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Abstracts from the 12th International Symposium on Modern Concepts in Endocarditis & Cardiovascular Infections

Session 1 – *Staphylococcus aureus* goes molecular

SY.1.1
UNDERSTANDING *STAPHYLOCOCCUS AUREUS* EPIDEMIOLOGY

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Staphylococcus aureus is one of the most important causes of healthcare associated infections worldwide. In mean, 20% of persons are asymptomatically colonized with *S. aureus*. Due to risk factors for colonization (e.g. wounds, catheters), *S. aureus* can be found also in other locations. Most infections due to *S. aureus* occur endogenously, i.e., the *S. aureus* originates from the colonizing reservoir of the patient itself.

In addition to methicillin-susceptible *S. aureus* (MSSA), the antibiotic-resistant variant, methicillin-resistant *S. aureus* (MRSA) has challenged healthcare since many years. Different international and cross-border studies have shown the differences between MSSA and MRSA epidemiology and that MRSA prevalences have been stable or even declining in recent years. In parallel, there is still a high diversity in prevalences, as the Netherlands and Denmark have up to 25 times less MRSA in blood cultures than countries like Germany, UK and France. The reason lies in the clonal difference between the countries. Molecular subtyping has shown that MRSA clonal lineages differ not only in epidemiological behaviour and clonal origin, but also in clinical importance and carriage of resistance and virulence genes. Therefore, MRSA are often divided into 3 different "epivars": (i) hospital-associated (ha-MRSA), (ii) community-associated (ca-MRSA) and (iii) livestock-associated (la-MRSA).

These epivars occur in different prevalence in different countries, reflecting differences in MRSA epidemiology. Different to the endogenous infection route, the primary acquisition of MRSA follows an exogenous transmission way via direct contact or via the hands of healthcare workers. Recent studies using network analysis revealed that the transmission is driven by the referral of patients between healthcare institutions. La-MRSA and ca-MRSA instead seem to use other transmission ways. Successful intervention strategies have focused on the prevention of colonization by rapid identification of carriers, infection prevention, antibiotic stewardship and interventions within the regional healthcare network. As boundaries between the three main epivars are not static under "one health"-aspects, we need to look especially at the epidemiological dynamics of la- and ca-MRSA, which show to change rapidly their epidemiological and clinical behavior at the moment. Further adaptation to the host and the hospital environment can rapidly lead to an increase of MRSA infections.

SY.1.2
DIAGNOSTIC AND TREATMENT IMPLICATIONS OF DIFFERENT STRAIN AND MEC TYPES

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Methicillin resistant *Staphylococcus aureus* (MRSA) continues to pose treatment problems for clinicians especially in complicated infections such as infective endocarditis. For more than 50 years, vancomycin has been the workhorse for treatment of MRSA infections. Today there is a general agreement that VISA isolates (MICs of 4–8 mg/L) are resistant. The implication of hVISA strains (MICs $\leqslant$ 2 mg/L but with subpopulations of resistant colonies) is less clear and in addition detecting of hVISA poses large problems for routine microbiological laboratories. In concordance a number of smaller studies have shown that infections with isolates with MICs of 2 mg/L are associated with poorer outcome. These studies question the present breakpoint of S $\leqslant$ 2 mg/L. However, when judging the MIC it should be recalled that MIC determination of vancomycin is method dependent, with Etest giving higher MICs compared to MICs obtained by broth microdilution (BMD). BMD is presently considered to be the gold standard; however, a number of small non-randomized studies have found better correlation between Etest and outcome. Despite these issues no randomized studies have found vancomycin to be inferior to alternative antibiotics such as daptomycin, linezolid or the recently licensed ceftaroline. A recent Australian study furthermore showed that for vancomycin there was a lack of correlation of outcome versus drug concentration/isolate MIC (AUC/MIC) and concluded "that multiple factors apart from the vancomycin AUC/MIC influence outcome, including strain-specific genotypic differences" (Holmes et al. 2013). It is thus noteworthy that VISA isolates frequently belong to strains of MLST clonal complex 5 although VISA and hVISA isolates are seen in a range of other MLST lineages too. The implications of these characteristics for diagnostics and for choice of treatment will be discussed in the talk.

SY.1.3
WHOLE GENOME SEQUENCING AND MRSA PATHOGENESIS

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Whole genome sequencing (WGS) of microorganisms is evolving from a research tool to valuable tool for any large clinical microbiology laboratory. The value of WGS lies in its universal applicability for identifying, typing, profiling and setting any microorganism into a possible infection control context.

Current challenges are costs, but while the first genome we sequenced cost €6700, a genome in our laboratory today costs £200 on a MiSeq and €55 on a HiSeq. On a MiSeq you can be up and running for about €30,000.

While the price for data production is getting lower, the higher throughput creates challenges for data analysis on computers and for bioinformatics to generate and handle results. A layout for establishing a WGS facility will be briefly described. Currently used software solutions, pipelines and internet-based services for WGS will be discussed.

With MRSA as a model we will describe typing methods, confirmatory tests, genotypic antimicrobial testing, virulence profiling, single nucleotide polymorphism typing and comparison between isolates in outbreak handling.

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Session 2 – Staphylococcal endocarditis

SY.2.2
HIGH-DOSE DAPTOMYCIN IN THE THERAPY OF STAPHYLOCOCCAL INFECTIVE ENDOCARDITIS AND WHEN TO APPLY IT

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MRSA bacteremia and endocarditis represent some of the most challenging and difficult infections to overcome with antibiotics. Understanding the relationships between antibiotic pharmacokinetics and pharmacodynamics, target organism, site of infection and the potential for resistance development is key for successful patient outcome. Daptomycin is a bactericidal concentration-dependent killing antibiotic that is indicated for complicated bacteremia including right-sided endocarditis at 6 mg/kg/day. Although infrequent, daptomycin non-susceptible *S. aureus* has been reported to emerge on therapy especially following vancomycin exposure. In vitro PK/PD models using simulated endocardial vegetations (SEV) and infective endocarditis animal infection models have demonstrated improved *S. aureus* killing and reduction in the potential for emergence of daptomycin non-susceptible strains with higher daptomycin dosages. Although clinical trial information is limited, multicenter observational data suggests that high-dose daptomycin may be safe and potentially efficacious.
This lecture will discuss data from PK/PD SEV and animal models that have investigated high-dose daptomycin alone and in combination for both susceptible and daptomycin non-susceptible *S. aureus* strains. Data from clinical experience regarding safety and efficacy will also be presented and discussed.

SY.2.3
UNDERSTANDING AND CIRCUMVENTING DAPTOMYCIN RESISTANCE IN TREATMENT OF STAPHYLOCOCCAL ENDOCARDITIS

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The bactericidal, cell membrane-targeting lipopeptide antibiotic, daptomycin (DAP) is an important agent in treating invasive *Staphylococcus aureus* infections. This agent is anionic, but is unambiguously inactive until it is calcium-complexed within the blood stream. Thus, DAP is an exogenous cationic antimicrobial peptide, analogous to endogenous host defense peptides. Of note, there have been many recent reports of development of daptomycin resistance (DAP-R) during therapy with this agent, leading to failed treatment. The mechanisms of DAP-R in *S. aureus* appear to be multifactorial. DAP-R strains often exhibit progressive accumulation of single nucleotide polymorphisms in the **m**ulti**p**eptide **r**esistance **f**actor gene (*mprF*) and the *yycFG* components of the *yycFGHI* operon. Both loci are involved in key cell membrane (CM) events, with *mprF* being responsible for the synthesis and outer CM translocation of the positively-charged phospholipid, lysyl-phosphotidylglycerol (L-PG), while the *yyc* operon is involved in the generalized stress response, including to antibiotics. In addition, other CM perturbations have been identified in DAP-R strains, including: extremes in CM order (including enhanced fluidity or rigidity); resistance to CM depolarization and permeabilization; and reduced surface binding of DAP. Moreover, modifications of the cell wall (CW) appear to also contribute to DAP-R, including enhanced expression of both the *dlt* operon (involved in d-alanylation of CW teichoic acids, leading to increased relative surface positive charge) and the *tag* operon (involved in production of CW teichoic acid and progressive CW thickening). Prevention of the evolution of DAP-R during therapy, as well as the treatment of established invasive staphylococcal infections caused by DAP-R strains is complex, and includes: combination therapy with agents such as rifampin, trimethoprim–sulfamethoxazole, or various β-lactams. The mechanisms of such combination effects range from classical synergy, as well as drug-induced membrane sensitization to enhanced daptomycin binding.

Case presentation

Case-5
THERAPEUTIC HYPOTHERMIA IN THE TREATMENT OF *HAEMOPHILUS APHROPHILUS* ENDOCARDITIS COMPLICATED WITH ISCHEMIC STROKE

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Background: Treatment with hypothermia is not common in patients with infective endocarditis complicated with ischemic stroke. We describe a patient with *Haemophilus aphrophilus* endocarditis, complicated with severe stroke and paravalvular abscess, who was treated with antibiotics, surgery and therapeutic hypothermia (TH).
Case presentation: A 37-year-old, previously healthy man presented with a two-week history of fever, chills and rigors. He was treated ambulatory with azithromycin for three days, then with co-amoxiclav, with no success. At admission, the patient had fever of 37.4°C and petechial rash on right shoulder and back. No murmur was heard during cardiac auscultation. Dental examination showed a good dental status. Laboratory tests showed erythrocyte sedimentation rate of 70 mm/hr (normal rate, 0–15 mm/hr) and elevated C-reactive protein of 81.5 mg/dL (normal level 0–5 mg/dL). The white-cell count was 15,900 per cubic millimeter with 91% neutrophils. Blood cultures were obtained, and the patient was started on ceftriaxone. Two of the conventional blood cultures turned positive approximately 4 days after incubation and were consistent with *Haemophilus aphrophilus* sensitive to ceftiraxone. On the fourth day of hospitalization, the patient collapsed and developed sensomotor aphasia with right-sided hemiplegia and coma followed by respiratory failure. He was transferred to the ICU where he was intubated and mechanically ventilated. Due to the patient's severely impaired consciousness associated with severe intracranial hypertension and carbon dioxide reactivity loss measured by transcranial Doppler, TH was started. Mild hypothermia (rectal temperature of 32–34°C) was maintained with continuous veno-venous hemofiltration. CT scan and MR of brain showed ischemic stroke in left temporal lobe with excessive brain edema with compression of ventricles. TH was conducted for 72 hours, gradual recovery of consciousness followed and the patient was extubated on the eighth day of hospitalization. Transoesophageal echocardiography revealed paravalvular abscess associated with endocarditis of the aortic valve. After solving the problem of excessive brain edema, the patient underwent cardiac surgery and valve repair. After overall six weeks of antibiotic therapy, the patient was discharged from hospital with sensomotor aphasia. The hemiparesis symptoms resolved. No relapses were observed during the 14 months of follow up.
Conclusion: This is the first case of *Haemophilus aphrophilus* endocarditis complicated with ischemic stroke treated with TH. This method of treatment could be a promising tool for treatment of patients with infective endocarditis complicated with ischemic stroke and severe brain edema.

Session 3 – Infections on cardiac implantable electronic devices

SY.3.1
CLINICAL CHARACTERISTICS AND OUTCOME OF INFECTIVE ENDOCARDITIS INVOLVING IMPLANTABLE CARDIAC DEVICES

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Context: Infection of implantable cardiac devices is an emerging disease with significant morbidity, mortality, and health care costs.
Objectives: To describe the clinical characteristics and outcome of cardiac device infective endocarditis (CDIE) with attention to its health care association and to evaluate the association between device removal during index hospitalization and outcome.
Design, Setting, and Patients: Prospective cohort study using data from the International Collaboration on Endocarditis–Prospective Cohort Study (ICE-PCS), conducted June 2000 through August 2006 in 61 centers in 28 countries. Patients were hospitalized adults with definite endocarditis as defined by modified Duke endocarditis criteria.
Main Outcome Measures: In-hospital and 1-year mortality.
Results: CDIE was diagnosed in 177 (6.4% [95% CI, 5.5–7.4%]) of a total cohort of 2760 patients with definite infective endocarditis. The clinical profile of CDIE included advanced patient age (median, 71.2 years [interquartile range, 59.8–77.6]); causation by staphylococci (62 [35.0% 95% CI, 28.0–42.5%] *Staphylococcus aureus* and 56 [31.6% 95% CI, 24.9–39.0%] coagulase-negative staphylococci); and a high prevalence of health care-associated infection (81 [45.8% 95% CI, 38.3–53.4%]). There was coexisting valve involvement in 66 (37.3% [95% CI, 30.2–44.9%]) patients, predominantly tricuspid valve infection (43/177 [24.3%]), with associated higher mortality. In-hospital and 1-year mortality rates were 14.7% (26/177 [95% CI, 9.8–20.8%]) and 23.2% (41/177 [95% CI, 17.2–30.1%]), respectively. Proportional hazards regression analysis showed a survival benefit at 1 year for device removal during the initial hospitalization (28/141 patients [19.9%] who underwent device removal during the index hospitalization had died at 1 year, vs 13/34 [38.2%] who did not undergo device removal; hazard ratio, 0.42 [95% CI, 0.22–0.82]).
Conclusions: Among patients with CDIE, the rate of concomitant valve infection is high, as is mortality, particularly if there is valve involvement. Early device removal is associated with improved survival at 1 year.

SY.3.2
REMOVAL OF INFECTED DEVICES – STRATEGIES AND RISKS

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Management of patients with cardiovascular implantable electronic devices (CIED) includes strategies to reduce the intrinsic morbidities of these therapies. The inherent nature of these devices includes a battery and the replacement of the device which means that we need to reduce the consequences of device replacement and the risk of device infection. Also, since these devices are tethered to the heart through wires, designated leads, these infections are linked to fibrosis, occlusive venous disease, sepsis and endocarditis. The first priority is to reduce the frequency of infection, the second priority is to reduce the risk of treating the infection. Unfortunately the frequent comorbid conditions, including left ventricular dysfunction, poor functional capacity, diabetes, renal dysfunction, vascular stenosis, other venous catheters and prior infections increase both the frequency and risk of therapy. The first obstacle is making the diagnosis as both under- and overdiagnosis is an issue. However once the diagnosis is made then the only consistently effective therapy is total removal of all of the hardware – transvenous, subcutaneous and epicardial. The pathogens are at least 80% staphylococcal, often methicillin resistant. Diagnosis, removal, antibiotics and reimplantation are all important topics to be addressed during the discussion. Unfortunately these patients have a high mortality with or without aggressive therapy and if done appropriately the risk of complications with removal is not high. Therefore, strategic approaches to avoiding infection including patient selection and prophylaxis, choosing appropriate number and types of leads with the devices, diagnosis, extraction and reimplantation are all important. Appropriate antibiotic therapy should be considered for prophylaxis and therapy.

Session 4 – Embolizations and coagulation

SY.4.1
THE ROLE OF HEMOSTASIS IN INFECTIVE ENDOCARDITIS

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Infective endocarditis, still characterized by significant morbidity and mortality, has pathogenic, clinico-pathological and therapeutic features that are highly relevant in terms of hemostasis function.
The endocardial vegetation is thought to arise as a sterile endocardial thrombus. Detachment of a vegetation fragment causes septic embolization, one of the most common and harmful complication of the disease. Several clinical and experimental studies have looked at the effect of hemostasis system modulation in infective endocarditis, with the aim to prevent the onset or reduce the risk of embolic complications.
In this paper, the most recent evidence on the role of hemostasis in infective endocarditis is reviewed, with special attention to the possible role of pro-thrombotic conditions.

SY.4.2
MODIFIERS OF SYMPTOMATIC EMBOLIC RISK IN INFECTIVE ENDOCARDITIS

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Systemic embolization may occur in one-third of the patients with infective endocarditis and is associated with significant morbidity and mortality. Historically, antimicrobial therapy is the only medical intervention proven to reduce the risk of embolization in infective endocarditis. More recently, aspirin and statins have generated considerable interest as modifiers of embolic risk in endocarditis due to their anti-inflammatory, anti-infective and anti-platelet activities. Aspirin has been shown to reduce bacterial density in vegetations and decrease embolic events in experimental models of endocarditis. Although an earlier, randomized trial that employed high-dose aspirin failed to demonstrate any benefit of adjunctive aspirin therapy in established endocarditis cases, more recent cohort studies suggest that ongoing aspirin therapy prior to onset of endocarditis may be associated with reduced risk of embolization. In another study, the rate of symptomatic emboli associated with endocarditis was reduced in patients who received continuous daily statin therapy before onset of endocarditis. Further evaluation of these drugs in prospective studies for their potential impact on risk of embolization among endocarditis patients is warranted.

SY.4.4
EMBOLIZATIONS OF THE CENTRAL NERVOUS SYSTEM – IS THERE MORE THAN WE OBSERVE?

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Embolization from vegetations is a characteristic feature of infective endocarditis (IE), with the highest numbers seen in studies where asymptomatic embolism has also been investigated. The most frequent localization of symptomatic embolism in IE is the cerebral vascular bed. Central nervous system (CNS) symptoms in IE are variable and IE patients with CNS involvement often exhibit more than one type of lesion and/or neurological sign, although they may also be asymptomatic. Neurological complications in IE are usually referred to as either ischemic events, hemorrhagic complications or infections, but cerebral infarction, micro- and macroabscess formation, meningitis, septic vasculitis, infectious (mycotic) aneurysms and cerebral hemorrhage have been suggested to represent a pathogenetic continuum caused by septic embolism.
The reported incidence of neurological complications in IE varies greatly among series and is influenced by how a CNS event is defined, what diagnostic methods are used, study population constitution and referral bias. Systematically performed cerebral magnetic resonance imaging (MRI) in IE patients has found cerebral lesions in at least 80% of the patients, most having no neurological symptoms. Apart from ischemic lesions, cerebral microbleeds and asymptomatic infectious aneurysms have been found. In older studies, IE patients with less well-defined neurological manifestations including diffuse encephalopathic symptoms and minor focal signs, to a much larger extent were examined by lumbar puncture, revealing a high degree of CNS meningeal involvement. Studies based on autopsy examination also have documented cerebral engagement and combinations of brain lesions in up to 90% of IE patients. To our current knowledge, cerebral embolization in IE is more frequent than clinically evident but the influence on the course of the disease is mainly predicted by severity of neurological impairment rather than number of lesions detected.

Session 5 – Hot topics in the surgical treatment of infective endocarditis

SY.5.2
OPTIMAL TIMING FOR CARDIAC SURGERY IN INFECTIVE ENDOCARDITIS – IS EARLIER THE BETTER?

