibility testing of 283 isolates (272 + 11) was performed to the following antimicrobials: amoxicillin, metronidazole, clarithromycin, azythromycin and tetracycline. Resistance to metronidazole was 25.4% and the corresponding values for clarithromycin and azithromycin 9.5%. No resistance to amoxicillin or tetracycline was observed. Urease test and Gram staining are two easy-to-perform tests and when taken together allow the microbiological diagnosis of Helicobacter pylori infection. Culture should be performed to know the evolution of resistance to antimicrobials used for treatment of this infection.

Lopez E.L. et al. *Shigella and Shiga toxin-producing Escherichia coli causing bloody diarrhea in Latin America.* Infect Dis Clin North Am. 2000; 14(1) : 41-65, viii.p Abstract: In Latin America, Shigella and shiga toxin-producing Escherichia coli are the two leading agents in the cause of bloody diarrhea. The already high and increasing antimicrobial resistance of Shigella also is a significant problem. Shiga toxin-producing E. coli is an emerging disease with life-threatening complications: hemolytic uremic syndrome. Although E. coli O157:H7 remains the most commonly recognized serotype, recently emerging, non-O157 bacteria may be the cause of a similar spectrum of disease in humans.

Lopez-Lozano J.M. et al. *Modelling and forecasting antimicrobial resistance and its dynamic relationship to antimicrobial use: a time series analysis.* Int J Antimicrob Agents. 2000; 14(1) : 21-31.p Abstract: To investigate the relationship between antimicrobial use and resistance in our hospital, we collected antimicrobial susceptibility and use data from existing microbiology laboratory and pharmacy databases for the period July 1st, 1991-December 31, 1998. The data was analyzed as time series and autoregressive integrated moving average (Box-Jenkins) and transfer function models were built. By using this method, we were able to demonstrate a temporal relationship between antimicrobial use and resistance, to quantify the effect of use on resistance and to estimate the delay between variations of use and subsequent variations in resistance. The results obtained for two antimicrobial-microorganism combinations: ceftazidime-gram-negative bacilli and imipenem-Pseudomonas aeruginosa, are shown as examples.

Lopez-Navidad A. et al. *Successful transplantation of organs retrieved from donors with bacterial meningitis.* Transplantation. 1997; 64(2) : 365-8.p Abstract: BACKGROUND: The shortage of organs for transplantation is the most important factor limiting the number of transplants performed. Consequently, in recent years, criteria for considering a patient as a potential organ donor have been broadened. METHODS: From 1995 through 1996, we have retrieved organs from five donors who were brain dead because of bacterial meningitis. The causative microorganisms were Neisseria meningitidis in one patient, Streptococcus pneumoniae in three patients, and Escherichia coli in one patient. Fifteen organs were retrieved and transplanted into 16 recipients. All the donors and recipients received adequate antibiotic therapy. RESULTS: None of the recipients developed infectious complications caused by the meningeal pathogens. After a follow-up ranging from 4 to 30 months, 12 patients are alive with functioning grafts. The cause of death was noninfectious in the four patients who died. CONCLUSIONS: Our study demonstrates that patients with brain death caused by bacterial meningitis due to meningococci, pneumococci, or E coli may be suitable organ donors. Transplantation of organs from such donors does not increase the risk of infection transmission to the recipient, provided that both donor and recipient had received adequate antibiotic therapy.

Lopez R. et al. *The pneumococcal cell wall degrading enzymes: a modular design to create new lysins?* Microb Drug Resist. 1997; 3(2) : 199-211.p Abstract: Autolysins are enzymes that degrade different bonds in the peptidoglycan and, eventually, cause the lysis and death of the cell. Streptococcus pneumoniae contains a powerful autolytic enzyme that has been characterized as an N-acetylmuramoyl-L-alanine amidase. We have cloned the lytA gene coding for this amidase and studied in depth the genetics and expression of this gene, which represented the first molecular analysis of a bacterial autolysin. Two observations have been fundamental in revealing further knowledge on the lytic systems of pneumococcus: (a) The well-documented dependence of the pneumococcal autolysin on the presence of choline in the cell wall for activity, and (b) the early observation that most pneumococcal phages also required the presence of this amino-alcohol in the growth medium to achieve a successful liberation of the phage progeny. We concluded that choline would serve as an element of strong selective pressure to preserve certain structures of the host and phage lytic enzymes which should lead to sequence homologies. We constructed active chimeras between the lytic enzymes of S. pneumoniae and its bacteriophages using genes that share sequence homology as well as genes that completely lack homologous regions. In this way, we demonstrated that the pneumococcal lytic enzymes are the result of the fusion of two independent functional modules where the carboxy-terminal domain might be responsible for the specific recognition of choline-containing cell walls whereas the active center of these enzymes should be localized in the N-terminal part of the protein. The modular design postulated for the pneumococcal lysins seems to be a widespread model for many types of microbial proteins and the construction of functional chimeric proteins between the lytic enzymes of pneumococcus and those of several gram-positive microorganisms, like Clostridium acetobutylicum or Lactococcus lactis, provided interesting clues on the modular evolution of proteins. The study of several genes coding for the lytic enzymes of temperate phages of pneumococcus also highlighted on some evolutionary relationships between microorganisms. We suggest that lysogenic relationships may represent a common mechanism by which pathogenic organisms like pneumococcus should undergo a rapid adaptation to an evolving environment.

