

### 3. Issues in Antibiotic Usage

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#### Treatment of complicated urinary tract infections or acute pyelonephritis with once-daily Levofloxacin 750 mg for 5 days compared to Ciprofloxacin twice daily for 10 days

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**Background;** Appropriate antibiotic use in urinary tract infections (UTIs) has traditionally been based on choosing an agent that covers the spectrum of suspect organisms. With increasing resistance of urinary pathogens to many antibiotics, pharmacokinetic properties are becoming more important in selecting an appropriate antibacterial. Agents with high antibacterial activity, good bioavailability and predominant renal excretion are advantageous and should be administered at sufficiently high doses to achieve eradication of the pathogens. Levofloxacin is primarily excreted as unchanged drug in the urine, achieving high urine levels that exceed those measured in the serum. Once-daily, levofloxacin 750 mg takes advantage of the concentration-dependent bactericidal activity of the quinolones and it is well-suited for shortening the duration of therapy. It is expected that short-course levofloxacin 750 mg will be an effective therapy for treating UTIs.

**Methods;** Patients with cUTI or AP were randomized to one of six strata, depending on the diagnosis, site of residence, and presence or absence of an in-dwelling catheter to treatment with either IV/oral levofloxacin 750 mg q.d. for 5 days or IV/oral ciprofloxacin 400/500 mg b.i.d. for 10 days. Enrolled patients had to have study entry cultures containing > 10<sup>5</sup> CFU/mL of a uropathogen(s) to remain in the study. Assessments were conducted at: Study Entry (Day 1), End-of-Therapy (Study Day 11 ±1), Posttherapy (Study Days 15-19) and Poststudy (Study Day 38-45). The primary efficacy outcome was microbiologic eradication at the posttherapy visit. Non-inferiority was assessed in the microbiologically evaluable and modified intent-to-treat (mITT) populations.

**Results;** As of January 17, 2006, 988 patients were enrolled at 109 centers: 709 patients had a diagnosis of cUTI and 279 had AP. 53.8% of enrolled patients had a uropathogen at study entry and received at least one dose of study drug (mITT population). The majority of uropathogens were *E. coli*, *K. pneumoniae*, *S. faecalis*, and *P. mirabilis*. Nineteen quinolone-resistant pathogens were isolated from baseline cultures in microbiologically evaluable patients.

**Conclusions;** Final study results will be reported.

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#### Multiple-antibiotic resistance of gram-negative bacteria associated with surgical and urological practice.

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**Objectives:** To determine the antimicrobial susceptibility profile of gram-negative bacteria isolated from patients in surgical and urological clinics; to optimize the antibacterial therapy of gram-negative nosocomial infections.

**Methods:** The gram-negative bacteria isolated from patients in the surgical and urological clinics of Sechenov Moscow Medical Academy in 2005 were analyzed for susceptibility to antibiotics using the disc diffusion method. Minimal inhibitory concentrations (MICs) of ampicillin, ampicillin/sulbactam, cefuroxime, cefoxitin, cefotaxime, ceftazidime, ceftazidime/clavulanate, cefepime, meropenem, aztreonam, gentamicin, amikacin, ciprofloxacin, levofloxacin, doxycycline and co-trimoxazole were determined. Clinical isolates were screened by PCR for the presence of extended-spectrum  $\beta$ -lactamase (ESBL) genes belonging to the TEM, SHV or CTX-M groups.

**Results:** Isolates included 481 strains from the surgical and 314 from the urological clinics. Among these, 34% were Enterobacteriaceae, and 12.5% were nonfermentative bacteria. The main sources of gram-negative bacteria were urine (17%), post-surgical wounds (13.2%) and bile (8.1%). Antibiotic susceptibility profiles of strains isolated in the urological and surgical clinics were similar. Among Enterobacteriaceae, 38.3% were resistant to third-generation cephalosporins but were susceptible to meropenem (MIC<sub>90</sub>)

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#### Effects of mixing program on antibiotic prescribing patterns in a surgical/trauma intensive care unit

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**Introduction:** Antibiotic cycling or rotation of antimicrobial classes has been proposed as one method to combat antimicrobial resistance. However, it is unclear whether the beneficial effects of antibiotic rotation are attributed to cycling or simply the introduction of antibiotic heterogeneity. A prospective cohort study was designed to evaluate the effectiveness of a mixing strategy based on day of the month in maintaining antibiotic heterogeneity over a two year period.

**Materials and Methods:** During the initial two year study period (12/1/01-11/30/03) a quarterly hybrid cycling regimen incorporating four gram-negative agents (ciprofloxacin, meropenem, piperacillin/tazobactam, cefepime) and two gram-positive agents (vancomycin, linezolid) was utilized for the empiric treatment of all infections in a university surgical/trauma intensive care unit (STICU). This was followed by implementation of a mixing protocol (12/1/03-11/30/05) utilizing the same antibiotics whereby day of the month determined the empiric antibiotic agent. Patterns of antibiotic prescription were compared between the two time periods. Results: 2,691 patients were admitted to the STICU during the study period, 1,429 during period 1 (quarterly cycling) and 1,262 during period 2 (mixing). The prescribing patterns between the two periods were significantly different. Of the patients receiving cycling antibiotics during the initial two year period, an average of 69.9% received an on-cycle gram-negative drug and 75% received the on-cycle gram-positive drug per cycle. During the second two year period, the distribution of the four protocol gram-negative agents was 25% for piperacillin/tazobactam, 19% cefepime, 25% meropenem, and 31% ciprofloxacin. The distribution for the two protocol gram-positive agents was 51% for vancomycin and 49% for linezolid. There was no difference in the total usage of any individual protocol drug between the two study periods ( $P > 0.05$ ).

**Conclusion:** Switching from a quarterly cycling regimen to a mixing protocol resulted in significant changes of antibiotic prescription patterns within a university STICU. Implementation of a mixing strategy based on day of the month successfully maintained antibiotic heterogeneity over a period of time without changes in total antibiotic consumption.

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#### Antimicrobial susceptibility patterns and macrolide resistance genotypes of $\beta$ -hemolytic streptococci from various wound specimens during the period of 2003-2004

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**Objectives:** This study evaluated the antimicrobial susceptibilities and macrolide resistance genes of  $\beta$ -hemolytic streptococci isolated from various wound specimens.

**Methods:** The minimal inhibitory concentrations of seven antimicrobials were determined for 101 stocked isolates of  $\beta$ -hemolytic streptococci between January 2003 and December 2004. The organisms were identified by latex agglutination test and API Strep 32 (bioMérieux, Marcy-l'Etoile, France). Resistance genes of erythromycin-resistant isolates were detected by polymerase chain reaction.

**Results:** The overall rates of non-susceptibility to tetracycline, chloramphenicol, erythromycin and clindamycin were 56.5%, 6.9%, 19.8% and 17.8% of the isolates, respectively. Among the  $\beta$ -hemolytic streptococci tested, *Streptococcus agalactiae* showed the highest non-susceptibility to tetracycline (88.9%), erythromycin (59.3%) and clindamycin (63.0%). In contrast, resistance rates of *Streptococcus pyogenes* to tetracycline, erythromycin and clindamycin were 28.6%, 7.1% and 3.6%, respectively. Of 20 erythromycin non-susceptible isolates, eight isolates had cMLS<sub>B</sub> phenotypes (constitutive resistance to macrolide-lincosamide-streptogramin B [MLS<sub>B</sub>]) carrying *erm*(B), and five isolates had M phenotypes with *mef*(A). One *S. agalactiae* had *erm*(B) and *erm*(TR), and one *S. pyogenes* carried *erm*(B), *erm*(TR) and *mef*(A) genes. The other five isolates of *S. agalactiae* showed no resistance genes.

**Conclusion:** Resistance rates to erythromycin and clindamycin in *S. agalactiae* were drastically higher than other  $\beta$ -hemolytic streptococci. Resistance rates of MLS<sub>B</sub> antibiotics were different by serogroup in  $\beta$ -hemolytic streptococci.

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### The role of subcutaneous gentamycin in wound management after ileostomy closure

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**Objectives:** After loop-ileostomy closure subcutaneous wound infection is the most frequent postoperative complication. It seems that preoperative antibiotic prophylaxis such as implantation of local antibiotics, significantly reduce the incidence of postoperative wound infection after different surgical procedures such as elective colorectal surgery, and is a recognized part of surgical management. We know that closure of ileostomy is considered a contaminated operation. The purpose of this study is to determine the effectiveness of a subcutaneous gentamycin-collagen implant to reduce wound infection after ileostomy closure.

**Methods:** we studied on 52 patients were admitted to our hospital for closure of ileostomy. The ileostomies were taken down by the same team using the same surgical technique in their operations. We randomly divided the patients into two groups to evaluate the effectiveness of a subcutaneous gentamycin-collagen implant to reduce wound infection after loop-ileostomy closure. Patients had the same perioperative treatment and standardized anastomotic and closure technique. A collagen sponge with gentamycin was used in group 1 (n=26) and an identical collagen implant without antibiotics was used in the group 2 (n=26).

**Results:** There was no difference between the groups with respect to demographics or in the postoperative course. The total wound infection rate was about 24 percent with no difference between the gentamycin (n=6) and the control group (n=7) (P = 1.0).