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For the first time, the 2009 European Society of Cardiology guidelines on infective endocarditis (IE) included recommendations on the timing of cardiac surgery (emergency: <24 h; urgent: within a few days; elective: after at least 1 or 2 weeks of antibiotic therapy). As there were no randomized trials at that time, these recommendations are based on expert consensus solely. Propensity analyses have shown benefits of early surgery in some subsets of patients. Earlier surgery may be better than later surgery in terms of vital prognosis; on the other hand, it may be technically more difficult and it exposes to a higher risk of relapse of IE and prosthetic dysfunction.
The three main situations at risk are heart failure, uncontrolled infection and high risk of embolism.
Heart failure is frequent and it is the strongest predictor of death. In case of pulmonary edema or cardiogenic shock, surgery is needed emergently. Even if heart failure responds well to medical treatment, surgery is urgently needed as heart failure will relapse. In patients with severe regurgitation but without clinical heart failure, echocardiography may identify patients at high risk of developing heart failure.
Surgery is needed urgently in case of locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation) and in case of persisting fever and positive blood cultures >7–10 days that are not related to an extracardiac cause.
Emboli are a frequent complication of IE. The risk mainly depends on vegetation size and on duration of antibiotic treatment. A recently published randomized trial showed that very early surgery decreased the 6-week rate of embolic events form 21% to 0%. Surgery must be performed urgently if the vegetation size is >10 mm in patients who already had $\geqslant$1 embolic event and >15 mm in patients who had no embolic event.

SY.5.4
NEW ENTITY: INFECTIVE ENDOCARDITIS AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION

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Transcatheter aortic valve implantation (TAVI) has developed during the last ten years as a safe and technically feasible alternative to conventional aortic valve replacement (AVR) surgery, particularly in high-risk populations such as the very elderly and frail. However, first results of long-term follow-up in large series of patients who underwent TAVI revealed that it is not free of infectious complications, including infective endocarditis (IE). Cases of IE over TAVI devices are being increasingly reported in the literature in recent years. In a PubMed review using the keywords of TAVI and IE we have identified until March 2013 34 cases of TAVI IE (8 in large follow-up series of TAVI and 26 from case reports).
Current lack of experience on this issue and scarce available data still preclude a firm definition of this entity. However, some features are repeatedly confirmed in these patients, and a new and particular profile of prosthetic valve endocarditis (PVE) is emerging. It includes some peculiarities related to: technical characteristics of the procedure, epidemiological aspects of patients, echocardiographic features, spectrum of causing microorganisms, treatment options and outcome. Placement of the collapsible valve over the damaged aortic native valve implies a sudden mechanical aggression that restructures the aortic ring and root, probably leading to higher risk of fistula formation. Use of either transfemoral or transapical approach appears to be differently associated to mitral valve involvement. Most cases are late TAVI IE. The prototypical patient is an old patient with several comorbidities. High rates of chronic renal failure, cancer, hemodialysis and health-care acquisition could explain the etiologic pattern noted so far, led by *Enterococcus* spp. (39%) and coagulase-negative staphylococci (19%). Apparently, only a little portion of patients received antibiotic prophylaxis prior to TAVI. Thickening of subvalvular apparatus after TAVI placement entails some challenges in the interpretation of perivalvular involvement on echocardiography. Besides, some of these elder patients with poor clinical status do not undergo transesophageal echocardiography, adding more complexity to the diagnostic process. Almost a third of patients were operated, maybe pointing to an inaccurate initial TAVI indication. Overall mortality was 30% but increased to 39% in non-operated patients. Conversely, mortality rate was only 12% in those patients who underwent cardiac surgery.

Session 6 – Controversial topics in antimicrobial therapy of infective endocarditis

SY.6.1
MULTIDRUG-RESISTANT PATHOGENS – HOW BIG IS THE THREAT?

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The evidence of a rapid development of complex and increasingly spread antibiotic resistance among strains of Gram-positive cocci causing infective endocarditis (IE) has led to growing concern. More than half of the *S. aureus* strains in the USA causing IE were methicillin-resistant (MRSA). Although cases of vancomycin-resistant MRSA (VRSA) IE are anecdotal, 29% of MRSA showed a heterogeneous vancomycin-intermediate (hVISA) phenotype, with higher rates in Europe and Oceania. Respectively, around 30% and 80% of MRSA strains with vancomycin minimum inhibitory concentrations (MIC) of 1 and 2 mg/L were hVISA. While an association between higher

vancomycin MIC and poorer clinical outcome in MRSA and MSSA bacteremia treated with vancomycin is well known, recent data show that vancomycin MIC $\geqslant$ 1.5 mg/L (43% of strains in our cohort) also conferred a worst prognosis in left MSSA IE treated with cloxacillin.
Among coagulase-negative staphylococci (CoNS) resistance to oxacillin reaches 70% in some series, especially in *S. epidermidis* (MRSE). Although vancomycin-resistant CoNS isolates were not detected, our group recently found a higher mortality among patients with CoNS IE treated with vancomycin than in patients treated with cloxacillin. Among the former, those with vancomycin MIC $\geqslant$ 2 mg/L presented the highest mortality. Besides, resistance was found in 20–30% for clindamycin, gentamicin and ciprofloxacin and in 10% for rifampin. This fact implies a big handicap in the treatment of MRSE prosthetic valve IE, which requires triple combined therapy with vancomycin and two other agents (gentamicin and rifampin).
Enterococcal IE also represents a challenge since high-level aminoglycoside resistance has increased in *E. faecalis* during the last decade, reaching 50% in some settings. Vancomycin resistance is found in almost 80% of *E. faecium* strains in the USA and is also growing in other species. Meanwhile, resistance to daptomycin, a promising antibiotic alternative, has also been described in enterococci. Thus, multidrug-resistant enterococci are becoming almost untreatable.
Finally, the rate of penicillin-resistant Viridans group streptococci from patients with IE has remained low during last years. However, although these strains are susceptible to daptomycin, our group has recently described a rapid "in vitro" and "in vivo" development of high-level daptomycin resistance (MIC $\geqslant$ 256 mg/L) after daptomycin exposure, mainly in *Streptococcus mitis* group.

SY.6.2
WHAT IS NEW IN THE PATHOGENESIS AND TREATMENT OF ENTEROCOCCAL ENDOCARDITIS

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Enterococci continue to be the third most common cause of community-acquired infective endocarditis (IE), behind staphylococci and streptococci, and are second when IE is hospital-acquired. *E. faecalis* causes the vast majority of enterococcal IE and, fortunately, less than 5% of *E. faecalis* isolates are resistant to vancomycin or ampicillin. While aminoglycoside high-level resistance has caused considerable clinical concern for the treatment of IE by this species in the past, recent published data strongly support the use of ampicillin plus ceftriaxone even for isolates lacking this resistance. Many bacterial factors are known to be important in the pathogenesis of experimental IE, including pili, collagen adhesins, gelatinase, and aggregation substance, among others. Our recent efforts have been directed towards passive prevention against experimental *E. faecium* IE by targeting some of these factors in this more problematic species. In the USA, 80% of clinical isolates of this species are vancomycin resistant and 90% are highly ampicillin resistant; the recent emergence of vancomycin-resistant *E. faecium* that are also resistant to daptomycin threatens our usual "go to" alternative for life-threatening VRE infections, such as endocarditis. Given the paucity of new antibiotics in the drug development pipeline, effective preventative measures such as passive immunization or prevention of GI colonization, the predecessor of infection, has the potential to play an important role in controlling this multi-drug resistant species.

SY.6.3
PRESENT CHALLENGES IN THE TREATMENT OF FUNGAL ENDOCARDITIS

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The last few decades have witnessed profound changes in the topic of fungal endocarditis:
Epidemiology: While it used to affect mostly intravenous drug users and patients who underwent valvular surgery with sub-optimal infection control procedures, fungal endocarditis is now mostly observed in patients with severe immunodeficiency (onco-hematology), in association with chronic central venous access. Overall, its incidence has probably decreased, at least in developed countries with access to harm reduction policies (i.e. needle-exchange programs).
Diagnosis: The use of specific blood culture bottles for the diagnosis of fungal endocarditis has decreased due to the optimization of media and automated culture systems. Meanwhile, the advent of rapid techniques, including polymerase chain reaction (including universal fungal PCR, targeting 18S rRNA genes), spectroscopy, and antigen detection – galactomannan, mannan/anti-mannan antibodies and (1,3)-β-d-glucans – shall improve sensitivity, and reduce diagnosis delay, although limited data are available on their use for the diagnosis of fungal endocarditis.
Treatment: Some of the antifungal agents available since the early 2000s represented dramatic improvement in the medical treatment of fungal endocarditis: (i) voriconazole significantly improved survival in patients with invasive aspergillosis, as compared to amphotericin B, and it probably applies to *Aspergillus* sp. endocarditis as well, although its prognosis remains dismal; (ii) a new class, echinocandins, is now regularly used for the treatment of invasive candidiasis, and has the potential to significantly improve candida endocarditis, due to its fungicidal effect on yeasts, and the tolerability and linear pharmacokinetics of increased dosages for some candins (e.g. micafungin). The combination with flucytosine remains advised by some experts, despite limited evidence-based data.
All together, these improvements shall improve the prognosis of fungal endocarditis, and even allow selected patients to be cured with prolonged medical treatment alone, when surgery is considered too risky.

Session 7 – Resistance and cidality in Gram-positives

SY.7.1
CURRENT RESISTANCE IN GRAM-POSITIVES

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Sixty years of antibiotics have marked an epochal change in the treatment of infectious diseases, bringing some authors, in the past, to make positive predictions on the disappearance of infections, at least in industrialized countries. Not only was this prediction shown to be false, but the use and misuse of these important weapons in veterinary, animal and plant agriculture and aquaculture have contributed to increase the selective pressure responsible for the survival and spread of resistant bacteria, now more frequently defined as multi-drug resistant. Bacteria have established a complex and diverse pool of genes, called the *resistome*, which protects them against antibiotics used therapeutically. But the bacterial response to antimicrobial use has not been limited to the acquisition of resistance genes: bacteria have also developed means for stabilizing the resistance phenotype, sometimes in a multi-step fashion, thus dashing initial hopes of possible reversion to susceptible phenotypes by simply reducing antibiotic use.
Mechanisms and genetics of resistance in Gram-positive cocci (above all staphylococci and enterococci) are many and various, ranging from the role of target site alterations, hydrolytic and efflux mechanisms, adaptive resistance to antibiotics, subtle changes in metabolic gene targets, and the fitness and virulence of resistant strains. These have almost paralleled the current use of antimicrobial agents.
In *Staphylococcus aureus,* above all methicillin-resistant, *one* of the most important human pathogens that is a major cause of hospital-associated infections, multiple resistance is now common. The globally distributed 34 major distinct lineages of MRSA possess a complex genetic machinery able to facilitate host specificity, resistance behaviour and virulence. Genetically, they undergo a continuous shuffling process so that new lineages can show advantages in survival in different hosts and in different environments, and this is demonstrated by the changing epidemiology that has transformed a classical nosocomial pathogen – dealing with hospital hygiene and infection control problems – into a community pathogen with all

the associated problems of massive diffusion. MRSA has recently become heteroresistant to both glycopeptides (hVISA and VISA); some of them are linezolid-resistant and strains with a profile of non-susceptibility to daptomycin are emerging in clinical practice. With regard to enterococci, many studies in recent years have indicated that nosocomial strains have acquired traits involved in resistance and virulence, rendering these strains impervious to any antibiotic therapies.

In conclusion, mechanisms of resistance are becoming even more complex and require a different view in terms of approaching the problem: continuous monitoring is necessary, but also studies on interactions with hosts and multidisciplinary strategies are absolutely necessary.

SY.7.2
MIC CREEP: DOES IT EXIST?

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The term MIC creep commonly refers to vancomycin mean or modal MIC elevation, within the susceptible range over a number of years, in clinical isolates of *Staphylococcus aureus* (meticillin susceptible – MSSA, or resistant – MRSA) in a given population. It is a widely observed and published observation all around the world, but some papers do not describe it and it seems most likely that methodology of published studies is critical as to whether it is observed. Strain or clone type may also be a critical factor.

There are many technical issues to be considered in measuring vancomycin MICs. The drug has a very narrow therapeutic window and with the recent reduction in breakpoint to 2 mg/L, this is only two doubling dilutions from the wild type MIC, so there isn't much room for experimental variation. MIC is also method dependent, with gradient tests usually yielding higher results than the commonly used microbroth dilution methods, possibly due to a better ability to detect low numbers of cells with elevated MIC as gradient methods use a higher inoculum. Elevated MIC within the susceptible range certainly seems clinically important in yielding a poorer clinical response on vancomycin treatment. This is also true when a semi-synthetic penicillin is used for MSSA, which suggests more changes are occurring in these organisms than just an elevated vancomycin MIC. These issues are heightened by the narrow therapeutic window of vancomycin and its poor activity, even for fully susceptible strains. So both the technical measurement of the vancomycin MIC and its therapeutic efficacy are on a knife edge, and hence the great debate about whether MIC creep really exists.

Probably the most important issues in discussion at the moment are the influence of organism storage prior to measurement of MIC, the mechanisms of a raised MIC, and are these resistance mechanisms stable on storage. I am not aware of any work on the last point, although it is well described that VISA and hVISA strains can lose their reduced susceptibility on freezing over time. The mechanisms of elevated MIC to vancomycin are complex and many but basically seem to take the form of multiple mutations, sequentially acquired as the MIC elevates until ultimately perhaps, full VISA status may be obtained.

SY.7.3
COMBINATION TG+HERAPY FOR GRAM-POSITIVES – WHAT ARE THE ADVANTAGES?

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Background: Severe, life-threatening infections often urge physicians to use a combination of antibiotics in order to increase the probability of a successful outcome. A number of contemporary guidelines suggest the use of such combinations without proper evidence for its utility. The objective of this presentation is to review recent papers on the clinical utility of combined treatment for Gram-positive infections.

Methods: Extensive review of papers reported on PubMed. Key words used are: combined treatment, Staphylococcus, Enterococcus, Streptococcus, gentamycin, aminoglycosides, rifampicin, endocarditis, blood stream infections.

Results: In the treatment of endocarditis even the newest guidelines suggest the use of gentamicin in the treatment of staphylococcal native-valve endocarditis admitting that such a suggestion is not supported by appropriate clinical trials. In recent years there has been an increase in the amount of data suggesting that the risk of nephrotoxicity might outweigh its potential benefits. Future guidelines will probably reconsider the value of addition of gentamycin to beta-lactams or glycopeptides in the treatment of staphylococcal endocarditis. Although combined ampicillin–gentamycin treatment is strongly recommended for the treatment of enterococcal endocarditis, new studies show that a combination of ampicillin and ceftriaxone improves outcome of patients with enterococcal endocarditis compared to an ampicillin combination with aminoglycosides, particularly in patients with a high level of aminoglycoside resistance. In the treatment of viridans streptococci associated IE aminoglycosides are recommended although the only clinical trial available did not support their use. However, numerous experimental data both *in vitro* and *in vivo* justify their administration. New combinations are emerging. Tygecycline combined with rifampicin for the treatment of infections associated with biofilm formation, and daptomycin plus rifampicin in the treatment of enterococcal and staphylococcal endocarditis are challenging.

Conclusion: Although a number of suggested combinations is scarcely supported by evidence from clinical trials, we may expect that the use of combinations will in increase in the future due to the emergence of new resistance problems.

Session 8 – Controversies in the prophylaxis of infective endocarditis

SY.8.2
INCIDENCE OF INFECTIVE ENDOCARDITIS DUE TO VIRIDANS GROUP STREPTOCOCCI BEFORE AND AFTER PREVENTION GUIDELINES CHANGES

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Due to recent restrictions in antibiotic administration promulgated by guidelines that address the prevention of infective endocarditis, continued monitoring of the incidence of infective endocarditis was deemed warranted at the time of publication of the restrictions. To date, four investigations from three different countries have provided data on incidence of infective endocarditis, particularly that due to viridans group streptococci. Three of the four studies were population-based and involved cohorts in the United Kingdom, France, and the United States. Findings were consistent across the four surveys; no increase in infective endocarditis due to viridans group streptococci has been demonstrated. A major limitation of these studies is the lack of verification that antibiotic administration did not occur, particularly in high-risk patients (those with prosthetic valves), despite guidelines recommendations that recommend that no prophylaxis be given in the setting of dental procedures. Continued monitoring of the incidence of infective endocarditis is being done.

SY.8.4
CAN WE REDUCE THE INCIDENCE OF HEALTH-CARE ASSOCIATED IE?

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The incidence of health-care associated (HCA) native endocarditis (IE) in the largest available study from the International Collaboration on Endocarditis including the 2000–2005 period was 34% (Benito, Ann Intern Med. 2009). HCA IE patients had mainly *S. aureus* infections (half of them methicillin-resistant) and greater mortality rates. Forty-six percent of HCA IE were non-nosocomial. Most recent studies point to a notable progressive increase in the proportion of HCA IE. A third of the episodes are catheter-related, which confers a leading role to catheter-related bacteremia management, including its prevention in the hospital, but also in the outpatient setting (cuffed and tunneled

catheters for hemodialysis and chemotherapy in cancer patients, anti-infective surfaces, etc.). Notably, evidence-based strategies and interventions, also known as "zero bacteremia" protocols, proved to decrease the rate of infection from 2.7 per 1000 catheter-days to 0 in 3 months and a reduction of 66% of catheter-related infection at 16 to 18 months after implementation (Provonost, NEJM 2006).
Another essential pack of measures reflected on current guidelines (Bratzler, Am J Health-Syst Pharm 2013) are focused on the antimicrobial prophylaxis of cardiac device insertion procedures: valve replacement and implantation of cardiovascular electronic devices. Recent studies have confirmed that *S. aureus* decolonization of the anterior nares decreases the rate of surgical site infections (SSI) in many surgical patients. The data are most compelling in cardiac surgery patients. In addition to antibiotic prophylaxis, antiseptic preparation of the insertion field in a properly organized and sterile setting, accomplishing the conditions of a real operation room is indispensable for placing pacemakers and defibrillators. Remarkably, these measures should also be applied in generator system changes. Cephalosporins have been the most studied antimicrobials for the prevention of SSI in cardiac procedures. Both first-generation (cefazolin) and second-generation (cefamandole and cefuroxime) cephalosporins have been shown to be effective in reducing SSI in cardiac surgery. Vancomycin should be considered in patients who are colonized with MRSA or for beta-lactam-allergic patients.
Finally, health-care personnel training on strict hygiene measures, effective handwashing and well-established specific protocols for each centre are called for to be generalized. This includes isolation measures for resistant microorganisms, constant revision of antimicrobial empirical treatments and ensuring homogenous accomplishment of realistic goals under strict supervision. All these measures will reduce the rate of health-care associated infections and therefore the risk of bacteremia and HCA IE.