Lorenz R. et al. *Microbiological examinations and in-vitro testing of different antibiotics in therapeutic endoscopy of the biliary system.* Endoscopy. 1998; 30(8) : 708-12.p Abstract: BACKGROUND AND STUDY AIMS: Prior to endoscopic therapeutic procedures, no antibiotic prophylaxis is administered routinely. Because of the reported incidence of infectious complications, which may reach up to 10%, a prospective study was undertaken to investigate the effects of a prophylactic dose of cefuroxime on the incidence of bacteremia and clinical signs of infection, but no significant effects could be demonstrated. In addition to this published work, blood and bile cultures obtained in this trial were also investigated, and the in-vitro susceptibility to several antibiotics was tested in order to recommend the appropriate substances. PATIENTS AND METHODS: Ninety-nine consecutive patients (51 men, 48 women; mean age 61.4 +/- 17 years) with biliary obstruction who underwent an endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic cholangiography with drainage (PTCD) were included. Sequential blood cultures were taken before and up to 60 minutes after the endoscopic intervention. Bile cultures were obtained in 56 patients with biliary drainage. Aerobic and anaerobic cultures were prepared from all obtained specimens and the isolated organisms were identified. In the case of positive cultures, an in-vitro resistance test for 15 different antibiotics was performed. RESULTS: The incidence of bacteremia was 11.1% (n = 11), and 16 bacteria were isolated. Twelve different microorganisms were detected, with Escherichia coli found in four cases. From 41 positive out of 56 prepared bile cultures (73.2%), 91 isolates were found with 25 different species. A single agent was detected in eight cases (19.5%), while a mixed growth, with pathogens ranging from two to six species, was found in 33 cases (80.5%). The seven most frequently isolated germs were E. coli and Enterococcus (each n = 19), Klebsiella (n = 10), Streptococcus viridans (n = 9), Staphylococcus epidermidis (n = 5), Morganella morganii (n = 4), and Bacteroides fragilis (n = 3), representing 76% of all agents. Examination for fungal infection revealed positive cultures of Candida albicans in 16.1% of bile cultures (nine of 56). Interestingly, the use of proton-pump inhibitors (PPIs), with a consequent rise in the gastric pH value, led to an increase in the rate of bacteremia to 26.2% (five of 19) compared to the other patients not on PPIs (n = 80), who developed bacteremia in only six cases (7.5%; p = 0.02). In-vitro testing of different antibiotics was carried out in 73 isolates. Imipenem showed the best antimicrobial activity (98.4%), followed by trimethoprim and sulfamethoxazole (90%), amoxicillin plus clavulanic acid (87.3%), vancomycin (82.4%), and ofloxacin (76.9%). CONCLUSIONS: Escherichia coli was found to be the pathogen most frequently detected in blood and bile following endoscopic interventions in the biliary tract. Enterococci, Klebsiella and Streptococcus viridans were found in bile cultures with an incidence exceeding 10%. In view of the in-vitro test results, possible side effects, and contraindications, amoxicillin plus beta-lactamase inhibitors or quinolones are considered to be suitable antibiotics for the prophylaxis of biliary infections.

Lotsu D.K. et al. *Current status of antimicrobial susceptibility in MRSA isolates typed by coagulase and phage typing in Okinawa.* Acta Med Okayama. 1995; 49(2) : 81-9.p Abstract: The incidence of nosocomial infections with methicillin-resistant Staphylococcus aureus is of great concern in Japan and the developed world as a whole.

Simple typing techniques like coagulase and phage typing are quick and useful for monitoring and evaluating these organisms. In view of this, the current status of antimicrobial susceptibility in Staphylococcus aureus (S. aureus) isolates in Okinawa typed by coagulase and phage typing was studied. Of 508 isolates, methicillin-resistant S. aureus (MRSA) comprised 54.3% (minimum inhibitory concentration (MIC) > or = 16 micrograms/ml). Coagulase type II and phage group III were the most prevalent, comprising 65.2% and 38%, respectively. These were followed by phage non-typable group and coagulase type III with 36.6% and 12.7%, respectively. Compared to a previous study conducted in 1989, there has been an increase of about 17% in the MRSA isolation rate with a concomitant increase of about 11% in the coagulase type II MRSA isolation rate and a decrease of about 27% in the isolation rate of coagulase type III MRSA. Using a panel of 16 antibiotics, coagulase type II MRSA were resistant to all except Arbekacin and Vancomycin. Arbekacin and Vancomycin were the sole antibiotics to which resistance was not expressed by any of the isolates. With regard to the methicillin-sensitive S. aureus (MSSA), coagulase type III and phase group III were the most prevalent, comprising 25.9% and 32.3%, respectively.

Louie M. et al. *The role of DNA amplification technology in the diagnosis of infectious diseases.* CMAJ. 2000; 163(3) : 301-9.p Abstract: Nucleic acid amplification and detection methods developed in the past decade are useful for the diagnosis and management of a variety of infectious diseases. The most widely used of these methods is the polymerase chain reaction (PCR). PCR assays can detect rapidly and accurately the presence of fastidious and slow-growing microorganisms, such as Chlamydia, mycoplasmas, mycobacteria, herpesviruses and enteroviruses, directly from clinical specimens. Commercial PCR assays for the diagnosis of tuberculosis and genital C. trachomatis infection are now routinely used in many diagnostic laboratories. Assays have also been developed that can detect antimicrobial resistance and are used to identify the cause of infection by organisms that cannot be cultivated. The value of viral load measurement by nucleic acid amplification in the management of patients with HIV infection or hepatitis C has also been well established. However, evaluations of this technology for rapid microbial diagnosis have generally been limited by small samples, and the cost of these assays may be as high as Can$125 per test. As nucleic acid amplification methods continue to evolve, their role in the diagnosis and management of patients with infectious diseases and their impact on clinical outcomes will become better defined.

Love D.N. et al. *Bacteriological warfare amongst cats: what have we learned about cat bite infections?* Vet Microbiol. 2000; 74(3) : 179-93.p Abstract: Cat bite infections are one of the most common infectious diseases presenting to veterinary practices and to emergency rooms at human hospitals. This review describes the disease in humans and cats, the origin of organisms involved in cat bite abscesses and the importance of selected organisms such as members of the genus Porphyromonas in the disease. It also discusses future directions, the importance of identifying significant organisms and why an understanding of antimicrobial susceptibility patterns is of consequence to the outcome of the disease in humans and cats.