**Conclusion:** Using subcutaneous implantation of a gentamycin no clinically relevant reduction of the wound infection rate after loop-ileostomy closure. therefore routine use is not recommended in ileostomy closure.

Key words: gentamycin, ileostomy, infection, wound

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### Timing of surgical antibiotic prophylaxis: compliance with national guidelines in Belgium

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**Objective:** To determine compliance with national consensus recommendations regarding timing of surgical antibiotic prophylaxis in Belgian hospitals.

**Methods:** Data were obtained from the hospitals participating in the national surgical site infection surveillance programme in 2001 to 2003. Fifteen hospitals provided optional detailed data on the use of antibiotic prophylaxis (AP) for the following NNIS surgical procedure categories: colon surgery, herniorrhaphy, hip replacement, laminectomy and vascular surgery. Only standard antibiotic prophylaxis was considered. First dosing within 2 hours before incision and discontinuation of antibiotics within 24 hours after surgery were considered as being in accordance with the national guidelines.

**Results:** For a total of 2552 surgical procedures, 2814 different antibiotics had been administered. Colon surgery (63%) and laminectomy (13%) were the categories where often more than one antibiotic was used. Cefazoline alone or in combination was used in 87% of all procedures. Correct timing of the first dose was found in 79% of procedures, in 15% AP was started at incision and in 3% during surgery. In most cases (81%) AP was discontinued within 24 hours after the procedure, but in 14% it was given until 48 hours and in 5% even more than 48 hours. Both timing of the first dose and duration of AP were in accordance with guidelines in 62% of procedures. Compliance regarding timing and duration of AP varied between hospitals from 100% to 0%.

**Conclusion:** Use of AP in Belgian hospitals was found to be in accordance with the national guidelines with regard to timing of the first dose and duration in about 80% of procedures. More attention should be paid to the timely start of prophylaxis before incision since this is critical to the effectiveness of prophylaxis in the prevention of surgical site infections. Limiting the duration to the recommended period of maximum 24 hours is important to limit emergence of resistance, side effects in the patient and cost.

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### ***In vitro* activity of beta-lactams, polycationic antibiotics, trimethoprim/sulphamethoxazole and fluoroquinolones against isolates of the *Burkholderia cepacia* complex**

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**Objectives:** To determine and compare the *in vitro* activities of seven beta-lactams, four polycationic antibiotics, trimethoprim/sulphamethoxazole and two fluoroquinolones against isolates of the *B. cepacia* complex.

**Methods:** One hundred and forty-two isolates of the *B. cepacia* complex were collected from patients in two Bulgarian University Hospitals during a 10-year period. The prevalent number of strains was found in clinical specimens of patients admitted in surgical intensive care units. The minimum inhibitory concentrations (MICs) of cefotaxime, ceftazidime, imipenem, meropenem, gentamicin, tobramycin, amikacin, polymyxin B, trimethoprim/sulphamethoxazole and ciprofloxacin were determined by the agar dilution method. The *in vitro* activities of piperacillin/tazobactam, cefoperazone/sulbactam, ceftazidime and levofloxacin were evaluated by the disc diffusion method. Both analyses were performed according to guidelines of the Clinical and Laboratory Standards Institute.

**Results:** All strains of *B. cepacia* complex tested were susceptible to piperacillin/tazobactam, cefoperazone/sulbactam, ceftazidime, ceftazidime, ceftazidime, ceftazidime and meropenem. Ceftazidime and meropenem had the lowest MIC values and the narrowest MIC ranges. Ninety-nine percent of the strains were susceptible to levofloxacin, 98% were susceptible to imipenem and 97% were susceptible to cefotaxime, trimethoprim/sulphamethoxazole and ciprofloxacin. All isolates tested were resistant to gentamicin (MIC  $\geq$  16 mg/L), tobramycin (MIC  $\geq$  16 mg/L), amikacin (MIC  $\geq$  64 mg/L) and polymyxin B (MIC > 512 mg/L). Conclusions: Beta-lactams, trimethoprim/sulphamethoxazole and fluoroquinolones demonstrated very good *in vitro* activity against examined strains of *B. cepacia* complex isolated in Bulgaria. Ceftazidime and meropenem could be the drugs of choice for therapy of systemic infections caused by these bacteria. Further *in vivo* clinical studies are necessary in order to evaluate the efficacy of such therapy.

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### **Germ switch under current antibiotic therapy with Linezolid by MRSA-infection**

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**Objectives:** Does the monotherapy with Linezolid is sufficient in MRSA eradication of MRSA infection?

**Material and Method:** Since 2001 in our hospital 67 patients with microbiological evident MRSA infections were treated with Linezolid. Firstly the infections were treated with a surgical procedure. The antibiotic therapy began with the prove of the germ and has been continued until eradication or for a maximum of 28 days, respectively. The success of the antibiotic therapy was monitored through the tissue sampling during surgical revision.

**Results:** In average 19 days were required to erase the MRSA in 55 patients successfully with an accompanying Linezolid application.

However, 6 of these patients showed a changeover from the MRSA to *Pseudomonas aeruginosa* in the operative tissue samples during antibiotic therapy with Linezolid.

Due to that fact an additional corresponding antibiotic therapy was performed.

The last mentioned cases required a treatment duration of in average 12 days until the germ was finally erased.

**Discussion:** Although Linezolid is known as a successful antibiotic in MRSA infections, a monotherapy should remain an exception because of the danger of germ changeover in 10% of all cases.

## 4. Prosthetic Implant Infections

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### Biomaterial-related surgical site infections after open prosthetic mesh repair of inguinal hernias

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**Background:** For the last two decades open prosthetic repair has been the gold standard for the treatment of inguinal hernias throughout the world. It has reduced recurrence rates after hernia surgery but mesh repair also induced other problems. The most important is possibility of biomaterial-related surgical site infections (SSI). The aim of this study was to present the results of our over ten-years' experience with usage of non-absorbable polypropylene mesh in inguinal hernia surgery.

**Methods:** From November 1995 to April 2006, in our clinic 430 patients underwent elective inguinal hernia surgery with usage of polypropylene mesh. We followed the "mesh-plug" procedure applied by Ira M. Rutkow. Antibiotic prophylaxis (1g of cephazoline i.v.) was administered. The skin was saved immediately before surgery and prepared with povidone scrub. During hospitalisation, wounds in all patients were examined daily by a staff surgeon. Sutures were removed 6-9 days after surgery. The follow-up visits took place 6 weeks, 3 and 6 months and finally 1 year after operation. Wound infections were categorized by using definitions established by the Centres for Disease Control and Prevention. Mesh-related but non-infectious complications like seroma, were excluded from this study.

**Results:** 21 superficial wound infections were reported (4,9%). Infections were identified on the basis of clinical criteria and sometimes confirmed by positive culture from the wound. The usual causative organism was *Staphylococcus aureus*. Deep SSIs involving biomaterial were recognized in 4 cases (0,9%). 3 of these cases manifested as abscesses in the groin region and one as a discharging fistula, which required surgical revision.

**Conclusions:** The results of our study suggests that usage of foreign material can promote inflammation and increase susceptibility to surgical site infection.

**First report of a total knee arthroplasty (TKA) - periprosthetic infection with *Bacillus cereus* - Successful treatment with debridement and implant retention**

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**Objectives:** According to current guidelines early prosthetic joint infections can be successfully treated with debridement and retention of the prosthesis in a number of carefully selected patients using long-term oral antibiotics (N Engl J Med 2004; 351:1645-54 and CID 2006; 42:471-8). Experienced multidisciplinary teams achieve success rates of over 80 % in patients with staphylococcal or streptococcal infections. However, management of early TKA-infections caused by rare pathogens is often unclear due to the scarcity of published reports. Case reports on the individual management and outcome of such infections can guide the clinician in difficult treatment decisions. We therefore discuss management and outcome in a patient with an early TKA-infection caused by *B. cereus*. To our knowledge this is the first report of a clearly documented prosthetic joint infection caused by this pathogen.

**Patient and Methods:** A 69-year old otherwise healthy male patient with left sided gonarthrosis was treated with an Innex®-TKA using standard techniques, laminar airflow environment and perioperative prophylaxis with cefuroxime (Zinacef®). For the tibial component Palacos® bone cement was used, while the femoral component was implanted without cement. On the second postoperative day a haematoma was evacuated and on day 7 open revision due to purulent haematoma with radical debridement and lavage was performed. The patient was febrile (38.4 C) and a rise of CRP to 290 mg/l (<5 mg/l) was noticed.

**Results:** A preoperative joint aspirate and 3 of 4 intraoperative tissue specimens showed growth of *B. cereus*. Identification was done using biochemical methods (Manual Clin Microbiol, ASM 2006). Susceptibility to antimicrobial agents was performed by E-testing (MIC). Resistance was observed for clindamycin and all betalactam antibiotics except imipenem (0.094 mg/l) whereas ciprofloxacin (0.125 mg/l), cotrimoxazol (2.5 mg/l) and teicoplanin (3 mg/l) were active. On the 1. and 2. postoperative day iv flucloxacillin and po rifampin were given empirically followed by iv imipenem (Tienam®) 500 mg q 6h for 2 weeks. At that time local and systemic symptoms improved (CRP 8.9 mg/l) and oral ciprofloxacin (Ciproxin®) 750 mg q 12 h was given for 6 months. At the end of treatment and 4 months later clinical and radiographic assessment and values for CRP and sedimentation rate were all normal.