Poster abstracts

P01
INFECTIVE ENDOCARDITIS: EPIDEMIOLOGICAL AND THERAPEUTIC ASPECTS IN AN URBAN POPULATION – ROME, ITALY. RETROSPECTIVE STUDY

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Objectives: To evaluate the epidemiological and therapeutic aspects, both medical and surgical, in patients with native or prosthetic infective endocarditis.
Background: Infective endocarditis (IE) still represents an important disease. The incidence of IE ranges from 3 to 10 episodes/100,000 person-years. Prosthetic valve endocarditis (PVE) is the most severe form of IE. It accounts for 10–30% of all cases of IE. Surgical treatment is used in approximately half of patients with IE because of severe complications. Yet, surgical therapy during the active phase of the disease is associated with significant risk.
Methods: Between 2009 and January 2011, 45 patients were admitted at Cardiac Surgery Division or at Infectious Disease Department of Tor Vergata Hospital in Rome (Italy) with diagnosis of IE. All the data were retrospective collected.
Results: The study included 45 patients with IE, 39 men and 6 women, with a mean age of 59±15 years (1 DS). The main presenting symptoms or signs were episodic fever, bacteremia or sepsis, embolism and heart failure. The diagnosis based on Duke criteria could be considered definite in 37/45 patients (82%). 21 patients had a PVE and 24 NVE. *Streptococcus* spp. was the most important cause of infection in patients with NVE and *Staphylococcus* spp. in patients with PVE. An embolic complication occurred in 17 patients (10 with PVE and 7 with NVE; P = 0.05). Because of persistent valve infections and despite antibiotics treatment, 17 out of 45 patients underwent surgical operation: 11 out of 17 had a PVE (64%). Cerebral embolism (P = 0.05) and type of valve (P = 0.03) were the most important mortality risk factors.
Conclusions: IE still represents a cause of mortality, despite major advances in both diagnostic and therapeutic procedures. Severe complications of the infection are more common in patients with PVE. An optimal coordination between clinical and surgical physicians is needed in these difficult cases of IE.

P02
AN EPIDEMIC OF INFECTIVE ENDOCARDITIS AT THE CROSSROADS OF DRUG TRAFFIC

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Purpose: To analyze the recent changes in clinical picture and treatment of infective endocarditis (IE) of intravenous (i/v) drug users in Novosibirsk city.
Methods: Observational cohort study conducted from 2008 through 2012 at Novosibirsk city among 300 i/v drug users (morphine, heroin, hydromorphone, codeine, methadone, fentanyl, desomorphine; average age 26.1 yrs) with IE (Duke criteria).
Results: The incidence of IE increased 10-fold, reaching 150 cases per 1 mln/year – increasing share of i/v drug addicts. Etiologically the change is characterized by a reduction of streptococci and a much higher incidence of staphylococci (>70%), Gram-negative bacteria, fungi and mixed virulent organisms. In all patients the clinical course of IE was with systemic affection of internal organs of thromboembolic, microvascular and toxic genesis. Necrotic vasculitis of the lower extremities developed in 44% of patients. Eradication of staphylococci with vancomycin or daptomycin, >8 mg/kg/day for 4–6 weeks, was obtained in 85% of IE patients with replacing heart valves in 70%. Mortality at discharge was 25%, at six months 35%. Russia has now become an absolute world market for opiates in the world (20%). From Afghanistan to Russia are smuggled at least 12 tons of heroin – 3 billion single doses. Every day 100 people die from overdoses, 30,000/year. Now the probability that drug addiction hooks at least one of the children in the Russian families reaches 25%.
Conclusions: IE of i/v drug addicts are a new challenge in the way of drug trafficking from Afghanistan to Europe involving Novosibirsk city area. The exponential growth of this challenge because of changes in the drug traffic, the evolution of opiods, antibiotic resistance of pathogens and bad prognosis make it necessary to draw attention of the whole society to this problem.

P03
STAPHYLOCOCCUS AUREUS IN THE AETIOLOGY OF INFECTIVE ENDOCARDITIS IN SLOVAKIA DURING THE LAST SIX YEARS

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Objectives: In the 21st century infective endocarditis (IE) is more often an acute disease, characterized by a high rate of *Staphylococcus aureus* in aetiology. The aim of this study was to compare the risk factors and outcome of IE due to *S. aureus* (SAIE) in 2007–2012 in Slovakia.
Methods: In this study we compared risk factors and outcome of SAIE in Slovakia (population about 5 million) during last six years. Thirty-four medical centers participated in this longitudinal observation nationwide survey and 449 cases of infectious endocarditis were reported. Duke criteria were used as inclusion criteria. Chi-square test, Fisher's exact test and t-test computerized with the open-source statistical package "R" were used and a P value <0.05 was considered statistically significant.
Results: A total of 449 patients (73.5% male, average age 56.4±16.71, range 22–85 years) with definite IE were included. *Staphylococcus*

aureus in aetiology was identified in 98 cases (21.8%), of them only five cases of MRSA and one case of VRE. In 37 cases (37.8%) the aortic valve and in 32 (32.7%) the mitral valve was infected. There were only 46 cases of right-side endocarditis. The significant risk factors were previous bacteraemia (52.0% vs. 38.5%, OR = 1.74, 95% CI 1.12–2.73, P = 0.02), i.v. drug abuse (7.1% vs. 1.7%, OR = 4.42, 95% CI 1.45–13.48, P = 0.001), dialysis (14.3% vs. 4.8%, OR = 3.27, 95% CI 1.55–6.91, P = 0.002). Concerning complications, more patients with SAIE had heart failure (41.8% vs. 28.5%, OR = 1.81, 95% CI 1.14–2.87, P = 0.01). In-hospital mortality was 10.2% and did not differ comparing in-hospital mortality of IE with other aetiology (10.2% vs. 11.4%, P = 0.74).
Conclusions: Only a few MRSA were recorded in the aetiology of SAIE during the period 2007–2012 in Slovakia, and the majority of SAIE were identified in patients with previous bacteraemia, dialysis and drug abuse. Heart failure as a complication was more prevalent and in-hospital mortality reached 10.2%.
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P04
PREVALENCE OF ENDOCARDITIS AMONG PATIENTS WITH PROSTHETIC HEART VALVES AND *STAPHYLOCOCCUS AUREUS* BACTEREMIA

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Background: *Staphylococcus aureus* is a highly virulent pathogen and one of the leading causes of bacteremia. Infective endocarditis (IE) is a major concern in patients with prosthetic heart valves and who present with *S. aureus* bacteremia (SAB). The aim of this study was to define the prevalence and outcome of prosthetic valve endocarditis (PVE) in a cohort of patients with SAB and underlying prosthetic heart valves.
Methods: We performed a retrospective review of all adults (age ⩾18 years) hospitalized at Mayo Clinic from July 2006 through June 2011 with SAB who had prosthetic heart valves. Clinical manifestations, comorbidities and outcomes during a 3-month follow up period were reviewed. PVE was defined using modified Duke Criteria.
Results: A total of 47 patients with prosthetic valves and SAB were identified. Overall, 42% of patients had mechanical, 46% had bioprosthetic and 12% had annuloplasty rings. 94% of patients underwent transesophageal echocardiography (TEE) and 6% had transthoracic echocardiography only. 32% of patients met modified Duke Criteria for definite PVE. TEE showed evidence of para-valvular abscess in 4 patients (9%). The frequency of PVE was 62.5% in community-acquired SAB, 29.6% in community-onset healthcare associated SAB and 16.6% (2/12) in nosocomial SAB. The prevalence of endocarditis did not differ significantly in patients with aortic vs. mitral prosthesis (22.6% vs. 50%, p = 0.19) and mechanical vs. bioprosthetic valves (33.3% vs. 27.27%, p = 0.75). The 12-week all-cause mortality rate for patients with SAB and prosthetic valves was 36% and was higher among those with PVE (54% vs. 28%, p = 0.17).
Conclusions: One-third of the patients who presented with SAB and had underlying prosthetic heart valves had evidence of definite PVE. The prevalence of PVE was independent of the type and location of the prosthetic valve. Our findings support current guidelines that recommend TEE in all patients with SAB and underlying prosthetic heart valves.

P05
STAPHYLOCOCCUS AUREUS BACTEREMIA: FACTORS ASSOCIATED WITH INFECTIVE ENDOCARDITIS

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Background: In the context of recently increasing incidence of *Staphylococcus aureus* infective endocarditis (IE), we aimed to identify the factors associated with IE in case of *S. aureus* bacteremia (SAB).
Methods: The VIRSTA study is a prospective cohort enrolling all SAB observed in 8 University Hospitals in France between April 2009 and December 2011. Factors associated with definite IE according to Duke-Li criteria were analysed using multivariate logistic regression.
Results: A total of 2008 cases of SAB were included (men: 65%, median age: 70 years). SAB was nosocomial in 55%, non-nosocomial health-care related in 18% and community-acquired in 27% of cases. Presumed portal of entry was unknown in 20% of cases and the most frequent was vascular access (18%). *S. aureus* was methicillin resistant in 13% of cases. An echocardiography was performed in 60% of patients. A definite IE was diagnosed in 11% of SAB enrolled. The proportion of IE was 20% in community-acquired SAB, 12% in non-nosocomial health-care related SAB and 7% in nosocomial SAB; it was 7% in patients without predisposing cardiac condition. In-hospital mortality was 26% in the whole population and 35% in IE cases (p = 0.003). Factors significantly associated with IE were injecting drug use (IE: 38%, adjusted odds-ratio (aOR) = 5.7), community acquired SAB (aOR = 3.8), non-nosocomial health-care related (aOR = 2.4), presence of a prosthetic valve (IE: 33%, aOR = 9.8) or of a native valvular disease (IE: 20%; aOR = 4.3), time >24 hours between first symptoms of SAB and performance of blood culture (IE: 15%; aOR = 1.5) and C-reactive protein >190 mg/L (IE: 15%; aOR = 2.2).
Conclusions: IE is a severe complication of SAB. Its frequency is high, even in case of nosocomial infection and in the absence of known predisposing factor.

P06
STAPHYLOCOCCUS AUREUS INFECTION IN SURGICALLY TREATED ACUTE INFECTIVE ENDOCARDITIS: DIFFERENCES BETWEEN MULTIRESISTANT AND MULTISENSIBLE STRAINS?

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Background: Acute infective endocarditis (AIE) is a life threatening disease with a high mortality rate. Whether patients with multiresistant *Staphylococcus aureus* (MRSA) compared to multisensible *Staphylococcus aureus* (SA) are at increased risk is not known.
Methods: Between 10/1994 and 12/2012 a total number of 1710 patients (pts) (69.9% male, age 62±15 years) were operated due to AIE at our institution. 1383 (80.9%) of these had positive blood cultures: monoinfection was found in 1184 (85.6%). *Staphylococcus aureus* strains were isolated in 374 pts: SA in 355 (94.9%), MRSA in 19 (5.1%). For these two groups' perioperative risk factors, Cox-regression, Kaplan–Meier-curves were generated.
Results: Age, gender, number of infected valves and NYHA classification were not significantly different between SA and MRSA except for preoperative laparotomy (8.5% vs. 26.3%; p < 0.001), gastrointestinal focus (7.6% vs. 26.3%; p = 0.005), preoperative tracheotomy (1.4% vs. 10.5%; p = 0.004) and ejection fraction (55.7±12.5 vs. 53.6±16.9; p = 0.018). However, the SA group showed in the postoperative period significantly less need for catecholaminergic support (70.8% vs.

94.7%; p = 0.024) and gastrointestinal complications (7.0% vs. 21.1%; p = 0.026). Overall 30-day mortality was 22.1% with no differences between SA and MRSA (22.1% vs. 22.2%; p = 0.990). Sepsis as cause of death was seen in 58 pts (56 in SA and 2 in MRSA; p = 0.538). Gastrointestinal reasons for death were observed in 20 pts (16 in SA and 4 in MRSA); these were highly significant (p = 0.002). Kaplan–Meier survival curves showed no statistical differences (log-Rank = 0.170).

Conclusions: *Staph. aureus* is a common isolate in positive blood cultures from patients with AIE (32%); only 5% of them are MRSA. Laparotomy, gastrointestinal focus and associated tracheotomy for long-term ventilation before valve surgery may be the reasons for AIE due to MRSA and therefore hospital acquired. MRSA patients need in the postoperative period more catecholaminergic support and have significant more gastrointestinal complications. Therefore more MRSA patients died due to gastrointestinal causes. However, 30-day mortality and long-term survival is not different between SA and MRSA.

P07

STAPHYLOCOCCUS AUREUS PROSTHETIC VALVE ENDOCARDITIS (SAPVE): CURRENT FEATURES DEPENDING ON TIME TO DIAGNOSIS

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Prosthetic valve endocarditis (PVE) is a severe disease with a high mortality; knowing the clinical presentation may help to an earlier diagnosis.

Material and Methods: Prospective, observational, multicenter study. SAPVE was classified depending on the time from valve substitution as early (EPVE): ⩽8 weeks, intermediate (IPVE): 9 weeks to 1 year, or late (LPVE): >1 year. Diagnosis delay was defined as diagnosis made more than 15 days after presentation.

Results: 342 episodes of PVE from 1996 to 2013. SA was isolated in 54 (15.8%). EPVE: 11 cases, 20.4%; IPVE: 10, 18.5%; LPVE: 33, 61%. There was diagnosis delay in 16 patients (29.6%): 9% EPVE, 30% IPVE, 36% LPVE (p 0.17). 59.3% of SA were oxacillin sensitive, 55% in EVPE, 44% in IPVE and 82% in LPVE (p 0.06). EPVE presented as fever and severe dyspnea (EPVE 36%, IPVE 20%, LPVE 12%, p 0.22), fever plus septic shock (EPVE 36%, IPVE 10%, 12% LPVE, p 0.18). IPVE presented as fever plus new murmur (EPVE 0%, IPVE 30%, LPVE 6%, p 0.05) and fever plus auriculoventricular block (EPVE 0%, IPVE 20%, LPVE 9%, p 0.20). LPVE presented as systemic embolism (18% EPVE, 20% IPVE, 30% LPVE, P 0.64). There was valvular insufficiency in 45% EPVE, 90% IPVE and 72% LPVE (p 0.06). Absence of vegetation in 45% EPVE, 20% IPVE, 12% LPVE (P 0.08). 30 patients died (55.6%). Death during hospitalization was 36% EPVE, 70% IPVE, 51% LPVE (p 0.29). Acute heart failure was the cause of death in 40% EPVE, 0% IPVE and 27% LPVE (p 0.10). Multi-organ failure caused the death in 40% EPVE, 57% IPVE, 11% LPVE (p 0.05).

Conclusions: Some clinical, microbiological and echocardiographic features differ depending on the time of diagnosis. Frequency and causes of death are also different; EPVE seems to be the one with the best prognosis.

P08

PANCARDITIS AND BACTEREMIA BY *STAPHYLOCOCCUS AUREUS*

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The patient was a man, 35, who was diagnosed 15 days after birth with a congenital heart defect. At 5, an only ventricle was found with a pulmonary valve stenosis, levo-TGA, atrial septal defect and atresia of the right auricular appendix. He underwent a successful surgery (Fontán Clásico). When he was 24, he suffered from a pulmonary TB (he took a treatment for 6 months). Siince 2006, he suffers from atrial fibrillation. In May 2012, he was hospitalized in the cardiology service because of a cardiac insufficiency in partial treated bacterial meningitis, pneumonia and urinary tract infection.

His symptoms were fever, vomiting and jaundice with choluria. During examination, he presented a systolic murmur in mesocardium and no more important findings. In the blood test results stood out the hemolytic anemia and thrombocytopenia. *Staphylococcus aureus* sensitive to methicillin was found in the extracted blood cultures. Due to these results, several image tests were ordered:

- Transthoracic echocardiogram: no evidence of endocarditis. Left ventricle had normal size and worked properly. The right auricular appendix had moderate insufficiency. There were dilations on the inferior vena cava and the suprahepatic inferior vena cava.
- Abdominal ultrasound: there was an increase of the quality of the inferior vena cava and the suprahepatic inferior vena cava.
- Gammagraphy with labeled leukocytes: In the second reading there was a high pathological gathering in the cardiac shape and the beginning of big vessels suggesting **pancarditis**.

To sum up, the patient was a young man with a congenital heart defect who was hospitalized with hemolytic anemia and thrombocytopenia related with an infectious process (*S. aureus* sensitive to methicillin). After dismissing endocarditis through an echocardiogram, we decided to complete the study with a Gammagraphy in wich we observed signs compatible with **pericarditis**. We started an empiric treatment (ampicillin, cloxacillin and gentamicin) wich was readjusted later with antibiogram (cloxacillin and rifampicin). Nowadays, he is evaluated by the Cardiology service.

JC: PERICARDITIS. BACTEREMIA BY S. AUREUS. HEMOLYTIC ANEMIA AND SECONDARY THROMBOCYTOPENIA

Conclusions: *Staphylococcus aureus* is the second global cause of bacteremia and the first cause of bacteremia in Europe. It constitutes the most frequent etiologic agent of endocartitis. In the last few years, bacteremia has risen because of *S. aureus* in association with intravascular mechanisms and resistant strains to antibiotics. The most important thing about this case if that the patient has a *S. aureus* sensitive to methicillin, however; he is able to produce a pericarditis.

P09

FIBRIN DEPOSITION DUE TO *STAPHYLOCOCCUS AUREUS* COAGULASE ACTIVITY CONTRIBUTES TO THE PATHOGENESIS OF *S. AUREUS* CATHETER INFECTIONS

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Staphylococcus aureus, a frequent cause of catheter-related infections (CRI), induces fibrin formation through the secretion of the coagulases staphylocoagulase (coa) and von willebrand factor-binding protein (vWbp), which bind to and activate the host prothrombin. This resulting staphylothrombin is insensitive to heparins, but can be inhibited by small-molecule direct thrombin inhibitors such as dabigatran.

We studied the effect of pharmacological inhibition or genetic absence (coa-/vwbp-negative mutant) of coagulases on fibrin formation and bacterial retention to catheter fragments in vitro, as well as in a mouse model of jugular vein catheter infection.