Love R.M. et al. *Coinvasion of dentinal tubules by Porphyromonas gingivalis and Streptococcus gordonii depends upon binding specificity of streptococcal antigen I/II adhesin.* Infect Immun. 2000; 68(3) : 1359-65.p Abstract: Cell wall-anchored polypeptides of the antigen I/II family are produced by many species of oral streptococci. These proteins mediate adhesion of streptococci to salivary glycoproteins and to other oral microorganisms and promote binding of cells to collagen type I and invasion of dentinal tubules. Since infections of the root canal system have a mixed anaerobic bacterial etiology, we investigated the hypothesis that coadhesion of anaerobic bacteria with streptococci may facilitate invasive endodontic disease. Porphyromonas gingivalis ATCC 33277 cells were able to invade dentinal tubules when cocultured with Streptococcus gordonii DL1 (Challis) but not when cocultured with Streptococcus mutans NG8. An isogenic noninvasive mutant of S. gordonii, with production of SspA and SspB (antigen I/II family) polypeptides abrogated, was deficient in binding to collagen and had a 40% reduced ability to support adhesion of P. gingivalis. Heterologous expression of the S. mutans SpaP (antigen I/II) protein in this mutant restored collagen binding and tubule invasion but not adhesion to P. gingivalis or the ability to promote P. gingivalis coinvasion of dentin. An isogenic afimbrial mutant of P. gingivalis had 50% reduced binding to S. gordonii cells but was unaffected in the ability to coinvade dentinal tubules with S. gordonii wild-type cells. Expression of the S. gordonii SspA or SspB polypeptide on the surface of Lactococcus lactis cells endowed these bacteria with the abilities to bind P. gingivalis, penetrate dentinal tubules, and promote P. gingivalis coinvasion of dentin. The results demonstrate that collagen-binding and P. gingivalis-binding properties of antigen I/II polypeptides are discrete functions. Specificity of antigen I/II polypeptide recognition accounts for the ability of P. gingivalis to coinvade dentinal tubules with S. gordonii but not with S. mutans. This provides evidence that the specificity of interbacterial coadhesion may influence directly the etiology of pulpal and periapical diseases.

Lovgren M. et al. *Invasive Streptococcus pneumoniae infections: serotype distribution and antimicrobial resistance in Canada, 1992-1995.* CMAJ. 1998; 158(3) : 327-31.p Abstract: OBJECTIVE: To report current information about invasive pneumococcal infections, capsular types and antimicrobial resistance in Canada. DESIGN: Retrospective analysis. SETTING: Canada. PATIENTS: A total of 976 patients from whom Streptococcus pneumoniae was isolated from blood or cerebrospinal fluid between Jan. 1, 1992, and Dec. 31, 1995. OUTCOME MEASURES: Capsular type and antimicrobial susceptibility. RESULTS: Twenty types accounted for 90.8% of the isolates from patients over 5 years of age; all but type 15A are covered by the currently available 23-valent vaccine. Nine types accounted for 92% of the isolates recovered from children 5 years and less. Reduced susceptibility to penicillin was found in 7.8% of the collection and was associated with types 6B, 9V and 19A. Full resistance to penicillin was observed most frequently during 1995 and was associated with type 9V. Rates of reduced susceptibility over one 12-month period were 19.5% for trimethoprim-sulfamethoxazole and 4.5% or less for each of cefotaxime, ceftriaxone, chloramphenicol, erythromycin, ofloxacin and tetracycline. CONCLUSIONS: Over 90% of invasive pneumococcal infections are covered by the currently available vaccines (for people over 2 years of age) and the pneumococcal protein-polysaccharide conjugate vaccines under development for young children. The high frequency of antimicrobial resistance observed requires more complete investigation and confirmation; however, taken from a global perspective, it supports the need to develop better control strategies, including greater use of new and existing vaccines.

Low D.E. *Quinupristin/dalfopristin: spectrum of activity, pharmacokinetics, and initial clinical experience.* Microb Drug Resist. 1995; 1(3) : 223-34.p Abstract: In recent years, the prevalence of multiple drug-resistant strains of common Gram-positive pathogens has grown in many regions of the world. Increasingly, methicillin-resistant Staphylococcus aureus, coagulase-negative staphylococci, vancomycin-resistant enterococci, and penicillin-resistant pneumococci have been identified as causative organisms in serious and life-threatening infections. This increase in resistance highlights the need for new antimicrobial agents to expand the therapeutic armamentarium. Quinupristin/dalfopristin is the first of a unique class of antibiotics called streptogramins. It is characterized by a unique mechanism of action, intracellular activity, synergistic activity of its components, broad spectrum of activity against most Gram-positive cocci, common respiratory pathogens, and anaerobes, and demonstrated postantibiotic effect. Clinical evidence to date indicates that quinupristin/dalfopristin may be effective for the treatment of mul-

tidrug-resistant infections, especially those due to vancomycin-resistant enterococci and methicillin-resistant staphylococci. This article reviews the pharmacology, microbiology, and clinical experience with quinupristin/dalfopristin to date.

Low D.E. *Resistance issues and treatment implications: pneumococcus, Staphylococcus aureus, and gram-negative rods.* Infect Dis Clin North Am. 1998; 12(3) : 613-30, viii.p Abstract: During the last decade there has been an unexpectedly rapid evolution of antimicrobial resistance in the respiratory pathogens for community- and hospital-acquired pneumonia. In order to choose the most optimal therapy for their patients, it is essential that physicians be aware of the prevalence and mechanisms of resistance and their implications on the effectiveness of the various antimicrobials.