**Conclusion:** We report the first TKA - periprosthetic infection caused by *B. cereus* and its successful treatment with debridement and retention of the implant. The follow up is currently 10 months and ongoing.

### **Etiology, incidence and antibiotic resistance markers in bacterial infections occurred in Romanian hospitalized patients with cardiovascular prosthetic devices**

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The purpose of this work was to investigate the incidence, aetiology and antibioresistance features of bacterial infections occurred in patients with cardiovascular prosthetic devices.

**Material and methods;** The study was carried out at the Institute for Cardiovascular Diseases C.C. Iliescu, Bucharest, Romania during 2003 -2005 on a total number of 676 (464 Gram-positive and 212 Gram-negative) bacterial strains.

**Results;** The most frequent Gram-positive strains were staphylococci mainly isolated from nasal exudates, surgical wounds and blood cultures followed by enterococci isolated with lower frequency from urine cultures. Out of the 138 *S. aureus* strains, 31 were methicillin resistant (MRSA). The MRSA strains were concomitantly resistant to erythromycin (23), quinolones (18), rifampicine (12), aminoglycosides (7) and sensitive to doxycycline, tetracycline, imipenem. The most resistant MRSA strains were isolated from surgical wounds, blood cultures and tracheo-bronchical secretions. The *Enterococcus faecium* /*faecalis* were resistant to quinolones (6). It is to be noticed that two vancomycin resistant *Enterococcus faecalis* strains were recently isolated in our hospital from stool cultures. The most prevalent Gram-negative strains were enterobacteria mostly isolated from urine cultures while Gram-negative, non-enteric bacilli were less frequently isolated from surgical wounds and blood cultures. Out of the 164 enterobacterial tested strains, 104 were beta-lactamase producers inactivating ampicillin, 46 were producing extended spectrum beta-lactamases and 37 an inhibitor resistant beta-lactamase. The enterobacterial strains exhibited also high resistance rates to quinolones (56) and sulphametoxazole (67). The enterobacterial strains preserved their sensitivity to carbapenems and aminoglycosides. Gram-negative, non-enteric bacilli, *Acinetobacter* proved to be much more resistant than *Pseudomonas* strains, exhibiting high resistance rates to all tested antibiotics, excepting imipenem. The *Pseudomonas* strains exhibited high resistance rates to the 3rd generation cephalosporins (cephtriaxone/ceftazidime), quinolones, amikacine, and were sensitive to cefsulodine, imipenem and sulfametoxazole.

**Conclusion;** The present study highlighted a large spectrum of microbial strains implicated in the etiology of bacterial infections occurred in hospitalized patients with cardiovascular prosthetic devices exhibiting high antibioresistance rates.

### **The effect of the type of intraperitoneally implanted prosthetic mesh on the systemic inflammatory response**

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**Background:** The purpose of this study was to investigate the alterations of the systemic inflammatory response after the intraperitoneal implantation of 3 different types of polypropylene mesh in an experimental setting.

**Methods:** Thirty-two male New Zealand rabbits underwent a 6-cm midline incision and opening of the peritoneal cavity. The animals were randomly divided into four groups: group A (n=8): intraperitoneal placement of polypropylene mesh (Bardβ mesh); group B (n=8): intraperitoneal placement of titanium-coated polypropylene mesh (Ti-Meshβ); group C (n=8): intraperitoneal placement of composite (polypropylene + e-PTFE) mesh (Composixβ mesh); group D (n=8): sham operation (control group). After the mesh implantation, the abdominal walls were closed without tension. Blood was sampled preoperatively (time 0) and at 6, 24, 48 and 168 hours postoperatively to measure white blood cell count (WBC), tumor necrosis factor alpha (TNF-α) and malondialdehyde (MDA). TNF-α was estimated by a bioassay and MDA by the thiobarbiturate assay and passage through HPLC.

**Results:** Statistically significant elevations of the values of WBC, TNF-α and MDA were observed in all four groups at 6, 24 and 48 hours postoperatively, in comparison to their preoperative values (pConclusion: Intraperitoneal mesh implantation induces mild systemic inflammatory response, which is independent from the type of implanted mesh.

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### Prevalence and characterization of ESBLs produced in Enterobacteriaceae strains isolated from patients with cardiovascular prosthetic devices in a Romanian hospital

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**Objective:** to determine the prevalence and characterize ESBLs produced in enterobacteriaceae isolated from patients with cardiovascular prosthetic implants hospitalized in a Romanian institution.

**Material and methods;** Previous study carried out at the Institute for Cardiovascular Diseases 'C.C. Iliescu' between 2003 -2005, aimed to study the prevalence of enterobacteria on a total number of 676 bacterial strains tested. All Enterobacteriaceae strains were screened for ESBL production, on the basis of a positive double-disk synergy test or positive ceftazidime and cefotaxime clavulanic combination discs tests. Only one strain of each species were evaluated per patient. Isoelectrofocusing (IEF) and PCR for blaTEM and blaSHV genes were used to confirm ESBL-production. When IEF and PCR indicated concordant results, final identification of ESBLs was obtained by sequence analysis of PCR products. Pulsed-Field Gel Electrophoresis (PFGE) was used to delineate clonal relationships between strains of the same species recovered from different patients and showing identical ESBL profiles.

**Results;** Among 164 enterobacterial tested strains, 104 were beta-lactamase producers inactivating ampicillin, 37 are producing an inhibitor resistant beta-lactamase and 46 ESBLs [*Escherichia coli* (n=16), *Klebsiella pneumoniae* (n= 18), *Klebsiella oxytoca*, *Proteus mirabilis* and *Enterobacter cloacae* (n= 4 each). *K.pneumoniae* and *E.coli* represented 39% and 35% of ESBL-producing strains, respectively. IEF and PCR confirmed the presence of ESBLs in 40 (86%) of strains, 28 strains exhibiting both blaSHV and blaTEM genes and 12 strains only blaTEM gene. PFGE analysis revealed the absence of any clonal relationship between strains.

**Conclusion;** This study illustrates the diversity of type of ESBLs produced by a wide range species among Enterobacteriaceae implicated in the etiology of bacterial infections occurred in hospitalized patients with cardiovascular prosthetic devices, including the rising proportion of ESBL producing *K.pneumoniae* and *E.coli* strains. The large clonal variability between the majority of strains was also delineated.

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### The clinical peculiarities and microbiology of the prosthetic valve endocarditis

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**Objectives:** We sought to study the clinical peculiarities and microbiology of the prosthetic valve endocarditis (PVE).

**Methods:** Between 2001 and 2006, 64 patients with infective endocarditis were operated. Perioperative testing was included preoperative blood cultures estimation, intraoperative microbiology (excised valve or valve prosthesis, infected thrombi) in addition to physical examination, echocardiography and laboratory testing. Microorganism isolates were identified using test samples (Becton Dickinson "Crystal", Oxford, UK) and tested for susceptibility by disk diffusion method on Muller-Hinton agar.

**Results:** In the analyzed group 7.8% of the patients were with PVE (mean age 43.6± 3.6 years, 60% males, term after surgery was 6-178 months). All cases were associated with prosthetic valve dysfunction including significant perivalvular leaks (40%) and mechanical obstruction (60%), thus all patients were valve re-operated, in 60% of cases - urgently. PVE was microbiologically proven in 80% of patients. *Staphylococcus* spp. was the causative microorganism in all cases: found in blood (60%), in excised valve prosthesis (40%). The isolation of the causative agent both in blood and in intraoperative material was found only in 1 case. All of the isolates were methicillin-resistant. Antibiotic treatment was performed in accordance to the results of microbiological testing and found to be successful in all cases. But we found new resistance of the causative microorganism during the treatment. So, MRSA isolated from the blood during adequate treatment with vancomycin (2 g per day) with positive effect 5 day latter acquired vancomycin-resistance with new wave of fever, thus we were forced to administrate linezolid (1.2 g per day).

**Conclusion:** *Staphylococci* are the important causative agents of PVE. Thus it is necessary to predict and treat staphylococcal infections and to include the drugs with antistaphylococcal activity in modified antibiotic prophylaxis regimens for patients with prosthetic valves.

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### Mesh infection after incisional hernia repair- personal experience

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**Objectives:** The incidence of incisional hernia after previous operation in the abdomen varies, from 3.8-11.5%. In 90% of cases they occur during the first 3 years after operation. Due to high recurrence rate after conventional repairs (Mayo- repair, direct suture), after the year 1999 we started to use prosthetic material for the repair of large incisional hernias.

The aim of this study is to show our experience with mesh infection after repair of incisional hernia.

**Methods:** At Clinic of Surgery, Clinical Center Nis, from 1999- 2005 we have operated 110 patients with incisional hernias using mesh repair (Rives- Stoppa, Trabucco, Chevrel), ASA (I, II and III). The mean age of patients was 65 (28-74 years). There were 36 men (32.73%) and 74 women (67.27%). All operations were done under general anesthesia. We have analyzed the correlation between size of the defect and occurrence of infection and its microbiological cause.

**Results:** Majority of patient received preoperative one-shot prophylaxis. Average was 8.5 days (2-45). 64.55% of cases we have used 1-2 drains, which were extracted after 2-5 days. The rate of infection was 8.18% (9 patients) caused with: Staphylococcus aureus, Proteus mirabilis, Ech. colli, Bacterioides fragilis. All of infections occurred among abdominal wall defects that were larger then 10 cm. In those cases we were obliged to use large size meshes. Infections were treated with antibiotics and daily wound care. In 2 cases (1.81%) the mesh was extracted.