S. aureus catheter infections were characterized by early fibrin deposition, as noted on fluorescence microscopy and SEM of catheter fragments inoculated with a Newman wild-type (Figure 1A), but not with a coa-, vwbp- mutant (Figure 1B). Dabigatran, but not enoxaparin, prevented the formation of this fibrin sheat (Figure 1C). Staphylothrombin-mediated fibrin deposition increased bacterial retention on catheter fragments in vitro a 1000-fold (6.04±0.55 log vs 3.00±0.23 log CFU/mL, p < 0.001), and staphylothrombin inhibition significantly reduced the retention of *S. aureus* (4.20±0.42 log CFU/mL, p < 0.001). Prevention of fibrin deposition by genetic inactivation or pharmacological inhibition of coagulases improved the efficacy of vancomycin towards catheter-grown *S. aureus*. In the mouse model, staphylothrombin inhibition reduced the bacterial load on catheters (5.74±0.18 log vs 7.02±0.15 log CFU/mL, p < 0.05; Fig1D), as well as in the kidneys (4.80±0.50 log vs 6.61±0.37 log CFU/mL, p < 0.01; Figure 1E). The combination of staphylothrombin inhibition with vancomycin had an additional effect compared to either treatment

alone ($p < 0.001$ vs vancomycin alone and $p < 0.01$ vs dabigatran alone) (Figures 1D,E).
Activation of prothrombin by coagulases and subsequent fibrin deposition contributed to bacterial retention to catheters as well as metastatic infectious complications. Inhibition of staphylothrombin-driven fibrin deposition reduced bacterial load and improved antibiotic susceptibility of *S. aureus* grown on catheter fragments in vitro and in vivo.
[GRAPHIC]P09.tif[/GRAPHIC] [CAPTION]Figure 1.[/CAPTION]

P10
CONTRIBUTION TO INFECTIVE ENDOCARDITIS BY *STREPTOCOCCUS BOVIS* IN ALBANIA

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Introduction: *Streptococcus bovis* is now evidenced as a cause of infective endocarditis. The subjects of this specific infection are those suffering of gastrointestinal pathologies.
Aim: Introducing epidemiological, clinical and therapeutic aspects of the first cases with infective endocarditis by *Streptococcus bovis* in Albania.
Patients: Two cases of endocarditis by *Streptococcus bovis*.
Method: We analyzed infective, cardiological, therapeutic features of these cases.
Case 1. Male, 56 years old, hospitalized in 2010, as F.U.O., hepatosplenomegaly, with fever in the last 5 months and diarrhea, sometimes bloody stools during the last 8 months, treated ambulatory. Anamnesis vitae: prolapsed of mitral valve without endocarditis. Objective examination: systolic murmur in apex. Several blood cultures were positive for *Streptococcus bovis*. TTE suggested an infectious mitral verrucous endocarditis, confirmed with TEE. The patient was treated with ampicillin and gentamicin, which dominated fever on the third day. The persistent bacteremia and the intermittent disturbances of defecation required the exploration of the digestive tract which evidenced a rectal adenocarcinoma. It was decided to intervene by surgery initially in colon and then in heart, under antibacterial treatment. Both procedures were successful and the patient is in good condition.
Case 2. Male, 70 years old, hospitalized in March 2011, in Gastrohepatology as hepatic cirrhosis. Soon, the clinical situation was decompensated; the patient had fever with chills. He was treated for three weeks and there was a gradual improvement of hepatic dysfunction. However, the fever persisted and began to associate with dyspnea, fatigue, chest pain, palpitations. In this conditions, the patient was transferred to Cardiology, and TTE evidenced a moderate aortic stenosis, without endocarditis. The case was a good indication for surgery, but the clinical situation was not. Of six blood cultures, four were positive for *Streptococcus bovis*. According to antibiogram, ceftriaxone was started as a therapy with 2 g as daily dose. TEE evidenced 2 verrucas, on coronary sigma of aorta. The cardiosurgeons decided to intervene after antibiotic therapy, which improved toxicosis and the temperature on the fifth day. The replacement of the aortic valve had no complications and presently the patient is in good condition.

P11
MYOCARDIAL ABSCESS AND SUPPURATIVE PERICARDITIS CAUSED BY GROUP B BETA-HAEMOLYTIC STREPTOCOCCI

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Background: Myocardial abscess and purulent pericarditis without endocarditis have been rarely described in literature. Group B beta-haemolytic streptococci (GBS) infections are uncommon in adults and are most commonly associated with diabetes and malignancy. Here we present a 63-year-old patient with myocardial abscesses and purulent pericarditis in the setting of severe sepsis and multiple organ dysfunction syndrome (MODS) caused by GBS with no evidence of endocarditis shown on autopsy.
Case presentation: A 63-year-old female patient with known complications of type 2 diabetes mellitus presented with a two-week history of fever and chest pain. She had been started on clarithromycin three days earlier. At admission the patient was conscious, hypothermic and hypotensive. Physical examination showed marbled skin, an abdominal papular rash, chronic ulceration of her left foot and a systolic heart murmur over the mitral valve. Laboratory tests showed elevated ESR and CRP levels, leukocytosis with neutrophilia, mildly elevated troponine T, liver enzymes, urea and creatinine levels. The chest X-ray and urine sediment were unremarkable.
She was admitted to the ICU and started on ciprofloxacin and vancomycin. Blood cultures were obtained. Electrocardiogram showed ST elevation up to 0.15 mV in leads D2, D3, aVF, aVR and V5–V6. Transthoracic echocardiogram showed a pericardial effusion of 13.4 mm and 2nd degree diastolic dysfunction with no signs of endocarditis. PiCCO measurements showed a reduced cardiac index and reduced peripheral resistance with high central venous pressure (29 mmHg) suggesting shock of mixed etiology (septic and cardiac shock). Due to volume overload and anuria continuous veno-venous hemodiafiltration was initiated. After 18 hrs in the ICU the patient went into cardiac arrest and died despite resuscitation. All blood cultures were positive for GBS susceptible to all tested antibiotics. The autopsy showed a dark purple area 1.5 cm in diameter in the posterior wall of left ventricle and septum. Histological preparation showed large accumulations of leukocytes in myocardium and lots of bacteria. There was 300 mL of thick yellow fluid in the pericardium.
Conclusion: GBS is a pathogen most commonly associated with neonatal infections. The incidence of GBS infection in adult populations has been increasing in recent years. To our knowledge this is the first case of myocardial abscesses and pericarditis without endocarditis caused by GBS.

P12
CLINICAL CHARACTERISTICS AND OUTCOME OF INFECTIVE ENDOCARDITIS AT THE HOSPITAL UNIVERSITÁRIO CLEMENTINO FRAGA FILHO

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Objective: To describe the clinical characteristics and outcome of infective endocarditis (IE) at the Hospital Universitário Clementino Fraga Filho (HUCFF).
Methods: The clinical and outcome data of patients with infective endocarditis admitted at the HUCFF from 1978 to 2012 were reviewed.
Results: 683 episodes of IE were diagnosed in 620 patients from1978 to 2012 (459 definitive and 224 possible according the modified Duke criteria). The male-to-female ratio was 1.8. Patients' age range was 5–87 years (mean 45.9).
In 192 episodes there were one or more comorbidity conditions. Hemodialysis (52), drug addiction (43), diabetes mellitus (41), HIV (31) and cancer (22) were the more frequent comorbidities.
One or more underlying cardiac conditions were present in 396 episodes [prosthetic valve (120); bicuspid aortic valve (56); mitral valve prolapse (34), rheumatic valvulopathy (30), other acquired valvulopathy (101), previous episode of IE (79) among other less frequent].
Native valve (NVE) was involved in 70%, prosthetic valve in 14.6% and 2.9% in other locations. In 12.5% the site of the infection was not defined. The mitral, aortic and tricuspid valves were involved in 38.8%, 21.5% and 8.8% respectively. In 14 patients with prosthetic valve the infection was not in the prosthesis.
Echocardiography found vegetation or abscess or new valvular dehiscence in 553 episodes. Blood culture yielded positive results

in 368 (54%) episodes. The most common organisms were *Staphylococcus aureus* (141), *Streptococcus viridans* (99), *Enterococcus* (40), coagulase-negative staphylococci (28), Gram-negative bacilli (22), *Streptococcus gallolyticus* (18) and Fungi (14).
Cardiac surgery for active IE was performed in 212 episodes, with 77 (32.3%) deaths. In-hospital mortality was 33.5%.
Conclusion: IE was more frequent in males. Comorbidities and underlying cardiac conditions were common. *Staphylococcus aureus* was the most common causative organism. The number of negative blood culture was high. The in-hospital mortality was high.

P13
HEALTHCARE-ASSOCIATED INFECTIVE ENDOCARDITIS: ANALYSIS OF CASES AT A CARDIAC SURGERY REFERRAL HOSPITAL, RIO DE JANEIRO, BRAZIL, 2006–2011

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Background: Healthcare-associated infective endocarditis (HCAIE) is a severe complication of medical care, with a growing incidence.
Aim: To evaluate HCAIE as to its epidemiology, etiology, risk factors for acquisition, complications, surgical treatment and outcome.
Methods: Observational prospective case series study, 2006–2011, in a public hospital in Rio de Janeiro.
Results: Fifty-three patients with HCAIE in a total of 151 (35%) cases of IE were included. There were 26 males (49%), 27 females (51%). Presentation was acute IE in 37 (70%) and subacute IE in 16 (30%). Mitral valve was affected in 19 (36%) and the aortic valve in 12 (36%). Prosthetic valves were affected in 23 (43%), native valves in 30 (57%). Early prosthetic valves (2–12 months) were affected in 20/23 (87%). Deep intravenous access was used in 43 (81%). Negative blood cultures were seen in 11 (21%), *Enterococcus faecalis* in 10 (19%), *Staphylococcus aureus* in 9 (17%), *Candida* sp. in 7 (13%), coagulase-negative staphylococci in 6 (11%). Fever was present in 49 (92%), splenomegaly in 12 (23%), new regurgitation murmur in 31 (58%), elevated C-reactive protein in 44/53 (83%). Echocardiograms showed major criteria in 46 (87%). Thirty-four patients (64%) were submitted to cardiac surgery. Overall mortality was 17/53 (32%).
Conclusion: HCAIE in Brazil affected younger patients. Prosthetic and native valves were affected in a similar proportion. Non-cardiac surgery was an infrequent predisposition while intravenous access was common. *S. aureus* was significantly more frequent in native valve HCAIE. Mortality was high.

P14
TREND OF INFECTIVE ENDOCARDITIS IN TWO UNIVERSITY HOSPITALS IN RIO DE JANEIRO, BRAZIL

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Infective endocarditis (IE) remains a condition of important morbidity and lethality, despite new surgical techniques. The aim of this observational study was to report demographic, epidemiologic and clinical characteristics of 62 patients with IE, who were diagnosed at two University Hospitals, in Rio de Janeiro, Brazil.
Patients with community infective endocarditis (CIE) or with healthcare-associated infective endocarditis (HAIE) between June 2009 and February 2012 were followed by two professors of Infectious Diseases. The modified Duke criteria were incorporated with the echocardiography information, history, and physical examination for the diagnosis of IE. The median age of patients was 49.5 years (range 1–87); 33 (53.2%) were male. The most frequent microorganisms were *Staphylococcus aureus* (30.7%) and *Enterococcus* spp. (25%). Prevalence of Gram-positive cocci methicillin or vancomycin resistance was 1%; we had only one case of caMRSA HAIE. *Streptococcus* spp. were more frequent in the CIE (42.8% vs. 3.2% for community vs. healthcare onset) and *Enterococcus* spp. were more frequent in the HAIE ($p = 0.05$). The valve most frequently compromised was the mitral valve (48.1%), and both aortic and tricuspid valves had the same percentage (20.3%). We observed more damage of multiple valves in the HAIE group ($p = 0.05$). Most IE episodes occurred in native valves (90.3%); many patients had cardiopathy (46.7%), immunosuppressive diseases (40.3%), and end-stage renal disease (29%). The overall mortality in the IE group was 43.5%; 16 (44.4%) and 11 (42.3%) died of HAIE and CIE, respectively.
In a stratified multivariate analysis of risk factors related to mortality in IE episodes, age up to 60 years (OR: 8.9; 95% CI: 2.1–3.7; $p = 0.003$) and compromise of the mitral valve (OR: 2.26; 95% CI: 0.9–10.9; $p = 0.05$) were associated independently with mortality. Our group reported 26 (41.9%) CIE and 36 (58.1%) HAIE. We observed an increase of risk for HAIE episodes in immunocompromised patients (OR: 13.9; 95% CI: 3.1–62.1; $p = 0.001$).

P15
RISK FACTORS AND MORTALITY RATES IN DIFFERENT GROUPS OF PATIENTS WITH INFECTIVE ENDOCARDITIS

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Objective: The aim of this study was to assess the value of risk factors in predicting early and late mortality in groups of patients who underwent surgery for infective endocarditis (IE) on the base of single center results.
Methods: The prospective study from 1993 to 2012 represents 364 patients (280 male, 84 female) with IE. The study covered cases of left-sided IE, severe right-sided IE (RSIE), and prosthetic valve endocarditis (PVE). Long-term follow-up was 5 years. The following parameters were used to create subgroups: (1) single-valve infection, n = 176 (48.4%); (2) multivalvular infection, n = 68 (18.7%); (3) paravalvular infection, n = 44 (12%); (4) PVE, n = 37 (10.2%); (5) RSIE, n = 39 (10.7%). Patients with neurological complications were assessed separately. Multivariable logistic regression analysis was performed to find clinical parameters associated with death.
Results: Mean age was 45.4 (14–76) years. In-hospital mortality overall was 12.9%. General 5-year survival was 74.2%. The table presents mortality rates in the subgroups.

	Group 1	Group 2	Group 3	Group 4	Group 5
In-hospital mortality, %	11.36	13.24	18.18	22.3	0
Long-term survival, %	81.92	77.51	67.57	72.0	74.36

The factors for higher in-hospital mortality in general group were: severe heart failure with multisystem disease ($p < 0.05$), neurological complications ($p < 0.1$), multivalvular dysfunction ($p < 0.1$). Predictors of 5-year mortality in the entire group were paravalvular infection and PVE. In groups 1 and 2, patients with severe heart failure also had higher in-hospital mortality ($p < 0.05$). In group 4 the predictor of high in-hospital and late mortality was fungal endocarditis. Surgery of tricuspid valve IE gave good in-hospital and not favorable long-term results.
Conclusions: The results of surgical treatment of IE in Voronezh Region are not far from the conclusions of multicenter studies. We need to save up wider database and to use international registers to work up the ways of management of high-risk patients.

P16
CHANGING PROFILE OF INFECTIVE ENDOCARDITIS IN A TERTIARY UNIVERSITY HOSPITAL: A 6-YEAR EXPERIENCE (2005–2010)

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Introduction: Epidemiological trends in infective endocarditis (IE) are changing all over the world. We describe IE changes at a University Hospital in Athens, Greece, the capital that houses more than 50% of the country population.
Patients and Methods: From 1/1/2005 to 31/12/2010 data on IE from all hospitalized patients was prospectively collected via a registry form and evaluated by experts on the field. Comparison between the early period A (2005–2007) and the late one B (2008–2010) was performed by the Fischer exact test.
Results: From 101 IE patients, 37 referred to period A and 64 to period B. No difference between periods were found for gender (male n = 68, 67.3%), age [mean age 67 (range 23–86 years)], prosthetic valve IE (n = 10), pacemaker IE (n = 9), community acquired IE (n = 81), health-care IE (n = 20), viridans group streptococci (n = 13), enterococci (n = 12), *Coxiella burnetti* (n = 7), fungi (n = 9), Gram-negative bacteria (n = 8), peripheral embolization (n = 33), stroke (n = 12), valve abscess (n = 19), heart failure (n = 34), surgery for IE (n = 49, 48.5%), death (n = 24, 23.7%), and post-surgery death (n = 14). Fever >1 month before IE diagnosis, diabetes mellitus, intravenous drug users (IVDU) and *Staphylococcus aureus* (27% methicillin resistant) were more frequent in period B compared to period A (48.8% vs 62.5%, p = 0.06, 12.2% vs 25%, p = 0.04, 2.5% vs 18.5%, p = 0.03, 19% vs 29.6, p = 0.09, respectively). Empirical antibiotic administration for fever before diagnosis of IE fell from 67.5% in period A to 46.3% in period B (p = 0.02). However, multi-drug resistant (MDR) Gram-negatives (n = 3) emerged in period B at a University Hospital in Athens, Greece. Although surgery is generally available for patients with IE, overall mortality exceeded 20% in our series.

P17
RISING INJECTING DRUG USE ASSOCIATED INFECTIVE ENDOCARDITIS – A MAJOR REGIONAL CENTRE EXPERIENCE FROM 2003–2012

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Background: Infective endocarditis (IE) is associated with high morbidity and mortality. Injecting drug use (IDU) is an established risk factor for IE. A contemporary understanding of IE and IDU epidemiology is important for planning and delivery of health care for this disease. We examined the relationship between IDU and IE over a 10-year period in a single tertiary referral centre.
Methods: Retrospective analysis of two cohorts of consecutive patients (n = 199) admitted to the Geelong hospital diagnosed with Duke definite IE. We utilized the International Collaboration on Endocarditis (ICE) local dataset from 2003–2012. Total number of cases of IE and number of cases related to IDU were compared between two cohorts of patients over two 4-year periods (Cohort 1 2003–2006, Cohort 2 2009–2012). Case data was not available for 2007–2008. Numbers of cases were compared along with proportion of cases associated with IDU.
Results: Comparing from cohort 1 to cohort 2 there has been a notable rise in the proportion of cases associated with IDU, from 4.2% to 14.7% (a rise of 10.5%, 95% CI 1.3–19.7%) with a rise in the number of cases from 5 to 10. Total number of cases of Duke definite IE declined from 119 to 68.
Conclusion: In a large regional centre over the last ten years there has been a decrease in the total number of cases of IE but a significant rise in the total number and proportion of cases associated with IDU. This alarming change may provide useful information to inform clinical and public health care planning in the region.