Low D.E. et al. *A practical guide for the diagnosis and treatment of acute sinusitis.* CMAJ. 1997; 156 Suppl 6 : S1-14.p Abstract: OBJECTIVE: To develop guidelines for the diagnosis and management of acute sinusitis. OPTIONS: Diagnostic clinical criteria and imaging techniques, the role of antimicrobial therapy and duration of treatment, and the role of adjunct therapy, including decongestants, glucocorticosteroids and nasal irrigation. OUTCOMES: Improved accuracy of clinical diagnosis, better utilization of imaging techniques and rational use of antimicrobial therapy. EVIDENCE: A MEDLINE search for relevant articles published from 1980 to 1996 using the MeSH terms "sinusitis," "acute sinusitis," "respiratory infections," "upper respiratory infections," "sinusitis" and "diagnosis," "sinusitis" and "therapy," "sinusitis" and "etiology," and "antimicrobial resistance" and search for additional articles from the reference lists of retrieved articles. Papers referring to chronic sinusitis, sinusitis in compromised patients and documented nonbacterial sinusitis were excluded. The evidence was evaluated by participants at the Canadian Sinusitis Symposium, field in Toronto on April 26-27, 1996. VALUES: A hierarchical evaluation of the strength of evidence modified from the methods of the Canadian Task Force on the Periodic Health Examination was used. Strategies were identified to deal with problems for which no adequate clinical data were available. Recommendations arrived at by consensus of the symposium participants were included. BENEFITS, HARMS AND COSTS: Increased awareness of acute sinusitis, accurate diagnosis and prompt treatment should reduce costs related to unnecessary investigations, time lost from work and complications due to inappropriate treatment. As well, physicians will be better able to decide which patients will not require antimicrobial therapy, thus saving the patient the cost and potential side effects of treatment. RECOMMENDATIONS: Clinical diagnosis can usually be made from the patient's history and findings on physical examination only. Five clinical findings comprising 3 symptoms (maxillary toothache, poor response to decongestants and a history of coloured nasal discharge) and 2 signs (purulent nasal secretion and abnormal transillumination result) are the best predictors of acute bacterial sinusitis (level I evidence). Transillumination is a useful technique in the hands of experienced personnel, but only negative findings are useful (level III evidence). Radiography is not warranted when the likelihood of acute sinusitis is high or low but is useful when the diagnosis is in doubt (level III evidence). First-line therapy should be a 10-day course of amoxicillin (trimethoprim-sulfamethoxazole should be given to patients allergic to penicillin) (level I evidence) and a decongestant (level III evidence). Patients allergic to amoxicillin and those not responding to first-line therapy should be switched to a second-line agent. As well, patients with recurrent episodes of acute sinusitis who have been assessed and found not to have anatomic anomalies may also benefit from second-line therapy (level III evidence). VALIDATION: The recommendations are based on consensus of Canadian and American experts in infectious diseases, microbiology, otolaryngology and family medicine. The guidelines were reviewed independently for the advisory committee by 2 external experts. Previous guidelines did not exist in Canada.

Low D.E. et al. *Multidrug-resistant enterococci: a threat to the surgical patient.* Am J Surg. 1995; 169(5A Suppl) : 8S-12S.p Abstract: The enterococcus has become an important nosocomial pathogen, reported by the National Nosocomial Infections Surveillance System as the third most common pathogen associated with blood-stream infections and the second most commonly isolated pathogen overall. It is now more frequently recognized as a cause of superinfection in the surgical patient, as the possible result of the frequent use of ineffective antimicrobials for prophylaxis and treatment. Both of these findings are due, in part, to the intrinsic antimicrobial resistance of the enterococci. Of greater concern is the ready ability of this organism to acquire resistance traits. During the past 5 years, the appearance and rapid dissemination of strains with high-level resistance to vancomycin, ampicillin, gentamicin, and streptomycin have been reported; in some cases, no effective antimicrobial therapy was available to patients infected with these strains. Enterococci, in addition to their intrinsic and acquired tolerance to beta-lactams, have acquired the ability to inactivate penicillin and ampicillin via beta-lactamase production. Prompt recognition of such multiresistant enterococci, the implementation of effective infection control precautions, and rational use of antimicrobials may limit or even prevent the spread of such strains in the hospital setting.

Low J.C. et al. *Antimicrobial resistance of Salmonella enterica typhimurium DT104 isolates and investigation of strains with transferable apramycin resistance.* Epidemiol Infect. 1997; 118(2) : 97-103.p Abstract: An examination of salmonella isolates collected by the Scottish Agricultural College Veterinary Services Division from April 1994 to May 1995 was conducted to determine the extent to which Salmonella enterica serotype Typhimurium phage type 104 (DT104) occurred and to investigate the antimicrobial resistance patterns of isolates. Typhimurium DT104 was the predominant salmonella and was isolated from nine species of animal. All isolates of this phage type possessed resistance to at least one antimicrobial and 98% of the isolates were resistant to multiple antimicrobials with R-type ACTSp the predominant resistance pattern. Various other resistance patterns were identified and transferable resistance to the veterinary aminoglycoside antimicrobial apramycin was demonstrated in three strains. A retrospective study for gentamicin resistance in isolates from the Scottish Salmonella Reference Laboratory collection revealed a human isolate of Typhimurium DT104 resistant to gentamicin but sensitive to apramycin and a bovine isolate with apramycin and gentamicin resistance.

Lu C.Y. et al. *Penicillin-nonsusceptible Streptococcus pneumoniae infections in children.* J Microbiol Immunol Infect. 1999; 32(3) : 179-86.p Abstract: The emergence of penicillin-nonsusceptible Streptococcus pneumoniae (PNSSP) has brought a new clinical challenge. In Taiwan, reports of the prevalence and clinical features of PNSSP infections in children are limited. This study reviewed the resistance patterns of all clinical isolates of S. pneumoniae obtained from patients under 17 years of age from January 1993 through July 1998 in a medical center. Their clinical features and treatment responses were analyzed, with special attention paid to those patients with invasive PNSSP infections. Totally, 170 clinical isolates of S. pneumoniae were obtained from 168 patients aged under 17 years. Among those infections, there were 56 sinusitis (including 4 sinusitis with bacteremia), 44 pneumonia (including 23 pneumonia with bacteremia or empyema), 23 otitis media (including 5 otitis media with bacteremia), 9 simple bacteremia, 9 conjunctivitis, 8 meningitis, 4 peritonitis, 3 skin infections and the other 14 isolates were colonization. One hundred eleven isolates (65.3%) showed reduced penicillin susceptibility by the disk diffusion method. A trend of increasing percentiles of PRSP was noted: 27.3% (3/11) in 1993, 37.5% (9/24) in 1994, 55.5% (10/18) in 1995, 77.5% (31/40) in 1996, 66.0% (31/47) in 1997, and 87.1% (27/31) in 1998. Minimum inhibitory concentration (MIC) determinations by the E-test showed some of the isolates were intermediately resistant. Prior antibiotic usage was associated with a higher incidence of PNSSP

infections. However, most children responded well to antimicrobial treatment.