**Conclusion:** Tissue trauma, duration of operation as well as mesh size, increase the risk of infection. Infections were caused by intrahospital species. Taking all of this into consideration we could conclude that laparoscopic repair is superior to open repair.

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### Hyperbaric oxygen (HBO) treatment of infections after spine deformity surgery in children

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**Objectives:** Hyperbaric Oxygen (HBO) therapy has the potential to correct hypoxia, improve tissue perfusion, stimulate tissue repair and enhance leukocyte bacterial killing capacity. We have previously (Larsson et al. Neurosurgery 2002;50:287-296) reported the clinical usefulness of HBO treatment as an alternative to the traditional neurosurgical procedures in 39 consecutive adult patients with postoperative infections. Continued good results have been seen in an additional series of 122 consecutive patients with a wider range of severe and complex cranial and spinal infections, including 31 patients with brain/spinal abscesses. We present a subgroup of children with postoperative infections after spine deformity surgery.

**Methods:** Since 2003, five postoperative deep infections after major spine deformity surgery were treated with HBO. The age of the patients varied from 1 to 17 years. Their deformities were neuromuscular or congenital with intra- and extradural anomalies. All cases except one had gone through several spine surgeries with postoperative infections earlier and had chronic urinary tract infections. The time of the current surgery varied from 120 to 860 minutes, and the relative bleeding from 10 to 62 % of the calculated blood volume. 4/5 patients had combined neuro- and orthopedic surgery in the same séance. They were all treated in Sechrist monoplace chambers, initially 2,8 bar twice a day, with a range of 12 - 87 sessions. A member of the HBO staff or a parent often accompanied the younger children in the chamber. Early "prophylactic" HBO treatment was given in two additional cases with a similar medical history. Evaluation was performed through medical charts and clinical examinations.

**Results:** All seven patients reached infection control and healing with implants retained and without major revision surgery. No major side effects were seen. All were without antibiotics at 6 months follow-up. No recurrence of infection has occurred so far.

**Conclusions:** HBO treatment offers a powerful cure for post-operative infections also in pediatric spine patients.

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## Hyperbaric oxygen (HBO) treatment of neurosurgical infections

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**Objectives:** HBO has the potential to correct hypoxia, improve tissue perfusion, stimulate tissue repair and enhance leukocyte bacterial killing capacity. We have previously (Larsson et al. Neurosurgery 2002;50:287-296) reported the clinical usefulness of HBO treatment as an alternative to the traditional neurosurgical procedures. Golden standard involves removal of bone flap or foreign material in the presence of infection.

**Methods:** We have 1996-march 2006 treated 151 consecutive patients, admitted to the hyperbaric unit. 39 patients have previously been reported ( Neurosurgery 2002;50:287-296). Another 42 patients have been followed for a minimum of 6 months after HBO treatment series. The remaining 70 patients are yet to be evaluated.

**Results:** As previously reported (Larsson 2002) HBO improved outcomes, reduced the need for reoperations, and allowed infection control, especially in complex situations. In this new evaluated material ( n=42), a wider range of severe and complex cranial and spinal infections has been treated, including 9 cerebral infections/ brain abscesses/ empyemas. One patient died in tumor recurrence before evaluation. Continued successful results (infection control and healing without removal of bone flaps or foreign material) were achieved.

**Conclusion:** We conclude that HBO treatment offers a powerful cure for many complicated cranial and spinal infectious problems. It can be an alternative / adjunct to standard surgical procedures and help resolve complicated neurosurgical infections where no simple solution exists.

## 5. Intraabdominal Infections

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### Fibrin sealant prevents gastrointestinal dehiscence in intra-abdominal sepsis

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**Objectives:** The intraoperative use of fibrin sealant has been used prophylactically to prevent formation of gastrointestinal fistulas. We recognized the potential use of fibrin glue as a therapeutic modality for successful resolution of gastrointestinal anastomotic dehiscence in septic surgery.

**Methods:** 56 patients (38 male and 18 female) suffering from intra-abdominal sepsis were subjected to prophylactic appliance of fibrin sealant in intra-abdominal septic surgery with immediately primary anastomosis. Indications were acute generalized peritonitis in 49 patients (traumatic intestinal rupture in 11, traumatic duodenal rupture in 9, appendicitis in 4, bowel obstruction in 4, colorectal carcinoma in 4, cholelithiasis in 3, uterine cervix cancer in 2, Esophagogastric devascularization in 2, and ulcerative colitis, duodenal bulb ulcerative perforation, pelvic inflammation, gastric carcinoma, uterine-incision delivery, dilatation and curettage, traumatic splenic rupture, traumatic pancreatic collapse, hepatocarcinoma, mesenteric venous thrombosis in the remainder), chronic peritoneal abscess in 5 (spontaneous intestinal perforation of Crohn's disease in 2, and bowel obstruction, intestinal tuberculosis, appendiceal abscess in the remainder), and retroperitoneal abscess in 2 (traumatic colonic fistula and parapancreatic abscess due to acute severe pancreatitis).

**Results:** Of the 56 patients, the modus operandi contained intestinal resection and anastomosis in 30 cases, ileal-colostomy in 11, intestinal wedge resection in 8, gastrojejunostomy in 4, bilio-jejunostomy in 2, and pancrea-jejunostomy in the remainder. 48 of the 56 patients recovered smoothly without complications from intraperitoneal application of fibrin sealant. Anastomotic leakage occurred in 5 patients, one case was well controlled by conservative treatment, one case received a late definitive operation, the other 3 patients died due to the leakage complication in hospital. Another three patients with widespread metastasis were noted and received no special treatment up to late death during post-discharge. The total surgical related achievement ratio was 87.5% for the diversionary operation with fibrin sealant in intra-abdominal sepsis. The hospital days were 45.6±28.4 days. There has been no sign of recurrence over a follow-up period of 1-15months (average 4.6 months).

**Conclusions:** Fibrin sealant may be useful in preventing gastrointestinal dehiscence and promoting healing of the "high risk" anastomosis during intra-abdominal septic surgery.

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### **Inguinal hernia or Emphysematous pyelonephritis: report of two cases and review of the literature**

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**Objectives:** Emphysematous pyelonephritis is a necrotizing renal infection, which is diabetes mellitus related in almost all cases. These gaseous lesions can be localized in the renal parenchyma or in the perirenal or retroperitoneal space. Diagnosis became easier with the advent of CT scan. Treatment usually requires surgery and antibiotics. It is life threatening and has a high mortality rates despite aggressive management. We expose with two cases giving especial importance to clinical diagnose as treatment and evaluation. We also make a literature review trying to understand this entity and find pathways for its therapeutic management.

**Methods:** A 67-year-old man with diabetes mellitus was hospitalized for left inguinal herniotomy .he had a previous history of non specific abdominal pain and low grade fever and shivering from 1 year ago. Aspiration on inguinal bulging showed purulent liquid and a 29-year-old man without history of diabetes mellitus had flank pain and fever. 1 week after receiving wide-spread antibiotics he found right incarcerated inguinal hernia sings. He underwent inguinal operation. During the surgery purulent liquid drained from inguinal incision.

**Results:** The CT scan of both showed gaseous infection and hydronephrosis in involved kidneys with a perirenal inflammatory infiltrate and gas in the retroperitoneal space. The men underwent suitable treatment with antibiotics and drainage.

**Conclusion:** Emphysematous pyelonephritis is a serious infective disease. The condition is observed mostly in patients with diabetes mellitus or obstruction of the urinary tract. The most important thing in management is a high diagnostic suspicious and also a rapid treatment, percutaneous drainage and, if necessary, nephrectomy is paramount in the treatment based on immediate hemodynamic and antibiotic medical support, due to its serious prognosis such as is described in the literature In patients suspected of emphysematous pyelonephritis, computed tomography scan should be done promptly before any abdominal wall or abdominal cavity operation.

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### **Anterior sacral meningocele causing meningitis due to anal fistula**

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Anterior sacral meningocele is a rare type of spinal dysraphism causing a thecal herniation through bone defect in anterior sacral wall. If not complicated patients generally complains of chronic constipation and urinary complaints. In our case we overwiewed this rare pathology complicated with anal fistulisation of an anterior meningocele resulting with intractable severe meningitis. A 44 years old female patient presented to emergency with complaints of headache nausea and vomiting. She was hospitased by neurology department with the diagnosis of meningitis and intravenous meropenem, teicoplanin and acyclovir was started but in cranio-sacral computerised tomography which is performed due to urinary incontinance and paraparesis revealed hydrocephaly, pneumocephaly, meningoencephaly and anterior sacral meningocele. Patient is consulted to general surgery department on the 3rd day of medical treatment due to seropurulent discharge from anus. On anal examination there was a fistula orifice on posterior anal wall 2 cm's proximal to anus from where watery-purulent discharge was coming out. This orifice is catheterised and fistulography is performed with fluroscopy and the connection between the meningocele and the anal fistula is shown. As neurosurgery department decided that definitive surgical operation for the patient was too risky under these circumstances we decided to cease the connection between central nervous system and anal canal. Patient is operated by posterior sacral approach ; the fistula tract is dissected and repaired.