P18
TRENDS IN RISK FACTORS AND AETIOLOGY OF 1053 CASES OF INFECTIVE ENDOCARDITIS WITHIN 28 YEARS IN SLOVAKIA (1984–2012)

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Objectives: The characteristics of patients with infective endocarditis (IE) vary significantly by region of the world. The aim of this study was to compare the aetiology, risk factors and outcome of IE during seven periods of a nationwide survey on aetiology, risk factors and outcome of infectious endocarditis in Slovakia.
Methods: A longitudinal observation nationwide survey on aetiology, risk factors and outcome of IE in Slovakia (population about 5 million) was performed during 1984–2012. Thirty-four medical centers participated in the study and patients with a definite or possible diagnosis of IE (modified Duke criteria) were included. P-values for trend computerized with the open source statistical package "R" were calculated.
Results: A total of 1053 patients with definite IE were included. *Staphylococcus aureus* was the most common pathogen (34.1%). Negative-culture endocarditis despite better bacteriological techniques was frequently observed in all study periods (33.4%). We observed significant increasing tends in IE due to enterococci (P = 0.002) and persistent IE (3 or more positive hemocultures, P < 0.001). Concerning risk factors, rheumatic fever (P < 0.001), neoplasia (P = 0.002), dental surgery (P < 0.001), tonsillitis (P < 0.001), embolization (P < 0.001), as complications were less frequent in later periods. Vice versa diabetes mellitus (P < 0.001), vitium cordis (P = 0.003) and i.v. drug abuse (P = 0.006) as risk factors had significantly increased. In-hospital mortality was 13.4% and was lower in later periods because of increased proportion of cardiac surgery in treatment of IE in 2000–2012 in comparison to 1984–1997 (P < 0.001).
Conclusion: The majority of IE during the period 1984–2012 in Slovakia was caused by staphylococci and streptococci. The most frequently identified risk factors were age >60, rheumatic fever, diabetes mellitus and previous surgery. In-hospital mortality was 13.4%.
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P19
REVIEW OF THE INFECTIOUS ENDOCARDITIS IN OUR HOSPITAL IN THE LAST YEARS

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Objective: To know the epidemiology and management of infectious endocarditis in our area.
Methods: We analyzed the epidemiological data of all infectious endocarditis cases from our hospital between 2008 and 2012.
Results: We analyzed a total of 38 cases with a predominance of men (57.9%) on women (42.1%), all of Spanish nationality, with a median age of ~72 years. The average stay was 31 days. Only 23.7% were valve prosthesis carriers and they had a previous valvulopathy in 34.2% (mainly from rheumatic origin). Only four of them had a nonvalvular intravascular device like a pacemaker or DAI. Three patients had a central venous catheter while all patients

had at least a peripheral catheter. We performed transthoracic echocardiography in 97.4% and transesophageal echocardiography in 52.6% (with a higher chance of diagnosis). In more than 90% of cases the patients had fever, however only one person had vascular injuries typical of endocarditis, and the embolisms were infrequentl (13.9%). Blood cultures were obtained for all patients and were positive in 97%. Gram-positive cocci were most frequently isolated, *Staphylococccus and Streptococcus* both at a percentage of 34.2%. Most *Staphylococcus* microorganisms were *S. aureus* (23.7%) and most *Streptococcus* microorganisms were *S. bovis* (13.2%). 45.5% were nosocomial infections perhaps in relation with a catheter infection. 37.5% of patients had been admitted to a hospital in the previous month. The mortality rate reached 44.7% with a mean time of 6 weeks since diagnosis.

Conclusion: Infectious endocarditis (IE) in our area is predominant in 70-year-old men. Bacteremia from Gram-positive cocci persists as the most frequent etiology, probably originating in intravascular devices. Infectious endocarditis is associated with prolonged hospital stay with an elevated mortality.

P20
FEATURES OF VEGETATION AND OUTCOME IN CHILDREN AND ADOLESCENTS WITH INFECTIVE ENDOCARDITIS

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Aim: To study the features of vegetation (size, length of pedicle, morbility, area of location) in children and adolescents with infective endocarditis (IE) in order to determine predictors of outcome for this disease.

Methods: Included in this examination were 164 patients (age from 6 months to 18 years) with acute and subacute IE strictly fulfilling Duke criteria, studied from 1998 till 2011. Clinical, echocardiographic and bacteriological parameters were measured. Results were analysed using t-test, logistic regression and χ^2 test.

Results: Overall mortality was 36% and 8% in acute and subacute IE, respectively. Causes of death were: septic shock (15%), multiple organ failure (35%), intracranial embolization of brain vessels and fatal hemorrhage (50%). IE was associated with the mitral valve (25%), aortal valve (35%) or both (25%), or the combination aortal valve–mitral valve–tricuspid valve (15%). Multiple-valve involvement and localization of vegetation on the right leaflet mitral valve and *S. aureus* IE was profoundly connected with fatal outcome. Mitral valve localization of vegetation and long pedicles (>10 mm) tended to be associated with embolic complication (OR = 1.6, 0.7–2.6) and clear trends towards increased mortality were seen in children and adolescents with mobile vegetation (OR = 1.8, 0.7–3.6).

Conclusion: The features of the vegetation (localization, size and mobility) determine embolic complication of IE in our patients and in combination with other factors (causative pathogen, postponed diagnosis and surgery for IE) can define mortality in children and adolescents with IE.

P21
FATAL OUTCOME OF MITRAL NATIVE VALVE ENDOCARDITIS DUE TO MISDIAGNOSIS AND USING HEPARIN

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Background: Heparin administration is contraindicated in infective endocarditis (IE), but this medication is included in intensive care therapy even in unclear and difficult cases. We report on the importance, in view of the risks involved, of excluding IE before starting heparin medication.

Case report: We describe a case IE in a previously healthy 15-year-old non drug-using adolescent who was admitted to the surgical division of the children hospital from home with abdominal pain that had started 12–14 hours ago, then became persistent and more intensive. Temperature was 38.6°C. Picture of blood revealed signs of inflammation (CRP 55 mm/h, leukocyte count 16×10^9/l, neutrophil count 76%) and mild anemia: erythrocyte count 3.1×10^{12}/l, Hb 84 g/l. Thrombocytes and fibrinogen were low normal. After abdominal ultrasound and laparoscopic manipulation, mesenteric adenitis, hepatosplenomegaly was investigated; bone marrow aspiration was without signs of leukemia. The abdominal pain disappeared, but fever and weakness persisted. On the 5th day of his stay in hospital, muscle and joint pain and appearance of hemorrhagic rash became leading symptoms, and inefficacy of antimicrobial treatment was registered. Systemic vasculitis with high probability was suspected and a plasmapheresis procedure was started in order to prepare the patient for methylprednisone pulse therapy. Nearly an hour into this procedure, which according to protocol is accompanied by heparin (which had been administered to the patient before this procedure during all of the hospital stay as a component of intravenous infusions), the patient fell into coma. Intracranial bleeding was suspected and confirmed, causing a fatal outcome 36 hours after the procedure. Gross morphology identified small vegetation length 6 mm, 4 mm strongly fixed for posterior mitral valve leaf; the anterior leaf was deformed by erosion (locus of the detached vegetation). The microbial analysis of postmortem blood culture revealed *Streptococcus mitis* as the causative IE pathogen.

Conclusion: This case demonstrates the difficulties in delaying IE diagnosis and the importance of fully assuring the absence of this disease before administering heparin, which can provoke fatal embolic complications. Simple ultrasound investigation could be useful and necessary.

P22
PARAVALVULAR ABSCESS IN INFECTIVE ENDOCARDITIS: 30 YEARS EXPERIENCE

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Objective: The aim of this study was to determine the best surgical attitude for infective endocarditis complicated with paravalvular abscess.

Methods: Between October 1979 and December 2009, 808 patients underwent surgery for infective endocarditis in the department of cardio-thoracic surgery of Rennes (France), of whom 141 had annular abscess. Patients' mean age was 59.6 years and 78% were men. There were 99 (70%) native valve endocarditis, and 42 (30%) prosthetic valve endocarditis. Surgery consisted of radical resection of the infected tissue; the abscess was let opened, closed by stitches or a patch, or a reconstruction of the root was performed; a prosthetic valve was implanted when needed.

Results: There were 28 operative deaths (20%). Follow up was 96% complete. Survival at 10 years was 49% for all patients. Freedom of reoperation at 10 years was 80%. *Staphylococcus* endocarditis and age were independent risk factors for operative death; 22 patients (16%) underwent a reintervention mainly due to valve disinsertion. No surgical attitude appeared as a risk factor of operative death or reintervention.

Conclusion: The surgical treatment of infective endocarditis with periannular involvement remains a technical challenge with high mortality and morbidity. However, our experience shows that prosthetic valve is a good substitute for these patients, provided that a radical debridement of infected tissues is performed.

P23
A PATIENT WITH ENDOCARDITIS AND CARDIAC MELANOMA METASTASES

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We describe the case of an 83-year-old male patient who presented with signs of sepsis. His past medical history was significant for metastatic melanoma. Despite antimicrobial therapy the patient died after two weeks of treatment. The diagnosis of bacterial endocarditis and cardiac melanoma metastases were made postmortem.

P24
ASSOCIATION BETWEEN VALVULAR SURGERY AND MORTALITY AMONG PATIENTS WITH INFECTIVE ENDOCARDITIS COMPLICATED BY SEVERE SEPSIS AND SEPTIC SHOCK

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Background: Severe sepsis and septic shock are common complications of infective endocarditis (IE). However, clinical characteristics of these complications in patients with IE, use of surgical treatment, and their associations with patient outcome are scarcely presented.
Methods: A prospective, single-center observational study in patients with definite native or prosthetic valve IE admitted between January 1, 2000 and December 31, 2011. The main objective of the study was to estimate the safety of valve replacement in patients with severe sepsis and/or septic shock and its impact on patients' outcome. We compared clinical characteristics and outcome (in-hospital mortality) in surgically and only medically treated patients stratified on the severity of sepsis.
Results: The cohort included 294 patients with definite IE known septic status enrolled. Patients were stratified into two groups. There were 95 (32.3%) patients with severe sepsis and/or septic shock (SSS) and 199 (67.7%) with sepsis (S). Valve replacement was performed in 37 (38.9%) patients in the SSS group, and 71 (35.7%) in the S group, p = 0.587. APACHE II score was significantly higher among medically treated patients.
The impact of valve replacement was the most conspicuous in the SSS group. The mortality in this group was significantly higher in medically treated patients, 39/58 (67.2%) vs. 5/37 (13.4%), p < 0.001. However, solely medically treated patients in the SSS group had more severe disease: the APACHE II score was higher (median 19.5 vs. 13.0, p = 0.001) as well as SOFA score (median 7.5 vs. 3.0, p = 0.005). After adjusting for APACHE II score, SOFA score, age, and congestive heart failure, the beneficial impact of cardiac surgery remained significant. Cardiac surgery decreased the risk of in-hospital death about five times in the SSS group, OR = 0.096, 95% CI 0.027–0.335. Factors significantly associated with poor outcome were SOFA score (OR = 1.306, 95% CI 1.061–1.607) and congestive heart failure (OR = 3.270, 95% CI 1.150–9.303), while age and APACHE score did not show significant impact on in-hospital mortality.
Conclusion: Even in the most severe, septic patients with IE, cardiac surgery improves patients' outcome. SOFA score is a better predictor of patients' outcome than APACHE II score, and should be included in the evaluation of IE patients.

P25
PLASMA CHOLINESTERASE ACTIVITY IN CHILDREN WITH INFECTIVE ENDOCARDITIS

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Introduction: Although pre-existing heart disease in children is the most frequent predisposing factor for infective endocarditis (IE), we report 6 IE children with no apparent pre-existing cardiac disease.
Patients and Methods: Our study included six patients with infection acquired from a central catheter; the microbial pathogens were *Streptococcus viridans* (n = 3) and *Staphyloccocus aureus* (n = 3). The diagnosis of IE was based on positive blood culture (2 positive cultures of blood samples drawn >12 hours), evidence of endocardial involvement (positive ECHO), measuring raised erythrocyte sedimentation rate and plasma cholinesterase (PChE) activity. We measured PChE activity ($\mu mol\ min^{-1}\ ml^{-1}$) in children with IE (group A, n = 6) and in IE-free children (group B, n = 10). For determination of PChE activity vein blood samples were collected and stored at −20°C until analyzed. PChE activity was determined by the spectrophotometric method of Ellman using butyrylthiocholine as the substrate (Sigma Chemical Co., St. Louis, MO, USA). Statistical analysis was made by Student's t-test.
Results: In group A (children with IE) we measured decreased PChE activity (1.89±0.24) in relation to patients of control group B (3.97±0.20).
Conclusion: Our study indicates that PChE activity can be also an important parameter for the diagnosis of IE.

P26
HOMOCYSTEINE IN INFECTIVE ENDOCARDITIS

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Background: Infective endocarditis (IE) arises as a consequence of bacterial seeding on a non-bacterial clot at the site of endocardial damage. Risk factors for initial non-bacterial clot formation are unknown. Elevated plasma homocysteine levels (h-Hcy) cause endothelial stress and a thrombophilic state. A common genetic variant within the methylenetetrahydrofolate reductase gene (C677T MTHFR) favours h-Hcy. We assessed plasma Hcy levels in IE patients and investigated the relationship between h-Hcy and MTHFR genotype.
Methods: We studied 171 patients with 'definite' IE and 125 healthy blood donors as controls. MTHFR C677T mutation was sought by PCR-restriction fragment length polymorphism analysis. Plasma Hcy levels were measured by a chemo-enzymatic method.
Results: Patient median age was 61 years (13–87) and 78.4% were males. 107 (62.5%) had left- and 64 (37.5%) right-sided IE. Median vegetation length was 14 mm. Blood cultures grew Gram-positive cocci in most cases (staph 32%; strep 31%; entero 11%). Homozygous MTHFR C677T mutation was present in 19.8% of IE patients and 16.8% of controls (p = NS). Mean Hcy levels were 17.1±8.7 μmol/L in IE patients and 13.8±7.1 μmol/L in controls (p < 0.01). Prevalence of h-Hcy (Hcy > 13 μmol/L) in IE and control pts was 65% and 41% (p < 0.001). Hcy levels were related to the MTHFR genotype, being 21.7±10.8 μmol/L and 19.2±11.6 μmol/L (<0.001) in 677TT homozygous cases and controls versus 15.4±5.6 μmol/L and 12.7±5.2 μmol/L in non-homozygous IE patients and controls (p < 0.01). Hcy levels significantly differed according to the heart side involved: 17.9±8.0 μmol/L in left-sided IE vs 15.6±6.0 μmol/L in right-sided IE (p = 0.043). Hcy levels were not associated with stroke, embolic complications or larger vegetations.
Conclusions: Hcy may play a role in the pathogenesis of IE. Patients with involvement of the left heart side showed higher Hcy levels than those with right heart disease. Higher Hcy levels were associated with the MTHFR C677T homozygous variation.

P27
THE IMPACT OF PREOPERATIVE LIMB EMBOLISATION IN ACTIVE INFECTIVE LEFT-SIDED ENDOCARDITIS

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Objective: Active infective endocarditis (AIE) is a life-threatening disease showing a variety of preoperative embolisation rates for different organ systems such as brain, spleen, kidneys and limbs. This study focused on the impact of preoperative limb embolisation in AIE undergoing valve surgery.
Methods: Between October 1994 and December 2011 a total number of 1,523 patients underwent valve surgery due to AIE at our institution. In total 94.9% (n = 1,446) of the patients suffered from left-sided AIE affecting aortic (n = 710) and mitral valve (n = 474) exclusively. Patients' characteristics, intra- and post-operative parameters were collected and evaluated. Retrospective analyses were performed for preoperative embolisation, need for intervention and 30-day mortality rate.
Results: General preoperative embolisation was observed in n = 670 patients (45.8%) mostly affecting spleen (29.9%), brain (24.5%) and kidneys (11.3%). Limb embolisation, however, was observed in 90

individuals (6.2%). In these patients interventions due to septembolic events were necessary in 14 individuals (15.5%) before valve surgery: embolectomy in 8, rotablation in 1, amputation in 5. Overall 30-day mortality rate for these 90 individuals was 21.1% (n = 19); none of the 14 individuals with need for intervention died perioperatively after valve surgery.
Conclusion: Peripheral limb embolisation is a rare complication due to left-sided AIE, which needs emergence treatment including amputation. This aggressive treatment option does not increase 30-day mortality after valve surgery and should therefore be considered if necessary.

P28
THE EFFECT OF EARLY DIAGNOSIS ON THE OUTCOME OF THE TREATMENT OF PROSTHETIC VALVE ENDOCARDITIS (PVE)

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Objective: To analyze the role of early diagnosis of PVE in treatment outcome. To clarify the dependency between the time of PVE diagnosis after surgery and the survival of the patients during the in-hospital phase, 1-year follow up and 5-year follow up.
Methods and Results: Retrospective assessment was obtained on the basis of 85 patients with definite PVE. They were divided into 3 groups, according to the time at which they were diagnosed:
Group I: very early – up to 10 days – 37 patients (43.53%)
Group II: early – from 11 to 90 days – 19 patients (22.35%)
Group III: Late – after 90 days – 29 patients (34.12%)
The application of χ^2 analysis shows that there is a significant statistical dependency between the time of diagnosis and the treatment outcome. Three factors of the outcome have been observed in three different situations: (1) in-hospital period, (2) 1-year follow-up, (3) 5-year follow-up. In group I, 94.6% of the patients survive the in-hospital period, in Group II – 73.7% and in Group III – 69% ($p = 0.019$). Within the 1-year follow-up, 91.9% of the patients, diagnosed in group I, survive, in Group II – 63.2% and Group III – 69.0% ($p = 0.019$). In the 5-year follow up in group I, 81.5% survive, in Group II – 44.4%, and in Group III – 40% ($p = 0.009$). The strongest dependence is between the time of diagnosis and the survivors in the 5-year follow-up (Kramer V = 0.411).
Conclusion: Early diagnosis, up to 10 days after the surgery, is of crucial importance for the survival of the patients. The number of patients who survived in the 1-year follow up and in the 5-year follow up, and the in-hospital survivors, is significantly higher than the average number of patients who were diagnosed later in time.