Lu P.L. et al. *Bacteremia due to Campylobacter species: high rate of resistance to macrolide and quinolone antibiotics.* J Formos Med Assoc. 2000; 99(8) : 612-7.p Abstract: BACKGROUND AND PURPOSE: Although the rate of isolation of Campylobacter from stool specimens in Taiwan is similar to those in other developed countries, Campylobacter bacteremia has rarely been reported in Taiwan, and the patterns of antimicrobial susceptibility of blood isolates to various antimicrobial agents remain unknown in the Taiwanese population. The purpose of this study was to determine the clinical characteristics of patients with Campylobacter infection in a university hospital in Taiwan and the antimicrobial susceptibility patterns of the Campylobacter isolates. METHODS: We retrospectively reviewed medical records of all patients with Campylobacter bacteremia treated in a university hospital between January 1991 and March 1999. Minimum inhibitory concentrations of 13 antimicrobial agents to 10 stored blood isolates were determined using the E-test. RESULTS: Approximately half (52%) of the 21 patients had chronic liver disease and one-quarter had hepatobiliary or gastrointestinal malignancies. Thirteen (62%) patients had conditions that were associated with gastroenteritis. Other clinical manifestations associated with Campylobacter infection included cellulitis, perinatal sepsis, peritonitis, vascular catheter-related infection, and primary bacteremia. The duration of illness was generally short: approximately half (52%) of the 21 patients had fever lasting for only 1 day. Antimicrobial susceptibility testing of the 10 isolates revealed that most of the blood isolates were resistant to erythromycin and nalidixic acid (100% and 90%, respectively), while the rate of cross-resistance between erythromycin and azithromycin was 70%, and that between nalidixic acid and ciprofloxacin was 67%. CONCLUSIONS: Our observations suggest that Campylobacter bacteremia should be included in the differential diagnosis of patients with chronic liver disease or malignancies involving the hepatobiliary system or gastrointestinal tract who present with fever and gastroenteritis. Clinicians in Taiwan should be alert to the high rate of resistance of Campylobacter isolates to macrolide and quinolone antibiotics.

Luaces Cubells C. et al. *[Routes of endotracheal colonization in patients with mechanical ventilation].* An Esp Pediatr. 1997; 46(1) : 20-3.p Abstract: OBJECTIVE: We prospectively evaluated the frequency and route of endotracheal colonization in intubated children in order to know what microorganisms, either by primary infection or through previous colonization of oropharynx and/or stomach and progression towards the lower respiratory tract, are responsible for these infections. PATIENTS AND METHODS: Oropharyngeal, tracheal and gastric samples of 43 patients were collected for culture at the moment of intubation and at 24-h intervals for 4 days. The colonization route for each endotracheal microorganism was classified depending on the initial isolation site. Isolated microorganisms were considered as belonging to the same strain if the biochemical pattern and antibiogram were identical. RESULTS: Of the patients studied, 84% presented positive cultures the first day. Tracheal colonization was detected at day 1 in 22 patients (51%) and in 35 (82%) at the end of the study. A colonization sequence was seen in 18 patients (41%). The microorganisms most frequently isolated were S. aureus, P. aeuruginosa and C. albicans. CONCLUSIONS: The mechanisms of tracheal colonization in intubated children is similar to adults. Oropharynx colonization is the key antecedent. Prophylaxis measures should avoid the proliferation at the oropharyngeal and/or gastric level.

Lubbe M.M. et al. *Comparative activity of eighteen antimicrobial agents against anaerobic bacteria isolated in South Africa.* Eur J Clin Microbiol Infect Dis. 1999; 18(1) : 46-54.p Abstract: The in vitro activity of 18 antimicrobial agents was determined against 378 anaerobic bacteria isolated in Bloemfontein, South Africa, during 1996/97. Against the gram-positive isolates, MICs of penicillin and cefoxitin were >0.5 microg/ml and >16 microg/ml, respectively, for five and three strains of non-perfringens Clostridium spp. Seventeen Peptostreptococcus anaerobius strains were resistant to penicillin (MIC > or = 2 microg/ml). All gram-positive anaerobes tested except one Peptostreptococcus sp. and one Clostridium sp. were susceptible to dalfopristin-quinupristin (MICs < or = 1 microg/ml). The carbapenems exhibited excellent activity against the gram-positive isolates and were effective against most gram-negative anaerobes, with the exception of the fusobacteria. Only seven strains exhibited decreased susceptibility to trovafloxacin (MICs > 2 microg/ml). In mixed anaerobic/aerobic infections, carbapenems and the fourth-generation quinolone trovafloxacin were the agents most suitable for us as broad-spectrum monotherapy.

Lucci L.M. et al. *Decontamination of human sclera: an in vitro study.* Cornea. 1999; 18(5) : 595-8.p Abstract: PURPOSE: The human sclera is frequently used in ophthalmic surgeries and must be preserved in disinfectants that prevent its contamination. In this study the efficiency of glycerin, absolute alcohol (ethanol), and benzalkonium chloride (1:5,000) as human sclera disinfectants were compared. METHODS: Fresh human scleras were trephined, the scleral disks divided into three groups and contaminated with Staphylococcus aureus (ATCC 29213), Pseudomonas aeruginosa (ATCC 27853), or Bacillus cereus (ATCC 11778) for 24 h. Thereafter they were transferred to preservation vials each containing glycerin, absolute alcohol, benzalkonium chloride diluted in 70% alcohol (1:5,000) or Trypticase Soy Broth (control), respectively, and stored at room temperature. From each vial, two scleral disks were removed after 1, 2, 3, 4, 7, 10, and 14 days of immersion. Both were plated on blood agar, one being macerated, and both incubated at 37 degrees C for 48 h. RESULTS: Pseudomonas aeruginosa, S. aureus, and B. cereus were recovered from the glycerin-immersed scleral disks until the second, fourth, and fourteenth days, respectively. Bacillus cereus was recovered from those immersed in absolute alcohol until the fourteenth day, whereas disks infected with the other microorganisms and immersed in absolute alcohol presented no growth since the very first day of immersion. Bacillus cereus was recovered from scleral disks immersed in benzalkonium chloride diluted in 70% alcohol (1:5,000) only on the first day. CONCLUSION: Resistant microorganisms can survive in scleral tissue preserved in glycerin and absolute alcohol. We conclude that benzalkonium chloride diluted in 70% alcohol (1:5,000) in vitro is the best disinfectant for human sclera after 24 h.