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### **Bacterial isolates from acute cholecystitis cases**

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**Objectives:** The aim of this study to detect bacterial isolates in patients admitted to Afyon Kocatepe University ANS hospital with acute complicated cholecystitis and underwent surgery.

**Methods:** After two days follow up, patients with persistent symptoms and fever were operated. Bile cultures were collected during operation, and immediately sent to Microbiology laboratory. Bacterial isolation and identification were performed by routine microbiologic methods and API Systems.

**Results:** A total of 27 cases ( 14 male and 13 female) were investigated between September 2003 - March 2006. Of 16 patients, bile culture positivity was found. E.coli was the most common isolated bacteria (5/16), and gram (-) bacilli such as Klebsiella, Enterobacter and Serratia were growth on cultures. Also five gram(+) cocci including four Enterococ were detected.

**Conclusion:** Although bile cultures are positive for bacteria in 50-75% of cases, cholecystitis is defined as inflammation of the gallbladder occurred by obstruction and bacterial proliferation may be a result of cholecystitis. However in complicated cholecystitis, bacterial growth is a prognostic factor affecting morbidity and mortality. Therefore , for appropriate medical approach, it would be useful to be aware the spectrum of bacterial pathogens.

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### **Factors influencing adequacy of surgical source control in large international multicenter trials of an anti-infective in complicated abdominal infections**

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**Introduction:** The provision of adequate surgical source control for established infections is a cornerstone of therapy. Large clinical studies present unique problems for assessing adequacy of source control, which has led to considerable variability in assessments. For studies evaluating anti-infectives, inadequate source control may adversely impact study outcome. The purpose of this study was to evaluate factors that influence adequacy of surgical source control in the context of large international multi-center trials of an anti-infective in complicated abdominal infections.

**Methods:** Patients enrolled in studies evaluating the safety and efficacy of Tigecycline for complicated abdominal infections were evaluated for adequacy of surgical source control. Evaluation was performed on blinded review forms that included demographics, operative and percutaneous procedures, subsequent procedures, location and type of infection, primary surgeon's assessment of adequacy, and outcome. Source control evaluation reviews were performed by at least 2 surgeons with expertise in abdominal surgical infections. Data were analyzed by the 2-sided Fisher's Exact Test or by the Generalized Cochran-Mantel-Haenszel Test (ANOVA statistic) as appropriate with significance at the p.

**Results:** Two hundred and forty two patients were reviewed, 42 (17.4%) received inadequate surgical source control. Age, gender, and APACHE II score were not associated with increased risk for inadequate source control. Surgeon's assessment of extent of residual contamination was significantly associated with risk of inadequate source control (no residual contamination: 6% inadequate source control, minimal residual: 21%, moderate residual: 24%, extensive residual: 40%, p=0.01). Type of infection was also significantly associated with risk for inadequate source control (cholecystitis: 7%, appendicitis: 10%, perforated viscus: 22%, diverticulitis: 27%, and abdominal abscess: 48%, p

**Conclusion:** When an experienced surgical review is performed, inadequate surgical source control occurs frequently in the context of large anti-infective trials for complicated abdominal infections. Type of infection and primary surgeon's assessment were the primary factors associated with inadequate surgical source control. Large international multicenter trials of anti-infectives for treatment of complicated abdominal infections should have these findings considered in their study design.

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### Hyperbaric oxygen (HBO) treatment of severe intra-abdominal infections and complications in children

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**Objectives:** Infected and inflamed tissues have an impaired microcirculation and increased O<sub>2</sub>-consumption. This results in hypoxia with an impaired infection defence and wound repair. We use hyperbaric oxygen (HBO) for hypoxic conditions with acute or refractory infections and wound healing problems. Severe and widespread abdominal infection is a feared complication after surgery.

The Karolinska multidisciplinary protocol for severe soft tissue infections including active and repeated diagnostics, surgical intervention, antibiotics and HBO has now been used in four critically ill children.

**Methods:** We report four consecutive cases of life threatening abdominal infections in children treated in the ICU with an open abdomen and ventilator support. They received HBO-therapy (initially at 2.8 bar absolute, twice daily) with 41, 20, 93 and 23 sessions respectively. Indications for HBO (boy 10 y.o.) pancreatitis and refractory infection with multi-resistant micro-organisms: KNS and Pseudomonas spp. treated locally with acetic acid instillation, with complications such as multiple central vein thrombosis, repeated sepsis episodes and more than 8 months hospitalization, (boy 6 y.o.) intestinal ischemia/infection after operation for oesophageal atresia, (boy 4 y.o.) ischemia-reperfusion injury/ infection after colon surgery and (boy 10 m.o.) septic shock and multiorgan failure following colonic resection for pseudo membranous colitis (clostridium difficile and cystic fibrosis).

**Results:** After achieving infection control, all four cases healed and are fully rehabilitated. One patient (boy 4 y.o.) had an early recurrence (multiple abscesses, partially drained spontaneously through the abdominal suture line), which was treated conservatively with HBO in an additional series with good end result. Follow-up after completed HBO was 35, 32, 17 and 3 months respectively. No major side effects with HBO were seen.

**Conclusions:** Our four patients have clinically turned over into success due to a multidisciplinary approach & cooperation including the use of HBO. We recommend that HBO is considered in clinical praxis in similar cases.

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### Concordance of inter-rater assessments of source control in intra-abdominal infection

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**Objectives:** Accurate assessment of the role of antimicrobial therapy in the outcome of clinical trials for intra-abdominal infection depends on adequacy of source control. Surgical judgment, a key factor in source control, was analyzed for consistency of inter-rater agreement.

**Methods:** 262 patients who had failed treatment of intra-abdominal infection were selected from the 1642 modified intent-to-treat patients randomized in two trials of tigecycline versus imipenem. Both double blind trials had similar study design and methodology. The pooled analysis of the two trials demonstrated comparable efficacy of tigecycline to imipenem for complicated intra-abdominal infections, 86.17% versus 86.23% respectively in the microbiologically evaluable group. (CID 2005: 41; S354-S367). Adequacy of source control was evaluated by two independent surgeons who were not the same for each subject. Reviewers were provided copies of original consultations, operative, imaging, and pathology reports, progress notes and selected case report form pages. They were blind to antimicrobial regimen and identity of institution and surgeon. Concordance between reviewers was calculated by the kappa and Z statistics, measures of inter-rater agreement, for age, sex, APACHE II scores, residual contamination and diagnosis.

**Results:** Overall inter-rater agreement was greater than chance for patients with intra-abdominal infection. However, inter-rater agreement was not greater than chance for patients over 75 years (p=0.146), for APACHE II scores >15 (p=0.356), when residual contamination was stated as "extensive" by the operating surgeon (p=0.944) and for patients with diffuse peritonitis (p=0.979). Inter-rater agreement was highest for acute cholecystitis (pConclusion: Inter-rater agreement on the adequacy of surgical method for source control, while significantly greater than chance for patients with intra-abdominal infection, showed no concordance in evaluation of elderly patients who had diffuse peritonitis, residual gross contamination after intervention, or high severity of illness scores. This finding may be important to future design of clinical trials of antimicrobial efficacy for intra abdominal infection.

## 6. Fungal Infections

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### Osteomyelitis in an immunocompetent patient: first proven case by *Scedosporium aurantiacum*

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**Introduction:** Bacterial infections are a well known complication following traumatic amputations. In cases with contact with soil or water contaminated with manure, one must also be aware of infections with fungi, particularly *Scedosporium* species. Here we describe a patient with an infection with a recently described *Scedosporium* species, *S. aurantiacum*.

**Case report:** A 36 year old man, without medical history, had an entrapment trauma of his leg in an agricultural machine, resulting in a traumatic amputation just below the knee level and contamination of the wound with manure. Given the extensive soft tissue damage, a patella preserving guillotine amputation and extensive debridement was performed. On the second postoperative day another debridement was done for progressive necrosis of the soft tissue. Thereafter the wound granulated well and could be closed by a split skin graft, 3 weeks after the trauma. Six weeks after the accident the patient developed a phlegmone. Cultures of the wound revealed *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The patient was treated with ciprofloxacin and clindamycin. Within days, the symptoms of infection disappeared, yet a 6 centimetre deep fistula became present in the amputation stump. Roentgenographs demonstrated an osteomyelitis of the distal part of the femur. The infected part was removed, 10 weeks after the trauma. A subcutaneous pocket and the bone marrow was filled with gentamicin beads. Cultures of the removed bone segment revealed a pure culture of a *Scedosporium* species, with a MIC value of 1 mg/L for voriconazole. By use of DNA sequencing of the Internal Transcribed Spacer 1 (ITS1) region of the nuclear rDNA, the fungus was identified as *S. aurantiacum*. One month later, the patient was re-operated because of a persisting fistula. An abscess was found. The wound was drenched in polyhexamethyleenbiguanide 0.2%, a disinfectant with antifungal activity, for four minutes. Gentamicin beads were replaced. Finally, the defect was covered with a vacuum assisted closure system. Clindamycin, ciprofloxacin and voriconazole was started post-operatively. Voriconazol was continued for 3 months. A per-operatively taken culture showed only growth of *S. aureus*. At the last control 8,5 months after the trauma and 2 months after cessation of the antimicrobial agents, the patient had no signs of infection on roentgenographs and had normal CRP values.