P29
EFFECT ON HOSPITAL LENGTH OF STAY FOR CARDIOVASCULAR IMPLANTABLE ELECTRONIC DEVICE INFECTIONS FOLLOWING IMPLEMENTATION OF AN EVIDENCE-BASED TREATMENT ALGORITHM

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Background: Cardiovascular implantable electronic device (CIED) infections are associated with significant morbidity and mortality as well as considerable financial burden. Considering the contemporary economic climate with spiraling health care costs and diminishing reimbursement for provision of care, efforts are needed to contain costs without compromising the quality of care. In an effort to do this, we designed and implemented a standardized treatment algorithm based on AHA/HRS guidelines for management of CIED infections.
Methods: We implemented the treatment algorithm prospectively starting February 6, 2012 on all patients admitted with suspected CIED infection to Mayo Clinic, Rochester. Over the next 12 months, 56 patients with confirmed CIED infection were identified and received standardized care based on the treatment algorithm. We compared the hospital length of stay (LOS) for these patients with historical controls. These controls consisted of 288 patients who had received treatment for CIED infections at Mayo Clinic, Rochester from January 2007 to January 2012.
Results: The mean LOS for all patients with CIED infections was 17.8 days prior to and 14.8 days after the implementation of treatment algorithm ($p = 0.42$). On subgroup analysis based on the type of infection (pocket infection vs. lead/valve endocarditis) the mean LOS for patients with device pocket infection was 12.4 days prior to and 10 days after the implementation of the treatment algorithm ($p = 0.14$), whereas the mean LOS for patients with CIED lead or valve endocarditis was 26 days prior to and 19.1 days after the implementation of the treatment algorithm ($p = 0.39$).
Conclusions: There was a non-significant trend towards decreased LOS following implementation of the standardized treatment algorithm for CIED infections. Based on this data, the treatment algorithm has subsequently been revised with the expectation that outcomes, including LOS, should improve while maintaining patient safety and quality of care.

P30
DEVICE-RELATED INFECTIVE ENDOCARDITIS (IE): ANALYSIS OF CASES FROM A CARDIAC REFERRAL CENTRE IN RIO DE JANEIRO, 2006–2012

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Background: A growing number of intracardiac devices (ID) are inserted for rhythmn disturbances and heart failure. A disproportionate number of IE related to ID (DRIE) are being described.
Methods: Prospective cohort study including patients with definite DRIE admitted to Instituto Nacional de Cardiologia (INC).
Results: Twenty patients were included, of 181 episodes of IE (11%). Mean age was 53.5±17.4 years and 16 (76%) were male. Clinical presentation was acute in 11 cases and subacute in 9. Etiological agents were *Staphylococcus aureus* 7, MRSA 2 (one of which ca-MRSA), *S. epidermidis* 2, viridans streptococcus 1, *E. faecalis* 1, *Propionibacterium acnes* 1, *S. marcescens* 1, *Enterobacter aerogenes* 1, *Acinetobacter* sp. 1, *P. aeruginosa* 1, *Candida parapsilosis* 1, *Trichosporon beigelli* 1. Clinical findings were fever in 15/20 (75%), new regurgitation murmur in 5/20 (25%), generator pocket infection in 12/20 (60%). Transesophageal echocardiogram was done in 18 patients and showed vegetations in 17. It was not done in 2 patients whose TTE had shown vegetations. Complications were emboli to lungs in 6 (30%) and to spleen in 2 (10%), heart failure in 10 (50%). CRP levels were high in 16/20 (80%). For 18 patients where date of device insertion was known, infections occurred after 993 days (range 11 to 6570) and mean antibiotic therapy duration was 42 days (range). Surgical removal was done in 14 (66%), and percutaneous extraction in 4 (19%). Overall mortality was 9 (42.8%). One patient had a ventricular assist device, awaiting heart transplantation, and died with *Candida*-related device infection.
Conclusion: *Staphylococcus aureus* predominated (9/20 cases) and ca-MRSA was seen in one case. A variety of other etiological agents were seen, one of which, *P. acnes*, is the first case reported in Brazil. Fever was often absent, and time of presentation was highly variable. Mortality was higher than in early prosthetic valve endocarditis and in native valve IE, which may be due to comorbidities and late removal of the device.

P31
PROSPECTIVE STUDY OF CARDIAC IMPLANTABLE ELECTRONIC DEVICE INFECTIVE ENDOCARDITIS

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Introduction: Infection of cardiac implantable electronic device (CIED) leads is an emerging form of infective endocarditis (IE).
Methods: We present data on 94 consecutive patients (72M; 22F), median age 67 yrs (range 17–90), admitted to our unit (1999–2012) with definite IE on a pacemaker or a defibrillator.

Results: IE involved a pacemaker in 70 cases, a defibrillator in 24. Diagnosis was made within one month in 30 cases (32%). Fever occurred in 88%, pulmonary embolism in 33%. Comorbidities (obstructive lung disease, heart failure, diabetes, chronic kidney disease) were each present in >20% patients. Blood and/or lead cultures grew *Staphylococcus epidermidis* in 39 cases (44.8%), coagulase-negative non-*epidermidis* staphylococci in 12 (13.8%) and *S. aureus* in 23 (26.4%). Methicillin-resistant (MR) staphylococci were involved in 54% of cases. Only 25% of cases were community-acquired, 70% were nosocomial and 5% non-nosocomial, health-care related. Trans-esophageal echocardiogram displayed vegetations in 99% of cases whereas trans-thoracic study was positive in only 80%. Lead vegetations (median 19.5 mm, range 2–33) were observed in 85 patients (90.5%), while tricuspid involvement with valve vegetations and regurgitation was present in 21 (22%).
Treatment was with antibiotics alone in 14 cases (15%) and a combined medical and surgical approach in 80 (85%). Seventeen patients (18%) underwent open-heart surgery, 63 (82%) transvenous lead extraction. Antimicrobial treatment was based on amoxicillin–clavulanate (average dose 8.8 g/day) in 34 cases, daptomycin (median dose 8 mg/kg/day) in 27, a combination of them in 6 and on vancomycin, teicoplanin or linezolid in the remaining 27 cases. Total duration of treatment was on average 6 weeks, prolonged for >8 weeks in 24%. Lead extraction was complicated by pulmonary embolism in 6 patients while leads or vegetations persisted in the heart in 5 patients, 2 of whom subsequently underwent open-heart surgery. Overall, 9 patients died in hospital (9.5%): 2 in the medical treatment group (mortality 14%), 4 in the open-heart surgery group (mortality 23.5%) and 3 in the transvenous lead extraction group (mortality 4.8%).
Conclusions: CIED IE mostly affects elderly patients with comorbidities, and may present without ill-defining signs/symptoms. It is often associated with signs of pulmonary involvement. Delayed diagnosis is common and transthoracic echocardiography may be negative. As the prevalence of methicillin resistance is >50%, initial empirical antimicrobial treatment must cover for both MS and MR strains.

P32
CARDIAC IMPLANTABLE ELECTRONIC DEVICE ENDOCARDITIS: REPORT OF EIGHT CASES

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Background: Cardiac implantable electronic device (CIED) endocarditis is a rare, but potentially dangerous complication. Literature data shows mortality of 30–35% in CIED endocarditis and 20–25% in valve endocarditis. We describe clinical characteristics, type of microorganism, complications and outcome of CIED endocarditis in eight patients.
Methods: In our hospital between January 2006 to November 2010 CIED endocarditis was identified in eight patients, 4 male and 4 female, age 24–80 years, mean age 62.5 years. Criteria for CIED infective endocarditis are related to clinical findings, positive blood cultures with identical microorganism or echocardiographic evidence of vegetation associated with transvenous leads or right-sided heart valves.
Results: Clinical features of patients are fever in 8, heart failure in 2, pulmonary embolism in 1 and chills in 3 patients. Echocardiography demonstrated lead vegetations in all patients; two patients had concomitant valve vegetations. Mean interval between device implantation and first findings of infection was 3.3 years. Interval from fever to diagnosis of CIED endocarditis was 2–7 days, mean 4.0 days. All patients presented with recurrent fever and were treated as outclinic patients before addmittance in our hospital. Antibiotic treatment lasted 8–23 days (mean 15.3±8.5 days) before surgical lead extraction and 7–21 days after surgery. Blood culture was positive in 7 patients (87.5%). Isolated causative organisms in blood cultures and extracted leads are: staphylococci in 3 (42.8%), two MRSA, streptococci in 2 (28.5%), *Pseudomonas aeruginosa* 1 (14.2%), and *Corinebacterium* spec. 1 (14.2%) patients. Treatment with a combination of antibiotics and surgical lead extraction was performed in 7 patients with placement of new epicardial leads. Concomitant valve surgery was performed in two patients. One patient was treated only with antibiotics and was lost to follow-up after a year. Hospital and 2-year survival was 100%.
Conclusion: *Staphyloccocus aureus* and *S. epidermidis* were the most common causative organisms in CIED endocarditis. CIED infective endocarditis can be safely managed by surgical lead extraction with hospital survival and 2-years survival of 100% in our patients. Four weeks intravenous administration of antibiotic therapy, which is considered to be sufficient, is mandatory before and after lead extraction.

P33
IMPLANTABLE CARDIAC-DEVICE INFECTIONS

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Background: Various cardiac devices such as pacemakers and implantable defibrillators are used more and more frequently. Infections are a serious complication and when they occur they are usually difficult to treat.
Objective: The aim of the report is to describe clinical picture, treatment and outcome of the disease in patients with pacemaker-related endocarditis in our patients.
Methods: All patients fulfilling the Duke pathomorphological and clinical criteria for pacemaker-related infective endocarditis, treated at our department in 1984–2011, were included. Clinical and demographic data were recorded as well as the time since the implantation of pacemaker, causative agent, size and localization of vegetation, mode of operation and outcome of the disease.
Results: In the years 1984 to 2011 there were 675 episodes of endocarditis. In 494 patients (73%) native valve was affected, in 180 (27%) endocarditis occurred on prosthetic valves including pacemakers (122 of late and 58 cases of early postoperative endocarditis). There were 24 episodes of pacemaker-related endocarditis, representing 3.9% of all episodes of infective endocarditis. In 0.7% of valvular endocarditis there was pacemaker wire involvement as well. 50% of all pacemaker-related episodes were caused by coagulase negative staphylococci (CoNS) and 36% by *Staphylococcus aureus.* In 67% of episodes the complete pacemaker system or only retained leads were extracted. None of the patients who survived the operation had a relapse of the disease. Overall mortality in pacemaker-related endocarditis was 24%.
Conclusions: Pacemaker-related endocarditis is rare. Complete cure is usually impossible without combined surgical therapy and long-term antibiotic treatment.

P34
CARDIOVASCULAR IMPLANTABLE ELECTRONIC DEVICE INFECTION, COMPLETE DEVICE REMOVAL FOLLOWED BY LONG TERM ANTIBIOTIC TREATMENT; IS LONGER SAFER?

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Background: Cardiovascular implantable electronic device (CIED) infections are increasing along with increasing rates of device implantation and more complex procedures. Recently an AHA statement was issued to help unify diagnosis and treatment. Few of the studies published on CIED infection have more than short term follow-up. Longer follow-up is crucial to describe the prognosis, hence give recommendations on treatment duration.
Objective: To review the safety of a treatment regimen of CIED infections with long duration of antibiotic treatment during long follow-up time.
Methods: All device removals due to CIED infection during the period from 2005 to 2012 were retrospectively reviewed. Clinical

presentation of either "local pocket infection" or "systemic infectious response", microbiology, echocardiography results and duration of antibiotic treatment were recorded.
Results: Seventy-one device removals due to infection were recorded during a total of 14,431 procedures, resulting in an incidence of CIED infections of 0.5% per procedure. Treatment duration with antibiotics was 4 weeks after device removal followed by 2-week treatment after implantation of the new device. Median follow-up time was 26 months (IQR 9–41); 30-day and 12-month mortality were 4% and 14%, respectively. There was no difference in mortality when comparing clinical presentation of local pocket infection or systemic infectious response. During follow-up only 2 cases of new infections were recorded (2.8%), 13 and 21 months from last procedure, respectively. Both cases were re-infections with *Staphylococcus aureus*.
Conclusions: The present treatment regimen of complete device removal and antibiotic treatment of long duration resulted in low mortality and no cases of infection relapse. Longer duration antibiotic regimen of CIED infections than the present guidelines could be considered.

P35
SCANT SUPPORT FOR USE OF THE DUKE CRITERIA IN MANAGEMENT DECISIONS ABOUT PATIENTS SUSPECTED OF INFECTIVE ENDOCARDITIS: A LITERATURE REVIEW

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The specificity of the (modified) Duke criteria is high as they were primarily developed to identify patients qualifying for inclusion in epidemiologic or treatment trials of infective endocarditis (IE). However, in practice the criteria are often used for management decisions in patients suspected of IE. To learn about the sensitivity of the criteria we reviewed the literature.
Included were studies which applied the criteria prospectively to consecutive patients suspected of IE, used a reference standard other than the criteria themselves and provided information on follow-up of all patients, including "rejected" or "possible" IE patients.
387 Publications had "Duke" and "endocarditis" in title or abstract. After reading the abstract 174 papers were excluded because they did not concern clinical cohorts of IE cases or were non-English. Ninety of the remaining 213 articles provided information on the application of the criteria. Of these, 24 studies included all patients suspected of IE. However, 7 of 24 papers evaluated only specific patient groups, e.g. *Staphylococcus aureus* bacteraemia, 6 other studies were not prospective, 7 more studies had insufficient follow-up data and 1 study used the criteria as the reference standard.
Three studies remained that were of sufficient quality, two of which used the modified Duke criteria. The reference standard for the diagnosis of IE was expert opinion in one study and pathology combined with follow up in the two other studies. Sensitivity using the "definite" classification was 55% and 83%, respectively, for the modified Duke criteria and 79% for the original Duke criteria. The 79% and 83% sensitivity figures were based on cases confirmed by surgery or autopsy, and these numbers may be an overestimation as these events are more likely in severe IE.
In conclusion, the sensitivity of the criteria seems to be low; evidence for the use as a clinical management decision tool is lacking.

P36
PRELIMINARY STUDY ON THE DIAGNOSTIC VALUE OF PET–CT SCAN IN CARDIOVASCULAR INFECTIONS

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Introduction: Beyond its role in clinical oncology, positron emission tomography (PET) scan is emerging as a useful diagnostic tool in selected infectious diseases, including prosthetic joint and vascular graft infections. By targeting actively replicating cells, PET scan using radiolabeled glucose tracings may disclose occult or otherwise unachievable foci of inflammatory cell accumulation. The application of this newer imaging technique in infective endocarditis (IE) and other cardiovascular infections (CVI) is currently unclear. In this study, we report our center's preliminary experience with the use of PET scan in CVI.
Methods: Included in this study were all consecutive patients admitted to our unit for suspected EI/CVI who underwent a whole body PET–computed tomography (CT) scan using 18-fluoro-deoxyglucose as radiolabeled tracing. CT was used for anatomical location and cardiac PET images were both attenuation-corrected and non-attenuation-corrected. Studies were interpreted by highly experienced personnel and always provided maximal standardized uptake values (SUV). Multiple blood cultures, trans-esophageal echocardiography and body ultrasound were also performed in all patients.
Results: There were 16 patients, 69% males, median age 61 yrs (range 18–79). All had cardiac prosthetic material in place, including a mechanical valve in 3, a defibrillator in 3, a bioprosthetic valve in 5, a valvulated biologic or bioprosthetic tube in 4 and an aortic tube in 1. Eleven patients were classified as having IE, 3 vascular infection, and 2 both. Aortic involvement was most frequent (7 cases), followed by pulmonary valve/artery and defibrillator (4 and 3 cases). Pathogens isolated from blood were staphylococci in 7 cases, streptococci in 5 cases, enterococci in 2 cases. On PET–CT, tracing uptake was noted at the site of cardiac prosthesis location in 11 patients (69%), with a median SUV of 9.2. PET was positive in the absence of trans-esophageal echocardiographic diagnostic criteria in 4 of these 11 patients.
Conclusions: If used judiciously, PET–CT scan may be a useful diagnostic tool in IE and CVI, especially when a valvular or vascular prosthesis is in place. Further studies are warranted to more precisely assess its sensitivity and specificity. Caution should be used when taking definitive diagnostic judgments based on PET–CT scan.

P37
THE IMPACT OF ROUTINE BRAIN CT ANGIOGRAPHY ON TREATMENT DECISION AND MORTALITY IN PATIENTS WITH INFECTIVE ENDOCARDITIS

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Purpose: Cerebral embolization and hemorrhage secondary to intracranial mycotic aneurysms (ICMA) are common with infective endocarditis (IE) and are associated with poor outcome. However, routine screening by brain CT and CT angiography (CTA) is not standard practice. We aimed at studying the impact of routine cerebral CTA on treatment decisions in patients with infective endocarditis.
Methods: From July 2007 to December 2012 we prospectively recruited 81 consecutive patients with definite IE according to modified Duke criteria. All patients had routine brain CTA within 2 weeks of admission. All patients with ICMA underwent four-vessel conventional angiography. Clipping or coiling was performed for ruptured aneurysms, aneurysms $\geqslant$5 mm, or aneurysms persistent despite appropriate therapy.
Results: The mean age was 30.43±8.8 years and 60.5% were males. *Staphylococcus aureus* was the commonest organism (32.3%). 37% of patients had underlying rheumatic heart disease, 26% had underlying prosthetic valves, 23.5% developed IE on top of structurally normal heart and 8.6% had underlying congenital heart disease. The overall mortality rate was 18.5%. CTA revealed ICMAs in 26 patients (32%), of whom 15 were clinically silent. Mortality in ICMA was 5/26 (19%). The findings in brain CTA prompted changes in decisions in 17 patients (20.9%). The decisions were aneurysm clipping or coiling before cardiac surgery rather than follow up, valve replacement by biological valve instead of mechanical valves, and withholding anticoagulation for fear of aneurysm rupture.

Conclusions: Routine brain CT/CTA results in changes in treatment plan in 20.9% of patients with IE even those without clinically evident neurological disease. Managing ICMA before rupture could decrease mortality in this subset of patients. Routine brain CT/CTA may be indicated in all hospitalized patients with IE.