Lucet J.C. et al. *Control of a prolonged outbreak of extended-spectrum beta-lactamase-producing enterobacteriaceae in a university hospital.* Clin Infect Dis. 1999; 29(6) : 1411-8.p Abstract: Extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBLPE) were isolated from clinical specimens from 130 to 140 patients/year in 1989-1991 in our hospital. In February 1992, a control program was initiated: screening tests in 3 intensive care units (ICUs) and contact-isolation precautions in all units. The septic surgical unit served as an isolation ward for surgical patients from whom ESBLPE was isolated. In 1992, the incidence of ESBLPE acquisition failed to decrease, and most acquisitions occurred in 3 ICUs. Critical evaluation of implementation of isolation procedures in these ICUs prompted corrective measures for barrier precautions. The incidence of acquired cases subsequently decreased, and a second evaluation determined that these measures had been correctly applied. The incidence of acquired cases in the septic surgical unit was lower than those in the other units. Decreases were also found in the incidence of acquisition of other hand-transmitted multidrug-resistant organisms. Barrier precautions, screening tests for ICU patients, and grouping of cohorts after ICU discharge are effective in controlling the spread of multidrug-resistant microorganisms by cross-contamination. The outbreak was effectively controlled without restricting antimicrobial use.

Lucet J.C. et al. *Microbiological evaluation of central venous catheter administration hubs.* Infect Control Hosp Epidemiol. 2000; 21(1) : 40-2.p Abstract: We compared, in three intensive care units, colonization of hubs with hub protection boxes or hubs with needleless closed connectors; 137 central venous catheters and 451 hubs were randomized in two groups with similar characteristics. Catheter and hub colonization were not different between the two groups. Among 30 colonized catheters, the same isolate was found in only two hubs; hub contamination rarely is responsible for catheter colonization in short-term catheters. Further studies are required to evaluate the benefit of protected hubs compared with unprotected hubs.

Lucey B. et al. *Integronlike structures in Campylobacter spp. of human and animal origin*. Emerg Infect Dis. 2000; 6(1) : 50-5.p Abstract: Resistance to antimicrobial agents used to treat severe Campylobacter spp. gastroenteritis is increasing worldwide. We assessed the antimicrobial resistance patterns of Campylobacter spp. isolates of human and animal origin. More than half (n = 32) were resistant to sulphonamide, a feature known to be associated with the presence of integrons. Analysis of these integrons will further our understanding of Campylobacter spp. epidemiology.

Lucht L. et al. *Recovery of foodborne microorganisms from potentially lethal radiation damage.* J Food Prot. 1998; 61(5) : 586-90.p Abstract: A two-stage recovery protocol was examined for microorganisms following gamma irradiation in phosphate buffer at 0 degrees C. In the first stage, survivors were recovered on basal yeast extract agar and held at various temperatures suboptimal for their growth for 20 h (resuscitation protocol). In the second stage the survivors were incubated for an additional 24 h, but in this case at their optimum temperature for growth. Controls consisted of survivors which were not subjected to the resuscitation protocol (direct incubation at their optimum growth temperature). The ratio of survivors enumerated with and without the resuscitation protocol (control) at each specified temperature was used to formulate a recovery factor(RF). An RF was determined for each treatment dose. Results of this study indicated that the number of Escherichia coli, Salmonella serotype typhimurium and Brochothrix thermosphacta survivors increased following a resuscitation protocol (RF > 2.0). Overall, optimum resuscitation temperatures ranged from 14 to 22 degrees C. The extent of recovery also appeared dose dependent, with larger treatment doses giving rise to a higher RF. S. serotype typhimurium irradiated at 1.5 kGy exhibited the highest RF, 161, when resuscitated at 22 degrees C. Listeria monocytogenes, Yersinia enterocolitica, Staphylococcus aureus, Aeromonas hydrophila and Saccharomyces cerevisiae exhibited an RF < 2.0 regardless of resuscitation temperature. Results of this study indicated that the use of suboptimal holding temperatures as part of a recovery protocol may have advantages, especially with respect to the enumeration of E. coli and salmonellae survivors in irradiated foods such as poultry.

Luchtefeld M.A. et al. *Evaluation of transarterial embolization for lower gastrointestinal bleeding.* Dis Colon Rectum. 2000; 43(4) : 532-4.p Abstract: INTRODUCTION: Transcatheter arterial embolization has been used as a therapeutic maneuver for lower gastrointestinal bleeding. The availability of highly selective arteriography has made this procedure safer and warrants re-evaluation. METHODS: A retrospective chart review was done of all patients undergoing arteriography for presumed lower gastrointestinal bleeding at two acute-care community hospitals. Causes of bleeding, clinical outcome, and complications caused by transcatheter arterial embolization were recorded. RESULTS: There were 26 arteriographically identified bleeding sites in the colon and small bowel. The most frequent cause of bleeding was diverticulosis (12 patients), with the diagnosis being arterio venous malformation in two, and one unknown colonic source. Transcatheter arterial embolization was attempted for 17 separate bleeding episodes in 16 patients. Transfusion requirements were an average (+/- standard deviation) of 7 +/- 1.43 units per patient. Transcatheter arterial embolization was successful in stopping bleeding in 14 cases (82 percent). Two patients had surgery after transcatheter arterial embolization: one for colonic necrosis and one for persisting bleeding. There were two more unsuccessful procedures; one had a successful repeated transcatheter arterial embolization, and one stopped spontaneously. One patient rebled during the same hospitalization and was controlled with intra-arterial vasopressin. There were two deaths, both secondary to sepsis unrelated to the transcatheter arterial embolization or the gastrointestinal tract. CONCLUSIONS: Transcatheter arterial embolization is a relatively safe and successful procedure in patients with massive lower gastrointestinal hemorrhage. It is an excellent choice of therapy for patients that are poor candidates for surgery, but its role in other patients remains to be defined.