**Conclusion:** As far to our knowledge, this is the first described patient with an osteomyelitis with *S. aurantiacum*. It may be that surgery alone was enough as treatment in this immunocompetent patient, because a culture taken one month after the first operation for osteomyelitis was negative. Since in the literature ongoing infection and dissemination has been described in immunocompetent patients following osteomyelitis with *Scedosporium* species, we choose to treat the patient also with voriconazol.

## 7. Infections in Intensive Care

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### An outbreak in an intensive care unit with an ESBL strain of Escherichia coli

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**Objectives:** Description of one of the first documented outbreaks in a Norwegian intensive care unit (ICU) with a strain of extended-spectrum-beta-lactamase (ESBL) of E. coli.

**Methods:** Pus and bronchoalveolar lavage (BAL) from two males born 1947 and 1939 (hospitalized with conditions in the GI tract in March 2006) were cultivated on blood, chocolate, Sabouraud and lactose agar. Our algorithm is to test the susceptibility with the disk diffusion method, plus E-test® for ESBL identification.

**Results:** From both patients E. coli with ESBL properties were identified. The antibiogramme was identical: Imipenem: Susceptible.

Trimethoprim-sulpha, gentamicin, ciprofloxacin, aztreonam and beta-lactam antibiotics, including ampicillin, cefuroxime, ceftazidime, cefotaxime and ceftazidime: Resistant. Standard E-test panel for ESBL identification comprising: cefotaxime and cefotaxime + clavulanic acid: 16/0.25 and ceftazidime/ceftazidime+ clavulanic acid: 32/0.38. This is compatible with an ESBL profile. There was no growth of obligate anaerobic bacteria.

**Discussion:** Both our patients shared the same room in SIHF. Both had been subject to bronchoscopy. One of the patients had ESBL in his pus as well as BAL. The other had ESBL in BAL only. One patient had been hospitalized in Sri Lanka in 2005. The exact mode of transmission is unknown. It may be that the bronchoscope might have colonized in one patient originally without ESBL after the bronchoscope had been used in connection with a patient already colonized with ESBL; this due to insufficient disease control precautions. It may also be possible that pus containing ESBL colonized the second patient, due to the first patient having profuse secretion. Other explanations are also being investigated.

**Conclusion:** Both strains will be reference tested to elucidate the exact ESBL pattern. Testing will aim to establish whether both strains are identical or if they differ. This case story highlights the need for vigilance concerning infectious disease control in ICUs as well as good monitoring when it comes to resistance patterns, including ESBL.

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### Evaluation of mortality causes in pediatric surgery department of Tabriz Children Hospital (1998-2003)

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**Objectives:** the aim of this study is observation surgery department mortality in infants (less than 2 month's age) to determine of common causes and to find a way for reducing of them.

**Materials:** this study was descriptive cross sectional. From 1997-2003, all documents of 162 dead and less than 2 months patients were studied, after reading the files all information of them were gathered and analyzed.

**Results:** there were 162 patients. 16.25% of patients have been died before the surgery. 1.25% during the surgery and 82.5% after the surgery. The most common anomalies were esophageal atresia in 34% of patients followed by jejune ileal atresia in 10% of patients. The most important complication before the surgery was aspiration pneumonia (34%) and sepsis (28%) and after the surgery was sepsis (41%) and nosocomial infection (28%).

**Conclusion:** congenital anomalies in surgery department are the most common cause of mortality in less than 2 month's age patients. After operation the main challenging for patients is fighting against the infection. better and standard performance of essential cares in ward, attention to sterilization on time and suitable antibiotics therapy, more attention and to patients and ward condition may help to decrease the rate of mortality

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### **Nosocomial infections caused by bacteria from the *Burkholderia cepacia* complex (Bcc) in patients admitted in intensive care units (ICUs)**

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**Objectives:** To investigate risk factors for the emergence of nosocomial Bcc infections in ICU patients.

**Methods:** One hundred and eighteen ICU patients in a Bulgarian University Hospital were studied retrospectively. All had nosocomial Bcc infections, according to definitions of the Centers for Disease Control and Prevention. The following were registered as putative risk factors for acquiring the bacteria in the hospital settings: demographic information; length of ICU stay; diagnosis on admission, pre-existing co-morbidities, neutropenia; invasive diagnostic and therapeutic procedures, indwelling devices; prescription of antimicrobial, corticosteroid or cytotoxic therapy before the onset of infection.

**Results:** Patients aged from 7 days to 78 years. Two thirds were male. The most frequent diagnosis was surgical and 87.3% of patients were admitted to surgical ICUs. These included 14 patients with diabetes mellitus; no patients had cystic fibrosis, chronic granulomatous disease or neutropenia. The prevalent invasive procedures were operation and transfusion of blood products. Intravenous catheters were in place in 99.2% (85 patients with central lines, 47 patients with peripheral lines and 15 patients with both central and peripheral lines) and urinary catheters in 58.5% of cases. Antimicrobial agents were administered to 108 patients. Antibiotics mainly prescribed were aminoglycosides and broad spectrum cephalosporins. The duration of ICU stay varied from 3 to 116 days (median 12) and the length of ICU stay prior to Bcc nosocomial infection was from 0 to 48 days (median 6). There was a statistically valid association between duration of ICU stay prior to the onset of infection and the number of different antibiotic groups used in the 15 days before isolation of Bcc bacteria.

**Conclusion:** Intravenous catheterization, antimicrobial therapy, operation, transfusion of blood products and urinary catheterization are the main risk factors for the emergence of Bcc nosocomial infections in ICU patients.

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### **Bacterial contamination of intensive care units (ICU and NICU) in Hamadan hospitals, western Iran.**

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<sup>1)</sup> Iran

**Objectives:** The objective of this study was to identify the isolates and determination of antibiotics resistance patterns in bacteria isolated from intensive care units (ICU and NICU) in Hamedan hospitals, west of Iran.

**Methods :** In this study, 642 samples were randomly collected from different area including devices, apparatus, air, physical surfaces and staffs, uniforms. The samples were inoculated in EMB and Blood agar and were identified. 140 isolates were tested for antibiogram by Kirby-bauer method. The antibiotics disks were consisted of : Erythromycin, vancomycin, methicillin, ceftriaxone, cefataxime, penicillin, carbapenem, ampicillin, gentamicin, sulfamethoxazole, nalidixic acid and ciprofloxacin.

**Results:** The average rate of bacterial contamination in ICU and NICU was 42.9%. The most contaminated parts, were the staffs, uniforms (70.3%) and physical surfaces (58.4%) respectively. The most bacteria isolated were as follow: Staphylococcus epidermidis, Staphylococcus aureus, Streptococcus faecium, Pseudomonas aeruginosa, E.coli, Klebsiella, Enterobacter, Proteus and Acinetobacter.

In total, gram positive bacteria showed more resistance patterns, rather than gram negative bacteria. More than 80% of Gram-positive bacteria were resistant to penicillin, ampicillin and gentamicin.

**Conclusion:** Our results showed that Gram-positive cocci in particular Staphylococcus epidermidis, Staphylococcus aureus and Streptococcus faecium are the main causes of bacterial contamination in ICU and NICU. There was also high antibiotics resistance in strains particularly for Staphylococcus aureus and Pseudomonas aeruginosa, which isolated from ICU and NICU.

Key Words: Nosocomial infection, Antibiotic resistance, Intensive care unit.

## 8. Skin and Soft Tissue Infections

8:101

### Severe skin and soft tissue infections: Sequential intravenous and oral treatment with Moxifloxacin

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**Objectives:** The broad antibacterial activity, the favourable pharmacological properties and the good tissue penetration gave rise to the investigation into the use of a moxifloxacin (MXF) sequential iv/po therapy for severe skin and soft tissue infections.

**Methods:** 29 patients were examined in an open-label, prospective, randomised study. The primary endpoint was the clinical efficacy (improvement/recovery), secondary endpoints were the bacteriological eradication, duration of treatment, necessity of alteration of antibiotic therapy, and duration of hospitalisation. Patients with severe skin and soft tissue infections including diabetic foot infections and systemic symptoms of inflammation were included. Therapy consisted of MXF 1x 400 mg iv/d, followed by 1x 400 mg/d po, or amoxicillin/clavulanic acid (amoxiclav) 1200 mg iv every 8 hrs, followed by 625 mg po every 8 hrs, for a maximum of 21 days each. The time point to switch from iv to po was determined by clinical assessment and the development of serum CRP. The MXF group included 15 patients, the amoxiclav group 14 patients.

**Results:** Indications were: n = 19 (65%) diabetic foot infection, n = 7 (25%) arterial occlusive disease stage VI, and n = 3 (10%) infected ulcers with venous insufficiency (no statistical difference between the two groups). On day 7 the percentage of clinical cures was clearly higher under MXF with 45% (amoxiclav: 20%). Switching/complementing the antibiotic therapy (due to resistance, ineffectiveness) was required less often with MXF than with amoxiclav [4/15 (26%) vs. 10/14 (71%)]. The intent-to-treat analysis showed that iv therapy in the MXF group was significantly shorter, being 4.3 days as compared with 7.0 days in the amoxiclav group. The same result was found for the subsequent oral therapy (12.5 vs. 25 days) and the overall duration of treatment. Duration of hospitalisation was 15 days in the MXF group and thus shorter than in the amoxiclav group (19 days). We found a trend towards a quicker bacterial eradication by MXF than by amoxiclav. CRP and leukocytes tended towards a quicker decrease under MXF in the first week.