P38

THE USE OF LEUKOCYTE SCINTIGRAPHY AND FDG-PET IN SEARCH FOR A PRIMARY FOCUS IN INFECTIVE ENDOCARDITIS; EXPERIENCES FROM A SINGLE TERTIARY HEART CENTRE

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Purpose: In 50% of patients with infective endocarditis (IE) extracardiac infectious foci are present. Finding these foci is essential but the optimal strategy has yet to be established. The purpose of this study was to assess the diagnostic value of leukocyte scintigraphy (LS) and ^{18}F-fluorodeoxyglucose (FDG) PET/CT scans in discovering extracardiac foci of infection in patients with IE.
Methods: Patients admitted at a Danish tertiary referral centre from 1 January 2010 to 31 December 2011 with the diagnosis IE were studied. Records were reviewed for information on use of LS and FDG-PET scans; C-reactive protein (CRP) and leukocyte levels; and bacterial aetiology.
Experienced cardiologists reviewed all journals with positive findings on LS or FDG-PET to decide if the focus was unknown, and if the finding changed the clinical course for the patient.
Results: A total of 165 patients were admitted. LS was performed in 95 of the cases, and FDG-PET in 29. There were no demographic baseline differences between the groups in which LS was performed and was not performed.
In total, 14 (14.7%) of the LS showed pathological leukocyte accumulation, and 18 (62.1%) of the FDG-PET scans showed pathological FDG uptake. CRP levels [mg/L] were higher if an infectious focus was found both with LS (65.36 vs. 38.84, $p = 0.137$) and FDG-PET scans (45.33 vs. 34.36, $p = 0.589$). In patients with positive LS scans the examinations were performed earlier [days] from initiation of antibiotic treatment as compared with patients with negative LS outcome (12.6 vs. 16.7, $p = 0.540$).
Journal review showed that 8 of the 14 pathological LS turned out to be clinically insignificant or false positives, and 2 had inconclusive results. The final 4 patients all had ostitis, and they all had clinical signs of the final diagnosis before LS was performed. Only in two of the 95 cases did LS result in altered treatment.
There was a low level of agreement between the outcomes of patients who had both LS and FDG-PET done ($\kappa = 0.099$, 95% CI [−0.040; 0.238]). Of the 26 patients who had both LS and FDG-PET performed, only two patients had a positive finding in both LS and FDG-PET and in these cases the foci found with the two modalities were different.
Conclusions: This study suggests that the value of LS in the search for extracardiac foci of infection in IE is low. Also, there was no agreement between foci found with LS and FDG-PET scans.
Performing LS early in the time course of antibiotic treatment and choosing patients with elevated CRP-levels might result in higher rates of LS with clinically useful results.

P39

NEW SYSTEM OF MICROARRAY-BASED DETECTION OF BACTERIAL PATHOGENS IN HEART TISSUE SAMPLES

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Fast detection of the causative pathogen in infective endocarditis (IE) patients is extremely important for early initiation of targeted antibiotic treatment. In this retrospective study, we compared a newly developed system of universal PCR and microarray-based detection of bacterial pathogens (Endocardi-Gene, Hutman Diagnostics) with routinely used 16S rDNA broad-range PCR followed by sequencing (br-PCR) in tissue samples.
DNA extracted from heart tissue from patients surgically treated in a period from 3/2009 to 11/2011 ($n = 120$), and stored at −20°C, was used. At the day of surgery, 60 samples were tested positive and 10 samples negative in the group of IE patients and all 50 samples were negative in the group of patients with non-infective heart disease, using br-PCR. All the retrospective DNA samples were retested using br-PCR at the time they were analysed with Endocardi-Gene.
Seven samples originally tested positive were excluded from the study, because retesting by br-PCR failed to confirm previous results. Endocardi-gene showed positivity in 45 out of remaining 53 br-PCR positive samples (sensitivity 85%). Looking at the 8 false negative samples, 6 of them were found out to be stored more than 2 years. Out of 60 br-PCR negative samples, 12 showed borderline positivity in Endocardi-Gene (specificity 80%). Six samples tested positive by both methods were not identified to the species level using Endocardi-Gene, either they were not included in the panel or the signal after PCR was too low.
Endocardi-Gene is a sensitive and fast diagnostic tool, capable to identify bacteria involved in IE. The study indicated that the kit should not be used with DNA stored for a prolonged period of time, but this does not limit the clinical utility of the test as it is intended to be used with fresh tissue specimens.
The study was supported by Hutman Diagnostics AG.

P40

"ACUTE INFECTIVE ENDOCARDITIS BY AMPLATZER" – A NEW ENTITY: CASE REPORT AND LITERATURE REVIEW

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Introduction: The percutaneous closure technique for interatrial defects was described around 1976 by King and Mills. Since then there have been multiple devices, one of which is the Amplatzer. This device is considered effective and safe, with low rates of mortality and morbidity.
Case report: A 52-year-old man, on the 5th postoperative day after closure of atrial septal percutaneous device (Amplatzer) arrived in the emergency room with fever and septic shock. Blood cultures grew *Staphylococcus aureus* and oxacillin and rifampicin were started; scintigraphy with labeled leukocytes reported abnormal leukocyte concentration in the interatrial prosthetic material; invasive thoracotomy for removal of Amplatzer and surgical correction of CIA confirmed the same germ in the percutaneous closure device. The clinical outcome after 4 months of evolution has been satisfactory.
Literature review: Percutaneous closure devices for septal defects are still considered safe and effective devices, with lower complication rates than surgical management. The complications related to these devices can be divided into major and minor. Observational studies of percutaneous closure devices have reported between 0.2% and 1.5% for major complications; the most common complication is improper positioning of the device and embolization followed by arrhythmias. Chessa et al. found only 2 cases of infectious endocarditis (IE) as complication. There are few reports of IE related to such devices, most cases corresponding to reports, the majority in children, some case reports to as late endocarditis related factor is incomplete endothelialization of the device. Most reports agree on the need for surgery but there is no consensus on the best treatment.
Conclusions: This is the first case reported in literature of early-onset IE in adults (5 days) related to Amplatzer; still no final consensus to treatment future research is required.

P41
AN ALTERNATIVE SUSCEPTIBILITY METHOD AS PREDICTOR OF CLINICAL RESPONSE TO VANCOMYCIN (VAN) WITH METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA) INFECTIVE ENDOCARDITIS (IE)

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Background: MRSA IE is an infection associated with high morbidity and mortality. VAN continues to be the primary treatment for MRSA IE. Emergence of VAN heteroresistance (hVISA), defined as modified population analysis profile (PAP) $\geqslant$0.9, may affect outcomes. The objective of this study was to evaluate clinical outcomes of MRSA IE treated with VAN.
Methods: Retrospective cohort review of patients (pts) with MRSA IE from 2002 to 2012 at Detroit Medical Center. Modified PAP was used to measure VAN susceptibility, such as PAP-minimum inhibitory concentration (MIC) and PAP-area-under-the-curve (AUC) ratio. Pt characteristics, outcomes and molecular subtyping of isolates were also compared. Composite VAN treatment failure was defined as bacteremia $\geqslant$7 days on VAN or death by MRSA. Classification and regression tree analysis (CART) was used to select VAN failure breakpoint between PAP-AUC ratios.
Results: A total of 180 pts were included for evaluation. Median age and APACHE II were 51 years (interquartile range 44–58) and 11 (7–16), respectively. Forty-nine patients (27%) had left-sided IE, 101 (56%) were injection drug users, and 19 (11%) had valve-replacement. Ninety-one strains (51%) were *mec*-type 4, 74 (41%) were *agr*-type 1, and 34 (19%) were hVISA. There was no difference in PAP-MIC for left-sided compared to right-sided IE (p = 0.703). Overall VAN failure was 68%; 63% had persistent bacteremia and 30-day mortality rate was 21%. On logistic regression analysis, ICU admission (aOR, 3.0; 95% CI 1.5–6.1), and PAP-MIC $\geqslant$4 mg/L (aOR, 4.5; 95% CI 1.5–14.2) were associated with VAN failure (p = 0.002 and 0.009, respectively). CART breakpoint between VAN failures and successes for PAP-AUC ratio was 0.9035.
Conclusion: PAP-MIC of $\geqslant$4 mg/L and ICU admission were significant for VAN failure for pts with MRSA IE. hVISA with PAP-AUC ratio $\geqslant$0.9035 predict failure. Further research is warranted for PAP and PAP-MIC in pts with MRSA infections.

P42
ISOLATION AND ANTIMICROBIAL RESISTANCE OF *STAPHYLOCOCCUS AUREUS* STRAINS

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All over the world *Staphylococcus aureus* is the most dangerous pathogen isolated in humans. However, the treatment of staphylococcal infections has become more difficult because of the development of multidrug-resistant strains. These strains are difficult to treat, particularly when they cause heart infections. Determination of antimicrobial resistance of the *S. aureus* strains is important in aiding clinicians to select the most appropriate agent for treating the infections. Considering what we said above, we undertook such a study to demonstrate the antimicrobial resistance of the strains of *S. aureus* isolated in human infections in Elbasan city in Albania during the period January 2011 to December 2012. This study included 242 *S. aureus* isolates which were identified by conventional method in the National Microbiologic Laboratory. All the strains were tested using Kirby Bauer's disc-diffusion method according to CLSI with antibiotics: cefaclor, cefalexin, augmentin, clarithromycin, nalidixin, bactrim, ciprofloxacin, gentamycin, doxycycline, amoxicillin, chloramphenicol, amikacin, azithromycin, norfloxacin. Based on antibiotic susceptibility testing *S. aureus* isolates showed a high prevalence and increased occurrence of methicillin-resistant staphylococci.

P43
CHARACTERIZATION OF AMINOGLYCOSIDE MODIFYING ENZYMES AMONG *STAPHYLOCOCCUS AUREUS* ISOLATED FROM SURGERY DEPARTMENTS

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Background: *Staphylococcus aureus* remains a versatile and dangerous pathogen in humans, particularly in hospital settings. The importance of *S. aureus* as a human pathogen, apart from its ability to cause a diverse range of infections that may be life threatening, is its extraordinary potential to develop antimicrobial resistance. Aminoglycosides still play an important role in anti-staphylococcal therapy, although emerging resistance amongst *Staphylococcus aureus* is widespread.
Objectives: The objective of this work was to study the occurrence of *S. aureus* infection in the Surgery Departments of Zagazig University Hospital. Other objectives were to identify the susceptibility profile of *S. aureus* to methicillin and aminoglycosides (AGs), and to determine the relationship between them, if any. Finally to characterize the genes encoding for aminoglycoside-modifying enzymes (AMEs).
Methods: One hundred seventy clinical samples were collected from patients with different clinical conditions hospitalized in the Surgery Departments. Samples were processed and isolates were identified using standard microbiological procedures. Antimicrobial susceptibility testing was performed using disc diffusion method, according to the standard procedures of CLSI, using oxacillin and 5 aminoglycosides – kanamycin, tobramycin, gentamicin, amikacin and netilmicin. A multiplex PCR assay was used to identify AMEs-encoding genes.
Results: A total of 81 (47.6%) *S. aureus* strains were isolated. Forty-three (53.1%) of them were methicillin-resistant (MRSA). Thirty-one (38.3%) isolates were resistant to at least one of the tested aminoglycosides, and the highest incidence of resistance was to kanamycin (38.3%), followed by tobramycin (30.9%), gentamicin (29.6%), amikacin (9.9%) and finally netilmicin (8.6%). Multiplex PCR assay revealed the *aac(6')-Ie+aph(2)* gene encoding the bifunctional AME to be the most common, followed by the *ant(4')-Ia encoding the* ANT (4')-Ia enzyme, then the *aph(3')-IIIa* gene encoding the APH(3')-IIIa enzyme. A statistically significant agreement ($p \leqslant 0.001$) was found between resistance to methicillin and the presence of AMEs genes. The highest level of significance was for *aac(6')-Ie+aph(2)* gene, followed by *ant(4')-Ia,* and finally, *aph(3')-IIIa.*
Conclusion: *Staphylococcus aureus* is highly prevalent in our Surgery Departments, with high resistance to methicillin and aminoglycosides. The most prevalent gene of AMEs is *aac(6')-Ie+aph(2)* encoding for the bifunctional enzyme. We recommend continued surveillance of the bacteriological flora in that Department, as well as monitoring the presence of the genes encoding aminoglycoside resistance that may be produced within the *S. aureus* population. This will help to develop effective strategies for control and prevention.

P44

CANDIDA INFECTIVE ENDOCARDITIS (IE) IN A TERTIARY REFERRAL CARDIAC SURGERY HOSPITAL IN BRAZIL FROM 2006 TO 2012

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Background: Despite the high incidence of candidemia, *Candida* infective endocarditis (IE) is a rare disease, but is often fatal.
Methods: Prospective cohort study.
Results: There were 200 patients and 15 (7.5%) episodes of *Candida* IE in the study period. Only definite and possible cases (modified Duke criteria) were included; 4 were pathologically proven, 14 were associated with positive blood cultures. There were 8 adults (6 male, 2 female) and mean±SD age was 45.4±16.4 years. 6 episodes were hospital acquired, 1 was health care associated (haemodyalisis), and 1 was community acquired. Predisposing factors were previous IE (4), diabetes mellitus (1), renal disease (2), antibiotic use (4), recent surgery (3), recent intravascular catheter use (5). Causative organisms were *C. parapsilosis* 4, *C. albicans* 2, *C. tropicalis* 2. Involved structures were mitral prosthesis 5, native valves 3. Complications were abscess (1), prosthetic dehiscence (2), persistently positive blood cultures (2), cardiac failure (6), extracardiac mycotic aneurysm (3) and emboli (5). Five patients (62.5%) died; of these 3 (60%) had surgery. Of the 3 who survived, 3 had surgery. At the same time period there were 7 children with *Candida* IE, 5 male and 2 female (in 43 episodes of IE, 16%). Three were less than 1 year old. Mean age was 5.4±7.1 years. All 7 episodes were hospital acquired. Predisposing factors were congenital heart disease (CHD) in 6, previous IE (1), recent surgery (5), antibiotic use (4), recent intravascular catheter use (7). Causative organisms were *C. parapsilosis* 3, *C. albicans* 1, *C. tropicalis* 2 and C. *lypolitica* 1. Involved structures were mechanical mitral valve 1; pericardial patches 2, Blalock shunt 1; atrium wall 1; and native valves (M 1, M-T 1). Complications were abscess (1), intracardiac fistula (1), persistently positive blood cultures (3), cardiac failure (3) and emboli (3). Five patients (71%) died; of these, 1 had surgery (20%). Of the 2 who survived, none had surgery.
Conclusion: Patients with *Candida* IE were more likely to be male (73%) and more frequently were using vascular catheters (80%). Incidence of *Candida* IE in adults at INC is higher than that described in the literature (5.1% vs. 2–4%), and incidence is proportionally higher in children (16%). *C. parapsilosis* predominated in adults and children, which is possibly related to intravenous catheters. Most episodes were hospital acquired.

P45

FUNGAL ENDOCARDITIS: EARLY DIAGNOSIS AIMING AT BETTER OUTCOME AND PREDICTORS OF MORTALITY

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Fungal endocarditis is a devastating disease that is associated with multiple morbidities and high mortality. Diagnosis is difficult and usually very late. Studying characteristics of patients with fungal endocarditis (FE) can help identifying clinical predictors for early diagnosis which can result in better outcome.
Method: Retrospective analytic study that included 232 patients with definite IE between February 2005 and September 2011.
Results: 31 (13.3%) patients had FE. Patients were relatively young, mean age was 35 (13–74) in FE and 28.5 (15–50) in non-FE. In the FE group, 22 patients had *Aspergillus*, 6 had *Candida* [71% vs. 19.3%, $p<0.001$] and 3 had other fungi.
Native RHD was less prevalent in FE [9.7% vs. 42.8%, $p<0.001$]. The FE group had more cardiac prostheses [74.2% vs. 23.8%, $p<0.001$]. Early PVE was more prevalent among FE [64% vs. 38%, $p=0.059$]. Late PVE was more common in non-FE [61% vs. 36%, $p=0.059$]. Vegetations were more common in FE [100% vs. 84.6% in non-FE, $p=0.002$] and were also larger [20 mm vs. 12 mm, $p=0.002$]. Negative Bl. Culture was more common among FE [80.6% vs. 52%, $p=0.003$]. Health care associated infection (HAI) was more common in the FE group [90.3% vs. 58.2%, $p=0.001$]. Complications were high in both groups, however death was higher in FE [54.8% vs. 32.8%, $p=0.017$].
Through multivariate regression test the following variables were independently associated with FE:
– Cardiac prosthesis [OR: 14, 95% CI: 5 to 41, $p<0.001$]
– HAI [OR: 8, 95% CI: 2 to 29, $p=0.003$]
– Absent splenomegaly [OR: 0.174, 95% CI: 0.034 to 0.879, $p=0.034$]
– IVDU [OR: 12, 95% CI: 2 to 64, $p=0.004$]
– Larger vegetation size [CI: 0.011–0.002, $p=0.003$]
Only heart failure was associated with increased mortality.

P46

FUNGAL ENDOCARDITIS – REVIEW OF NINE CASES

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Background: Fungal endocarditis is a rare and difficult to cure infection. Only limited number of cases are reported.
Materials and Methods: A retrospective search through endocarditis database was performed and medical records of patients with confirmed fungal endocarditis were reviewed. Important data on demographics, medical history, clinical data, outcome and treatment were extracted.
Results: From 1984 to 2011 ten episodes of fungal endocarditis in nine patients were treated at our department (2.5% of all episodes of endocarditis). The age of the patients was from 19 years to 84 years. There were 6 women and 3 men. The causative agents were *Aspergillus* in 4 patients, *Candida parapsilosis* in 2 patients (3 episodes) and *Candida albicans* in 3 patients. In 2 patients with *C. parapsilosis* endocarditis the disease occurred in the early postoperative period after valve replacement. In 2 patients with *Aspergillus* endocarditis the disease occurred after heart transplantation. Underlying diseases in other patients were intravenous drug abuse in 2 patients, total parenteral nutrition in 2 patients and prolonged antibiotic treatment and cancer in 1 patient. All patients with *Aspergillus* endocarditis died. In 3, massive involvement of heart and other organs was documented after at least one month of treatment with amphotericin B. Of 5 patients with *Candida* endocarditis 3 were operated in the active phase of the disease (one of the patients died after operation), and 1 patient died just before the planned operation. A patient with 2 episodes of *Candida parapsilosis* prosthetic valve endocarditis was successfully treated conservatively. All patients except one with *Candida* endocarditis had multiple embolic episodes. Only three of nine patients with fungal endocarditis survived.
Conclusions: Fungal endocarditis remains a serious disease. *Aspergillus* endocarditis in our patients had 100% mortality rate. Whether the advent of new antifungal agents will change the prognosis of this infection remains to be seen.

P47

FEATURES OF INFECTIVE ENDOCARDITIS CAUSED BY AEROCOCCI

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Aerococci are Gram-positive bacteria that have been reported to cause urinary tract infections, bacteremia, and infective endocarditis (IE). The bacteria have also been shown to possess virulence properties of potential importance for IE, including the capacity to form biofilms and to aggregate human platelets. The identification of aerococci has been hampered by their resemblance to alpha-hemolytic streptococci and thus the incidence of aerococcal infections has been underestimated. Recently, a mass spectroscopic tool (MALDI-TOF) that correctly identifies aerococci has been introduced in many clinical microbiological laboratories.
We have previously shown that bacteremia with *Aerococcus urinae*, the most important human pathogenic *Aerococcus*, occurs mainly in older males with underlying urinary tract abnormalities and

that IE occurred in only three of sixteen patients. Here we employ the Swedish Registry for Infective Endocarditis to identify cases of aerococcal IE. We present the clinical characteristics of 19 IE episodes caused by aerococci, 17 of which were deemed to be definite. The patients were predominantly male (16/19) and had a median age of 79 years (range 35–92). The mitral valve was affected in eleven patients, the aortic valve in five patients, and both valves in two patients. In five patients embolic complications were recorded and valvular surgery was performed in three cases. There was one recorded fatality, in contrast to previous case reports in which eleven fatalities were reported among 24 patients.