Lumbiganon P. et al. *Comparison between the antimicrobial susceptibility of Burkholderia pseudomallei to trimethoprim-sulfamethoxazole by standard disk diffusion method and by minimal inhibitory concentration determination*. J Med Assoc Thai. 2000; 83(8) : 856-60.p Abstract: Melioidosis, an infection caused by Burkholderia pseudomallei, usually occurs in immunocompromised patients and requires prolonged antibiotic therapy. Previously, oral trimethoprim-sulfamethoxazole (TM/SM), an inexpensive and effective drug has been used as a maintenance therapy. The susceptibility of B. pseudomallei to TM/SM by the standard disk diffusion method is very low. However, some patients who were treated with TM/SM as a maintenance therapy despite the in vitro resistance showed good clinical responses. There were no data comparing the susceptibility of B. pseudomallei by the standard disk diffusion method with other quantitative susceptibility tests. The objective of this study was to determine the agreement between the antimicrobial susceptibility of B. pseudomallei to TM/SM by standard disk diffusion and minimal inhibitory concentration determination (MIC). We performed the susceptibility test of 144 strains of B. pseudomallei to TM/SM by both the standard disk diffusion and microbroth dilution MIC. The sensitivity results were 53.5 per cent and 84.0 per cent respectively. The agreement between the 2 tests was very poor (Kappa = 0.14; 95% CI = -0.01 to 0.29). The false resistant rate by the standard disk diffusion test was 67.9 per cent. Further in vitro susceptibility and clinical study are needed to define the interpretive criteria that correlate with clinical response.

Luna C.M. et al. *Community-acquired pneumonia : etiology, epidemiology, and outcome at a teaching hospital in argentina*. Chest. 2000; 118(5) : 1344-54.p Abstract: OBJECTIVE: To survey the etiology and epidemiology of community-acquired pneumonia (CAP) in relation to age, comorbidity, and severity and to investigate prognostic factors. DESIGN: Prospective epidemiologic study, single center. SETTING: University hospital at Buenos Aires, Argentina. PATIENTS: Outpatients and inpatients fulfilling clinical criteria of CAP. INTERVENTIONS: Systematic laboratory evaluation for determining the etiology, and clinical evaluation stratifying patients into mild, moderate, and severe CAP (groups 1 to 3), a clinical rule used for hospitalization. RESULTS: During a 12-month period, 343 patients (mean age, 64.4 years; range, 18 to 102 years) were evaluated. We found 167 microorganisms in 144 cases (yield, 42%). Streptococcus pneumoniae, the most common pathogen, was isolated in 35 cases (24%). Mycoplasma pneumoniae, present in 19 (13%), was second in frequency in group 1; Haemophilus influenzae, present in 17 cases (12%), was second in group 2; and Chlamydia pneumoniae, present in 12 cases (8%), was second in group 3. Etiology could not be determined on the basis of clinical presentation; identifying the etiology had no impact on mortality. Some findings were associated with specific causative organisms and outcome. A significantly lower number of nonsurvivors received adequate therapy (50% vs 77%). CONCLUSIONS: Age, comorbidities, alcohol abuse, and smoking were related with distinct etiologies. PaO(2) to fraction of inspired oxygen ratio < 250, aerobic Gram-negative pathogen, chronic renal failure, Glasgow score < 15, malignant neoplasm, and aspirative pneumonia were associated with mortality by multivariate

analysis. Local microbiologic data could be of help in tailoring therapeutic guidelines to the microbiologic reality at different settings. The stratification schema and the clinical rule used for hospitalization were useful.

Luna C.M. et al. *Impact of BAL data on the therapy and outcome of ventilator-associated pneumonia*. Chest. 1997; 111(3) : 676-85.p Abstract: STUDY OBJECTIVE: To define the impact of BAL data on the selection of antibiotics and the outcomes of patients with ventilator-associated pneumonia (VAP). DESIGN: Prospective observation and bronchoscopy with BAL, performed within 24 h of establishing a clinical diagnosis of a new episode of hospital-acquired VAP or progression of a prior episode of nosocomial pneumonia (NP). SETTING: A 15-bed medical and surgical ICU. PATIENTS: One hundred thirty-two patients hospitalized for more than 72 h, who were mechanically ventilated and had a new or progressive lung infiltrate plus at least two of the following three clinical criteria for VAP: abnormal temperature (> 38 degrees C or < 35 degrees C), abnormal leukocyte count (> 10,000/mm3 or < 3,000/mm3), purulent bronchial secretions. INTERVENTIONS: Bronchoscopy with BAL within 24 h of establishing a clinical diagnosis of VAP or progression of an infiltrate due to prior VAP or NP. All patients received antibiotics, 107 prior to bronchoscopy and 25 immediately after bronchoscopy. RESULTS: Sixty-five of the 132 patients were BAL positive (BAL[+]), satisfying a microbiologic definition of VAP (> 10(4) cfu/mL), while 67 were BAL negative (BAL[-]). The BAL(+) patients had no differences in mortality, prior antibiotic use, and demographic features when compared with the BAL(-) patients. More of the BAL(+) patients (38/65) satisfied all three clinical criteria of VAP than did BAL(-) patients (24/67) ($p < 0.05$). A total of 50 BAL(+) patients received antibiotic therapy prior to bronchoscopy, and when this prior therapy was adequate (n = 16), as defined by the results of BAL, then mortality was 38%, while if prior therapy was inadequate (n = 34), mortality was 91% ($p < 0.001$), and if no therapy was given (n = 15), mortality was 60%. When therapy changes were made after bronchoscopy, more patients (n = 42) received adequate therapy, but mortality in this group was comparable to mortality among those who continued to receive inadequate therapy (n = 23). A total of 46 of the 65 BAL(+) patients died, with 23 of these deaths occurring during the 48 h after the bronchoscopy, before BAL results were known. When BAL data became available, 37 of the 42 surviving patients received adequate therapy, but their mortality was comparable to the patients who continued to receive inadequate therapy. CONCLUSIONS: Patients with a strong clinical suspicion of VAP have a high mortality rate, regardless of whether BAL cultures confirm the clinical diagnosis of VAP. When adequate antibiotic therapy is initiated very early (ie, before performing bronchoscopy), mortality rate is reduced if this empiric therapy is adequate, compared to when this therapy is inadequate or no therapy is given. If adequate therapy is delayed until bronchoscopy is performed or until BAL results are known, mortality is higher than if it had been given at the time of first establishing a clinical diagnosis of VAP. When patients were changed from inadequate antibiotic therapy to adequate therapy, based on the results of BAL, mortality was comparable to those who continued to receive inadequate therapy. Thus, even if bronchoscopy can accurately define the microbial etiology of VAP, this information becomes available too late to influence survival.