**Conclusion:** In this investigation including patients with different types of severe skin and soft tissue infections moxifloxacin has been shown to be effective. Therefore, moxifloxacin is an option in the treatment of this indication.

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### The clinical efficiency of Ronkoleukin and Betaleukin in treatment of infected neuroischemic form of diabetic foot

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To analyze the clinical efficiency of recombinant forms of interleukin-1 and - 2 in treatment of diabetic patients with infected neuroischemic form of diabetic foot.

The recombinant form of interleukin-1 (Ronkoleukin, "Biothek", Russia) and interleukin-2 (Betaleukin, "Biothek", Russia) were used in the study. The drug dose of 500 000 UN was given thrice with 3 days interval to 123 diabetes mellitus patients with infected neuroischemic form of diabetic foot

In seven groups of patients the disturbance of T-cellular link was observed in 89% of cases, B-cellular link-in 23%; the decrease of phagocytic activity was registered in 34% of cases, the decrease of bacterial activity - in 42% (the increase of spontaneous level of neutrophils activation (HCT-TEST)- in 32% and the decrease of induced level-in 28%). The operative measures invoked stress-induced changes in 84% of the patients, which were accompanied by aggravation of T-cellular link disturbance, the change in activation index, and the decrease of several phagocytic indexes. In the postoperative period these tendencies appeared to be present during 12.4 +/- 5.2 days. The introduction of Ronkoleukin and Betaleukin into the treatment protocols resulted in the correction of secondary immunodeficiency in 78% of the patients for approximately 7 days after the last infusion. The preoperative (1-2 hours) and intraoperative applications rendered the stress protective influence, which was expressed by levels of AKTG excretion and catecholamines, as well as by corticosteroid dynamics. In all patients there were no registered allergic responses to the drug introduction. We have observed few side effects: 30 patients have shown body temperature increase after the drug infusion (only 2 patients had the body temperature above 39C); 5 patients developed cuboidal vein phlebitis.

The introduction of Ronkoleukin and Betaleukin to conventional therapy allowed: to increase the number of patients with preserved support function of the lower extremity from 52.6% to 80.5% ( $p<0.05$ ); to increase the number of operations without organ amputation from 26.3% to 36.1% ( $p<0.05$ ); to increase the number of operation without the expense of foot amputation from 26.3% to 44.4% ( $p<0.05$ ). The number of femur amputations decreased from 47.4% to 19.5% ( $p<0.05$ ); and the lethality rate also was decreased from 19.7% to 3.28% ( $p<0.001$ ).

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### Microbiology and clinical outcomes in necrotizing fasciitis: Recent 5 years experience

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**Objective:** Necrotizing fasciitis is an uncommon rapid progressing severe infection affecting subcutaneous tissues and fascia. This study investigated the microbiologic characteristics and clinical outcomes of necrotizing fasciitis.

**Methods:** The medical records of 28 consecutive patients with a diagnosis of necrotizing fasciitis from January 2001 to December 2005 were retrospectively reviewed.

**Results:** The average age was 53 years (range 32-76). A single pathogen was identified as the infectious agent in 14 patients (50%), multiple pathogens were identified in 9 patients (32%), and no organism was identified in 5 patients (18%). Group A streptococci (GAS), identified in 8 patients, was the most commonly isolated species. Twenty patients (71%) had precipitating event, such as previous infection (9), previous surgery (3), acupuncture (3), and other minor trauma (5). Among the patients with GAS infection, 6 patients (75%) had no identified precipitating events. Of the 28 patients, 5 died (17%) and 23 survived (83%). Duration of symptoms before hospitalization was no significant difference between survivors (9.9+/-12.5 days) and non-survivors (4.4+/-4.3 d). The mean length of hospital stay for non-survivors was 6.4+/-6.5 days (survivors: 64+/-38 days). Treatment modalities of the all patients were beta-lactam antibiotics (100%), extensive debridement (71%), limb amputation (11%), hyperbaric oxygen therapy (25%) and IV immunoglobulin (29%).

**Conclusion:** This study showed that GAS was the most common pathogen of necrotizing fasciitis. Rapid diagnosis and multimodality therapeutic approach remains the cornerstone of therapy because most mortality occurred rapidly.

## 9. Infections in Transplant Patients

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### Case report: Primary cutaneous cryptococcosis

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**Objectives:** We report a case of a 60-year old male renal transplant recipient with severe skin and soft tissue infection mimicking necrotizing fasciitis. Culture of aspirate from the wound and tissue samples revealed *Cryptococcus neoformans*. No signs of systemic cryptococcal infection were found.

**Clinical presentation, intervention:** A 60-year male renal transplant recipient was transferred to our hospital with severe skin and soft tissue infection of the right upper limb. His immunosuppressive regimen consisted of prednisone and cyclosporine. He suffered a minor cat scratch wound to the palm of his right hand by a domestic cat. Three days later he presented with local signs of inflammation at the site of the scratch wound. Amoxicillin/clavulanic acid was started. Inflammation rapidly proceeded. Two days later a small incision at the site of the primary wound was performed, followed by surgical debridement of the palm. The wound swab revealed growth of encapsulated yeasts. Patient's condition deteriorated, he showed signs of systemic infection, and was transferred to our hospital. He presented with bullous swelling of the right upper limb, with soft tissue necrosis. Elevated levels of CRP and PCT were detected, normal white blood cell count with shift to the left. Imipenem and liposomal amphotericin B were started. Soft tissue and muscle necrosis were present, so amputation of the arm above the wrist had to be performed. After surgical intervention and antimicrobial treatment patient quickly recovered. Blood cultures remained negative, positive antigen test for *C. neoformans* was found in blood. All wound swabs revealed *C. neoformans* but showed no signs of bacterial growth. Histological examination of the muscle tissue sample taken at the operation also revealed encapsulated yeasts. Chest X-rays were normal. Lumbar puncture was not performed, but patient showed no signs of CNS involvement during hospitalization and during a 9-month follow-up. He was treated with standard amphotericin B for 3 weeks, and was then switched to fluconazole per orally for three months. After 9 months he is without any signs of skin or systemic infection.

**Conclusion:** We present a case of primary cutaneous cryptococcosis. It is important to consider primary cryptococcal cellulitis in immunocompromised hosts presenting with skin and soft tissue infection that does not respond to broad spectrum antibiotic regimens.

## 10. Infection Control

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### Prevalence of hospital-acquired infection in a Moroccan hospital April 2005

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**Summary:** In order to estimate the prevalence of hospital acquired infection (HAI) and the research of factors associated with its occurrence, a one day survey was conducted at Ibn Sina University hospital, Morocco. We did deal with 658 patients of more than 15 years old in age, who had been in the same ward for at least 48h, and had also occupied a hospital bed from April first to April 7th 2005. The overall prevalence of HAI was 17.8% (117/658). The most frequently infected sites were the urinary tract with 35% , followed by surgical wound infection 21,5% and low respiratory tract in 16.2 % cases. In intensive care units the HAI prevalence among patients was 50% (11/22). 63, 5% had urinary tract infection, 27,5% had a low respiratory infection. besides, one patient 9% had catheter infection. Among 117 HAI cases, only 31.6% patients (37/117) had microbiological documentation. 49 samples were documented. And about 10% (12/117) of patients had two infection sites, in witch, we identify 2 micro-organisms at the same patient. The most frequent microorganisms were *Staphylococcus aureus* 30% (15/49), *Proteus mirabilis* 25% (12/49) and *Pseudomonas aeruginosa* 18% (9/49). By logistic regression analysis, Significant risk factors for HAI included surgery, adjusted odds ratio was (OR): 2.81; 95% CI: 1.87- 4.32), intravenous catheter, (OR 2; 95% CI: 1.07-3.90), urinary catheter (OR 2.30; 95% CI: 1.04 – 5.37) and more than 10 days stay at hospital (OR 4.43; 95% CI: 2-9.44). and more than 20 days stay (OR 5.51; 95% CI: 2.50-12). These results show that the hospital is needing multisectorial strategy to struggle HAI.

## Prevalence of carriers of methicillin resistance *Staphylococcus aureus* (MRSA) in 100 staff of Shahid Beheshti hospital of Kashan (Iran)

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**Background:** *Staphylococcus aureus* is recognized as one of the most important bacterial pathogens seriously contributing to the problem of hospital infections all over the world. The source of infection is nasal carrier hospital personnel. Determination of antibiotic resistance pattern of isolated strains is essential for treatment of carrier.

**Objective:** The aim of this study was access the incidence of methicillin resistant *S.aureus* (MRSA) carriage in the Shahid Beheshti University Hospital, Kashan (Iran).

**Material and Methods:** To find prevalence of MRSA carrier, A prospective survey was conducted over 100 personnel in Shahid Beheshti Hospital of Kashan, from March 2001 to Sep 2002 , total specimens were taken from the anterior nares of staff, were cultured on the selective media, isolates were identified based on coagulase and conventional biochemical reactions according in Standard Method.

All staphylococcus isolates were screened for methicillin resistance by in oculation of Muller-Hinton agar supplemented with salt and oxacillin 6 µg/ml, according to National Committee for Clinical Laboratory Standards (NCCLS) guidelines, other tested antibiotics included amoxicillin (20 µg), ciprofloxacin (5 µg), penicillin (10 units), gentamycin (10 µg), rifampin (30 µg) vancomycin (30 µg), then the results were presented by descriptive analysis.

**Results:** The results showed (12%) of Staphylococcal isolates were coagulase positive, of the total *Staphylococcus aureus*, 7 (58.3%) were resistant to methicillin.

**Conclusion:** Resistance pattern of *Staphylococcus aureus* to various antibiotics, especially methicillin is towards increasing trend, it seems the prevalence of MRSA clonisation in the staff of University Hospitale of Kashan (Iran) is increasing.

**Keywords:** Antibiotics, Carriage, Nasal, *Staphylococcus aureus*, Methicillin – Resistant *Staphylococcus aureus*

**Influence of cephalosporins usage in perioperative prophylaxis on occurrence of Enterococcus spp. infections**

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Enterococcus spp. started to play major role in nosocomial infections and now are the most common etiological factor of infections on surgical wards. Enterococcal natural resistance for cephalosporins and common application of I<sup>st</sup> and II<sup>nd</sup> generation cephalosporins in perioperative prophylaxis can lead to increase of infections with these strains.

The aim of the study was to evaluate frequency of perioperative infections with Enterococcus strains while cephalosporins for perioperative antibiotic prophylaxis were administered.

All the patients operated on because of illnesses in the abdominal cavity from April 2004 until September 2005 in the Department of General, Gastroenterological and Endocrinological Surgery in Poznan, where included in this study. The patients were treated with cephazoline and metronidazole. This perioperative prophylaxis of infections was administered to 2072 patients (1114 women and 958 men, average age: 64 years).

Antibiotic perioperative prophylaxis was administered to these patients where the cleanness of the operating site was assessed as a clean-contaminated or contaminated. In the few cases prophylaxis was used also in clean operations. Cephazoline and if there was a need also metronidazole were given in perioperative period, but in justified cases prophylaxis has been prolonged for 72 hours. If symptoms of infection occurred, material for microbiological tests was also taken. These collected materials were: smear tests from the operated site and content from the abdominal cavity drainages. As a measurement of increasing dynamics of the infections, on the basis of the average percentage basis increase ( $T/t-1$ ) according to formula:  $T/t-1=100(\bar{y} t/t-1-1)$ , the statistic analysis has been performed.

In evaluated group of patients positive cultures were affirmed in 212 tests. Enterococcus were seen as a single factor or with other pathogens. The most common where: 126 strains of Enterococcus faecalis, 23 strains of E. faecium and 22 strains of E. gallinarum. Average percentage basis increase of the infections of Enterococcus spp. during evaluated period of 18 months was negative (-1,0077). To confirm that tendency evaluated period of time has been shortened for last 12 months of observations and then negative increase of infections was affirmed (-2,5773). In these discussed time periods positive average increase rate in operated patients were observed, adequately 3,47 and 2,42%.

On the basis of our studies, we do think that properly carried out and monitored perioperative antibiotic prophylaxis with using cephazoline and metronidazole will not conduct to increase of infections caused by Enterococcus spp.

**Reduced rates of surgical site infection with the use of continuous incisional infusions of local anesthetics with ON-QPainBuster: A meta-analysis of clinical studies**

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**Objectives:** The use of continuous infusions of local anesthetics for postsurgical pain management is widely used. The benefit of aggressive postsurgical pain management includes a lowered rate of complications, faster recovery and greater patient satisfaction. Additionally, localized pain management with local anesthetic agents may reduce the risk for surgical infections by increasing tissue oxygenation and continuous tissue lavage. The local anesthetics have been shown to exhibit antimicrobial benefit in in-vitro and in-vivo studies. We conducted this systematic review to determine the effect this pain management modality has on the incidence of surgical site infections.

**Methods:** To provide an estimate of the natural incidence of infection, we used the National Nosocomial Infections Surveillance System (2004) database as resource for control groups. The National Library of Medicine's Medline database, Embase (Excerpta Medica) and known abstracts presented at the Scientific Sessions of Medical Societies were searched for the time period January 1996 to June 2005 for all completed trials on the use of a portable elastomeric continuous incisional infusion pump that delivers local anesthetic for incisional specific pain management. Our intent was to compare data of continuous wound catheters placed by the surgeon vs. no catheters for postoperative analgesia. Studies included met the following criteria: 1) prospective, retrospective, randomized, controlled, blinded or open; 2) end points of wound status including infections were reported. Studies were divided into therapeutic groups for sub-analysis. Comprehensive Meta Analysis V2 software (BioStat, Englewood NJ) was performed using various methods based on fixed effect models including the Mantel-Haenszel method; the Peto method and risk difference method for the quantitative systematic review, and qualitative review was performed by displaying data in table format.

**Results:** 48 studies with 3,011 patients were included for analysis. Meta-analysis associated significant benefit for continuous wound catheters lowering risk for surgical site infection (RR 0.494 p<0.001). Sub-analysis by therapeutic area confirmed these general findings.

**Conclusion:** Both quantitative and qualitative systematic review identified the benefit of continuous wound catheters reducing the risk of surgical site infection. The potential utility in taking a multimodal approach to infection risk reduction is similar to the approach to pain management. The use of continuous wound catheters for more consistent pain relief may enhance the overall response to the trauma of surgery and reduce the risk of surgical infections. Future large, homogenous RCTs will be valuable to confirm these findings.

**The effect of Ostene®, a new water soluble bone hemostasis material, on bone healing in a calvaria defect model**

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**Objectives:** Softened beeswax (bonewax) has been widely used for bone hemostasis for over a century. As beeswax is both insoluble and nonresorbable, it remains at the site of application indefinitely and is well known to potentiate infections, act as a foreign body causing a giant cell reaction and local inflammation as well as inhibiting osteogenesis. Ostene, a new bone hemostasis wax comprised of water soluble alkylene oxide copolymers, readily achieves bone hemostasis but does not remain at the site of application and thus should address all of the known adverse reactions associated with bonewax. The objectives of this study were to compare the effect of Ostene versus bonewax and the effect of Ostene versus no hemostatic agent on bone healing in a calvaria defect model.

**Methods:** Two 3-mm circular defects were made in the calvariae of Sprague-Dawley rats (n = 10) and sufficient Ostene or bonewax was applied to the defect to achieve immediate hemostasis. Control defects had no hemostatic material added. After 3 weeks, rats were sacrificed and the calvaria excised, fixed in neutral-buffered Formalin for 48 h, and stored and scanned in 70% ethanol by micro-computerized tomography (micro-CT, Scanco, PA). Isotropic voxel resolution of 15 µm and an X-ray energy of 55 kVp and 72 mA were used. Measurements are expressed as mineralized tissue (bone) volume.

**Results:** No evidence of Ostene was observed at the site of application, but bone wax remained unchanged with negligible healing. Micro-CT analyses of the Ostene, bonewax or control defects determined mineralized tissue volumes of 1.1, 0.11 and 0.59 mm<sup>3</sup> respectively. It is interesting to note that Ostene-treated defects showed increased mineralization volume and bone density compared to untreated defects at 3 weeks post-surgery. This may in part be due to the additional time required for clearance of a blood clot within the control bone defect prior to initiation of osteogenesis.

**Conclusions:** Ostene is an effective hemostatic agent that showed enhanced bone healing compared to untreated defects. Ostene is an excellent solution when immediate bone hemostasis is required while avoiding the complications of bonewax.

## Session: 10. Infection Control

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### Feedback of surgical site infections (SSI) in a university hospital

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**Objectives:** To investigate the diffusion of SSI data to individual surgeons in a Belgian university hospital (AZ VUB, Brussels) one year after the reintroduction of a SSI surveillance program.

**Methods:** Surgical site infections are detected through a prospective, computerized surveillance method based on microbiological sampling. Because of the presence of many surgeons in training and the high rotation rate of surgical teams in a university hospital, the results of this surveillance are communicated only to the chairmen of the surgical departments. During a yearly "SSI lunch", a written document of surgical site infection rates according to National Nosocomial Infections Surveillance (NNIS) operative procedures and risk indices is discussed. In order to investigate whether and how the chairmen of the surgical departments communicate this information to their team, they were asked to respond to a structured questionnaire within a 3-week period.

**Results:** The infection control team mailed the questionnaire to the chairman of the 11 surgical departments. Seven questionnaires were returned before the deadline was reached, the others could be obtained only after one or more telephone calls.

Six of the 11 chairmen reported to have discussed the results within their surgical team during a seminar. Two reported to have discussed the results with each surgeon individually. Another chairman combined both ways of communication: results were discussed in general during a seminar and surgeons who had unacceptable results were approached personally. Two chairmen did not yet discuss the results, but were planning to do so in the near future. Despite these encouraging findings, random interviews of surgeons by the infection control team revealed a lack of knowledge of the SSI rates of their department.

**Conclusion:** Surveillance can reduce the incidence of surgical site infections provided that the results are communicated adequately to health care professionals. Surgeon-specific rates should be reported. However, this sub-analysis is time consuming and difficult to perform in a teaching hospital. Communication of SSI data to the chairmen of the surgical departments is no guarantee of accurate diffusion to all team members. Chiefs of department are either not familiar with interpretation of SSI data or not sufficiently motivated to communicate the information to their staff members. More support from the infection control team in the final stage of information dissemination could be productive in terms of surgical infection control.