Lund E.S. et al. *[Aminoglycoside treatment II: Dosage regimes at the departments of internal medicine in Denmark]*. Ugeskr Laeger. 1997; 160(1) : 50-2.p Abstract: The aim of this study was to get a general view of the habitual practice of the usage of aminoglycosides in Danish medical departments, regarding choice of drug, dosage regimen and monitoring of drug-related toxicity, as this antimicrobial agent is commonly used in Danish hospitals against severe infections in spite of the potential for nephro- and ototoxicity. The survey, taking place in 1991 and in 1994, showed that gentamicin and netfilmicin were preferred as first choice with an equal frequency in university and county hospital department, whereas in departments in small hospitals gentamicin was preferred twice as often. From 1991 to 1994 the dosage regimen most commonly used had altered from thrice-a-day to once-a-day. Monitoring of serum levels of the drug was performed on all treated patients in fifty-two of the seventy-nine departments questioned. Most of the departments also monitored the kidney function.

Luther J.M. et al. *Utility of bone marrow biopsy for rapid diagnosis of febrile illnesses in patients with human immunodeficiency virus infection*. South Med J. 2000; 93(7) : 692-7.p Abstract: BACKGROUND: Histochemical staining of bone marrow biopsy samples for microorganisms may provide a presumptive diagnosis weeks before culture. METHODS: To identify predictors of histochemical positivity, we reviewed 161 bone marrow biopsies from febrile patients with human immunodeficiency virus (HIV) infection. RESULTS: By multivariate analysis, both hematocrit value <30% and white blood cell count <4,000/mm3 predicted biopsy positivity by culture or staining, but only anemia predicted histochemical stain positivity. Of cases with serum lactate dehydrogenase (LDH) levels >600 U/L, histoplasmosis was diagnosed in 31.6% versus 7.8% with lower LDH levels. Among histoplasmosis cases, staining showed fungi in all, with LDH levels >600 U/L versus 44.4% with lower levels. CONCLUSIONS: Bone marrow biopsy will most likely provide a rapid diagnosis in patients with anemia. Markedly elevated LDH levels suggest stain positivity for Histoplasma capsulatum. Histopathologic patterns may also guide empiric therapy.

Lutters M. et al. *[Antibiotic utilization in a university geriatric hospital and drug formularies]*. Schweiz Med Wochenschr. 1998; 128(7) : 268-71.p Abstract: Inappropriate use of antibiotics needlessly increases drug expenditures, enhances the emergence of antimicrobial resistance in hospitals and heightens the risk of toxicity, especially in elderly patients. This population is very sensitive to inappropriate drug treatment because of pharmacological and pharmacokinetic changes, reduced homeostatic functional reserve, multiple underlying diseases (e.g. renal failure) and polypharmacy (leading to drug interactions and side effects). To assess antibiotic prescription in a geriatric university hospital with a restrictive drug formulary, we analyzed data extracted from the Drug Kardex (a standardized synthesis of all prescribed medicines) during 4 cross-sectional drug utilization studies, carried out in 1996 on all hospitalized patients. RESULTS: 1138 patients' Kardex have been analyzed. 20% of these patients received one or more antibiotic treatments. In total 268 antibiotic treatments (AB) were prescribed, 84 in March, 44 in June, 71 in September and 66 in December. 21 different AB were used, the five most frequently prescribed AB being amoxycillin-clavulanic acid, ceftriaxone, ciprofloxacin, metronidazole, co-trimoxazole and representing 69% of all AB. Most of the AB were given in an oral form (63%) and in one standard dose. Dose adjustments in these very old patients with a high percentage of renal failure were apparently rarely done. The choice of rather broad spectrum AB may be due to the fact that obtaining an appropriate bacteriological culture from elderly patients with respiratory tract infections is difficult, but was also due to a lack of diagnostic subcategorization of the infection. Undesirable effects of the restrictive drug formulary were also noted: large utilization of ciprofloxacine (only fluoroquinolone on the hospital's drug list) for urinary tract infections instead of other more appropriate antibiotics. CONCLUSION: It is important to individualize antibiotic drug therapy with respect to underlying diseases, site of infection and antibiotic sensitivity patterns, especially in elderly patients. Restrictive hospital drug formularies are not sufficient to assure rational drug use, but should be associated with broader educative measures.

Lynch J.P. 3rd et al. *Community-acquired pneumonia*. Curr Opin Pulm Med. 1998; 4(3) : 162-72.p Abstract: Community-acquired pneumonia remains a serious cause of morbidity and mortality, particularly in the elderly or patients with coexisting diseases. Therapeutic strategies are usually empiric, based upon demographic and epidemiologic factors, acuity and severity of illness, comorbidities, and cost constraints. Recent guidelines may be used to discriminate