The bacterial aetiology in our case series was claimed to be *A. urinae* in eight patient, *A. viridans* in six patients, and *A. sanguinicola* in two patients. We have thus far been able to confirm species determination of five *A. urinae* isolates. In an attempt to identify additional cases of IE caused by aerococci, alpha-hemolytic streptococci from patients reported to the Registry will be reclassified with MALDI-TOF.

P48
INFECTIVE ENDOCARDITIS CAUSED BY *NEISSERIA MUCOSA*

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Background: *Neisseria mucosa* are normal inhabitants of the upper respiratory tract. Although these bacteria are regarded as having low pathogenicity, it has been reported to cause serious infections such as endocarditis. We report a case of infective endocarditis due to *N. mucosa* in a patient without predisposing risk factors.

Case report: A 62-year-old male, with a medical history of chronic atrial fibrillation, arterial hypertension and hypercholesterolemia, was admitted to our department because of right ankle arthralgia, fever, headache, tremor and ataxia.

Physical examination revealed ataxic gait, upper limb tremor, diastolic heart murmur left to the sternum, blood pressure was 95/64 mmHg, meningeal signs were positive, and there was a subcutaneous haemorrhage over the lateral side of the right ankle.

Laboratory tests: CRP 184 mg/l, WBC 15.5×10^9/l (6% bands) and mildly elevated liver enzymes. Lumbar puncture showed 49 WBC/mm^3. Treatment with ceftriaxone and vancomycin was started. Blood cultures were positive for *Neisseria mucosa,* sensitive to chloramphenicol and meropenem. Antibiotic therapy was changed for meropenem and gentamicin. TTE revealed mild aortic valve regurgitation and a vegetation (up to 9×9 mm) on the left coronary leaflet. On the 6th day a septic embolus appeared on the dorsum of his left foot. On the 8th day the patient complained about abdominal pain. A CT angiography revealed a septic embolism 4.5×4 cm in the spleen together with thrombosis of a. mesenteric superior. After an observation period of 4 days, the decision was made that surgery was not indicated. Abdominal ultrasounds were performed on a weekly basis to assess the changes in the spleen; there were no signs of colicvation or abscess formation. The rest of the treatment was unremarkable and after 42 days we discontinued meropenem and the patient was discharged.

P49
CARDIOVASCULAR SYPHILIS: REPORT OF TWO CASES

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Introduction: Tertiary syphilis is a rare disease in the 21st century. Cardiovascular involvement is still associated with high morbidity. Syphilitic aortitis is its most frequent form manifested by dilation of the ascending aorta, aortic regurgitation and involvement of the proximal coronary arteries sparing distal portions. Sometimes there is a history of untreated or incompletely treated syphilis but usually only medical suspicion guides the diagnosis. We present two cases of cardiovascular syphilis.

Case 1: A 60-year-old woman with a history of hypertension, hyperlipidemia and smoking was admitted for thoracic pain workup. On presentation she was in apparent distress with blood pressure of 160/70, heart rate of 130 bpm, O_2 saturation at 80% and bilateral crackles. The electrocardiogram showed elevated ST-segment in aVR and depression in v1–v6. Treatment for acute coronary syndrome was started and a coronary angiogram showed partially occluded proximal left main and right coronary arteries. Although surgery was considered because of proximal coronary disease and suspicion of aortic disease, percutaneous treatment was chosen due to instability. Laboratory results were consistent with latent syphillis (VDRL 1:32 dils, positive FTA-Abs) and the diagnosis of syphilitic aortitis was supported by multiple proximal coronary involvement.

Case 2. A 48-year-old man was referred for treatment of aortic regurgitation. The patient underwent aortic valve and ascending aorta replacement. During surgery the aortic walls appeared swollen and a penetrated aortic ulcer was found. The aortic root was calcific as far as the proximal portion of the right coronary artery. Syphilitic aortitis was suspected and confirmed by positive FTA-Abs and histology. He was treated with penicillin G with excellent results.

Conclusion: Tertiary syphilis is an infrequent presentation in our population. Nonetheless, its cardiovascular effects are potentially fatal and should always be considered in patients with acute aortic or coronary syndromes, especially with proximal disease.

P50
STAPHYLOCOCCUS LUGDUNENSIS ENDOCARDITIS: MULTICENTER STUDY OF 17 CASES

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Introduction: *Staphylococcus lugdunensis* (SL) is a rare cause of infective endocarditis (IE), but its course is often complicated, with high morbidity and mortality. The published experience mostly corresponds to isolated cases and few published series.

Objective: To describe the characteristics of IE caused by SL in a multicenter cohort.

Method: Prospective cohort study of IE episodes diagnosed in seven hospitals during the years 1984–2012, based on the modified Duke criteria (definite and possible). Demographic data, underlying diseases, underlying heart disease, clinical dates, echocardiographic features, microbiological treatment performed and prognosis. These variables were compared with those caused by other *Staphylococcus* spp.

Results: We diagnosed 17 episodes (1.30%) caused by SL from a total of 1240 episodes of IE. Twelve cases affecting native valves, 2 cases affecting prosthetic valves and 3 cases affecting pacemaker lead. In the same period 188 episodes were diagnosed caused by other coagulase-negative staphylococci (CoNS) and 265 episodes caused by *Staphylococcus aureus* (SA). Those caused by SL predominated more in males and had a predominantly community acquisition. These developed heart failure more frequently (59%, 56%, 52%, p = 0.693), severe valvular regurgitation (58%, 38%, 28%, p = 0.020), and needed surgery more often (64%, 53%, 31%, p = 0.001). In contrast, the proportion of patients with severe sepsis was intermediate (23%, 17%, 27%, P = 0.061). Overall mortality was high, similar to those caused by other *Staphylococcus* spp. (47%, 40%, 46%, p = 0.719). Mortality rate was 18% of the operated and 83% of those receiving medical treatment, although surgery could not be performed in 4 cases due to the patient's critical situation.

Conclusion: *Staphylococcus lugdunensis* is an uncommon etiology of IE in our cohort, but has serious complications resulting from valve destruction and hemodynamic compromise that requires in most cases, early surgical treatment.

P51
GRANULICATELLA SPP. ENDOCARDITIS: CASE SERIES

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Introduction: Nutritionally variant streptococci (NVS) are fastidious organisms that could be responsible for up to 6% of cases of streptococcal infective endocarditis (IE). We report four cases of IE caused by *Granulicatella* species.
Case 1: A 31-year-old male patient presented with fever in the past 15 days and weight loss in 5 months. Echocardiogram showed a bicuspid aortic valve with a 21 mm vegetation, abscess and fistula formation. Patient had valve replacement surgery, he was treated with teicoplanin plus gentamycin for four weeks, and was discharged asymptomatic.
Case 2: A 64-year-old male with diabetes was admitted with 30 days progressive dyspnea and loss of 25 kg in 6 months. Echocardiogram revealed two vegetations in the aortic valve (26 mm). Patient developed cardiogenic shock, requiring emergency valve replacement surgery. Postoperatively, he was treated with multiple antibiotic regimens including teicoplanin, meropenem, polymyxin and fluconazole, being discharged fully recovered. He was readmitted two weeks later and died due to heart failure and nosocomial pneumonia.
Case 3: A 75-year-old man was admitted with a 3-month weight loss. Echocardiogram showed vegetation (19 mm) and severe aortic regurgitation. Penicillin plus gentamicin were initiated. Patient died before cardiac surgery due to central nervous system embolization.
Case 4: A 59-year-old female reported a five-month fever prior to admission. At hospital admission, tomography showed spleen and kidney embolization. Echocardiogram identified a bicuspid aortic valve with severe regurgitation and vegetation (12 mm). Valve replacement surgery was performed and the patient was treated with vancomycin plus gentamycin for 30 days. She was discharged home asymptomatic.
Conclusion: NVS are important agents due to the difficulties in isolation and treatment response. We suggest that in IE cases with large vegetations (>10 mm), early surgery and combined antibiotic therapy should be considered, probably leading to more favorable outcomes in NVS endocarditis.

P52
STREPTOCOCCUS PYOGENES INFECTIVE ENDOCARDITIS

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Group A β-hemolytic *Streptococcus* is an uncommon agent in bacterial endocarditis with few cases described in the literature. We report 2 cases of acute infective endocarditis (IE) due to *Streptococcus pyogenes* with systemic complications.
Case 1: A 22-year-old woman was admitted with confusion and a 5-day fever history. The patient presented neck stiffness, altered mental status and mitral regurgitation murmur. Cerebrospinal fluid showed 1840 cells (82% neutrophils) and ceftriaxone was prescribed. Blood cultures yielded *Streptococcus pyogenes*. Echocardiography revealed 2 vegetations in the mitral valve and posterior cusp perforation with moderate reflux. She had no clinical or image signs of heart failure or embolization and was discharged after 4 weeks of ceftriaxone treatment.
Case 2: A 16-year-old boy, with a past history of corrected type II truncus arteriosus, aortic prosthesis and right ventricle–pulmonary artery tube presented with fever in the last week. Blood cultures yielded *Streptococcus pyogenes* and penicillin plus gentamicin was started. The patient developed hypotension, dyslalia and sepsis. A cranial tomography identified a small bleeding area in the left parietal region. Transesophageal echocardiography revealed no signs of vegetations. Abdominal tomography showed spleen abscess and kidney infarction. The patient was submitted to splenectomy on hospital day 30, and to cardiac surgery for aortic valve and right ventricle–pulmonary artery tube replacement on hospital day 36. He completed 4 weeks of antibiotic treatment after surgical procedures and was discharged.
Conclusion: Both cases were young people presenting with acute illness and several complications related to IE. According to current data, most cases of *Streptococcus pyogenes* IE occur in children or young adults, have rapid clinical progression and high rates of complications, just as our patients. This agent is associated with high virulence and high rates of complications and must be promptly recognized and treated to avoid high mortality rates.

P53
NEISSERIA GONORRHOEAE INFECTIVE ENDOCARDITIS. A CASE REPORT

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Background: Gonococcal endocarditis is a rare (1–2%) but serious manifestation that occurs in patients with disseminated gonococcal infection (DGI), which is also infrequent (0.3–5%).
Case report: A 56-year-old man, HIV+ (CD4 = 320/mm^3 [29%] – CV = 38,300 copies/ml) with HAART (abacavir/lamivudine/efavirenz) was admitted with fever, asthenia, anemia and low platelet count; he started the clinical picture 20 days before.
On physical exam: blood pressure 120/80 mmHg, heart rate 100/minute, axillary temperature 38°C, liver and spleen enlargement, groin and axillary lymph nodes. No signs of arthritis or urethritis. Laboratory analysis results: hematocrit 24%, WBC 8000, platelets 76,000, sed rate 68 mm/h; normal liver and renal function tests. Serology test: HBV, HCV, VDRL and Chagas disease were negatives. Blood cultures were negatives. Colonoscopy and upper gastrointestinal endoscopy screening were performed. Two days after these procedures the patient had fever and chills. *Neisseria gonorrhoeae* (beta-lactamase negative, ciprofloxacin resistant and penicillin intermediate) was isolated in 2/2 blood cultures obtained in this clinical scenario. Nasopharyngeal swab was negative for gonococci. TEE: aortic vegetation and thrombus in ascending aorta. TC scan angiography and cardiac MRI showed mural thrombus and pseudoaneurism of ascendenting aorta. Ceftriaxone 4g/d was started and cardiovascular surgery (ascending aorta replacement) was undertaken. Aortic biopsy was sent to the National Reference Laboratory and PCR confirmed the diagnosis of *N. gonorrhoeae*. The patient was discharge in good clinical condition and he is asymptomatic after 1 year of follow up.
Comments: *Neisseria gonorrhoeae* infective endocarditis is a rare complication of DGI and usually occurs in young male adults without previous valve disease. Although often associated with the arthritis–dermatitis syndrome, endocarditis may be the sole manifestation of DGI. Almost 23% had urinary symptoms and in 2/3 of cases arthritis or tenosynovitis precede the clinical picture. Mortality ranges from 20% to >50% (in patients who underwent valve replacement). Mycotic pseudoaneurism is an exceptional but severe complication of *N. gonorrheae* IE.

P54
ECHINOCOCCUS GRANULOSUS INFECTIVE ENDOCARDITIS. A RARE PRESENTATION OF AN HELMINTH INFECTION

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Background: Echinococcosis is a zoonosis that can cause invasive infection in humans. In Argentina are among the most prevalent helminthiases. The hydatid cysts of *E. granulosus* usually affect the liver or lungs but may be found in any organ of the body. Although

very rare (<2%), when the heart is involved, cardiac wall is the most frequent localization (myocardial cyst).
Case report: A 32-year-old woman with a history of treated lungs hydatid cysts in 2006 (surgery and albendazole) presented during pregnancy with progressive dyspnea. Cesarean section was performed after TTE showed a mass in right atrial endocardium and was derived to cardiac surgery. A TEE showed pedicled and mobile mass in the right atrium and PASP = 75 mmHg; TC scan angiography with multiple cysts in lungs, pulmonary artery compression by a cyst and calcified liver cysts. Cardiac MRI revealed two pedicled and mobile cysts on right atrial endocardium. Combinated treatment with albendazole plus praziquantel was started; cardiopulmonary surgery was done with atrial and lung cyst squeezing PA excised. No myocardial wall cysts were observed. Histopathologic analysis confirmed the diagnosis of *Echinococcus granulosus*. The patient was discharged in good clinical condition, with PASP = 50 mmHg and under prolonged treatment with combined anthelmintic agents.
Comments: Echinococcosis is frequent in rural areas where cattle and flesh-eating animals live together. The cyst is usually asymptomatic, but in certain location, as in the heart, can cause high morbility: rupture into the circulation with anaphylactic reaction, damage to the cardiac valves, ischemic syndromes, systemic or pulmonary embolization. Echocardiography is the most reliable test but cardiac MRI is currently a useful complementary diagnostic method. Hydatid cyst must be involved in the differential diagnosis of cardiac cysts in endemic areas. A multidiscipilinary approach should include surgery and combined anthelmintic agents active against this larval trematode.

P55
CA-MRSA AS A CAUSE OF LEMIERRE'S SYNDROME: FIRST REPORT OF TWO CASES IN ARGENTINA

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Background: Lemierre's syndrome (LS) is currently an uncommon disease and *Fusobacterium necrophorum* is responsible for two-thirds of the cases. From 1965 to the present, a total of 11 cases were reported in the literature caused by *Staphylococcus aureus*, one of them was recently associated to USA300 clone. Here we report two LS cases in Argentina associated with CA-MRSA.
Case reports: ***Case 1:*** a 17-year-old man, without any clinically relevant data, was hospitalized in September 2011 due to right internal jugular vein and right cavernous sinus thrombosis, brain abscess and septic pulmonary emboli. MRSA was isolated in 3/4 blood cultures. Antibiotic treatment and anticoagulation were administered with complete clinical resolution. ***Case 2:*** a 34-year-old man, without any clinically relevant data, was hospitalized in November 2011 with bilateral internal jugular vein, transverse sinus thrombosis, and septic pulmonary emboli. MRSA was isolated in 2/2 blood cultures and BAL. The patient died after multiple complications in spite of antibiotic treatment and anticoagulation.
Strains were not epidemiologically related. The type of staphylococcal chromosomal cassette (SCC*mec*) and PVL were determined by PCR as previously described. Genetic relationship among isolates and reference strains was established by *Sma*I-PFGE. Both strains were characterized as CA-MRSA, carried SCC*mec*IV, were PVL(+) and were not genetically related by PFGE. One of the CA-MRSA (case 2) was genetically indistinguishable by PFGE from CA-MRSA ST5-SCC*mec*IV-PVL+, the dominant CA-MRSA clone detected in Argentina since 2000. None of these strains was related to the USA300 clone (ST8) or the Southwest Pacific (ST30) clone. To the best of our knowledge, these represent the firsts two cases of LS associated with CA-MRSA reported in Argentina.
Comments: CA-MRSA could be an emerging cause of LS in addition to typically recognized organisms. Awareness of CA-MRSA will guide empirical antibiotic choice and may positively impact patient outcomes.

P56
THE NEW PROFILE OF GRAM-NEGATIVE BACILLI PROSTHETIC VALVE ENDOCARDITIS

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Introduction: Gram-negative bacilli prosthetic valve endocarditis (GNBPVE) is a rare but serious complication. We describe the current profile of GNBPVE.
Material and Methods: Prospective, observational and multicenter study. GNBPVE were classified depending on the time after valve replacement: early (EPVE, <1 year) and late (LPVE, >1 year). Diagnosis delay was defined as diagnosis made >15 days after clinical presentation.
Results: Among 342 episodes of prosthetic valve endocarditis, Gram-negative bacilli were isolated in 26 episodes (7.6%), 6 EPVE (23%) and 20 LPVE (77%). 14 episodes (53%) were community-acquired, 3 (11%) health-care associated and 9 (36%) nosocomial. No predisposing factor was found in 13 cases, most in community-acquired GNBPVE. An underlying disease was described in 14 patients (56%) mainly diabetes mellitus (9) and chronic anemia (3). None of the episodes was related to drugs. There was diagnosis delay in 13 cases (50%). The main clinical presentation was fever and malaise in 22 (85%), followed by cardiac presentation in 6 (23%). Five presented as constitutional syndrome (19%), all of them in LPVE (p 0.28). Systemic embolism was seen in 6 patients (23%), 3 presenting as stroke. Fourteen episodes were caused by Enterobacteriaceae (54%), 4 (15%) by non-fermenting GNB. Two episodes were caused by HACEK organisms. Prosthetic dehiscence was seen in 8 patients (31%), stenosis in 6 (23%) and moderate or severe insufficiency in 6 (23%). Five patients developed periannular extension (19%). Seven patients developed septic shock (27%). Twenty patients (78%) showed vegetation on echocardiography, 9 (45%) bigger than 10 mm. Fifteen patients (58%) underwent surgery. In-hospital mortality was 42%, 1 (16.6%) in EPVE vs. 10 (50%) in LPVE (p 0.18).
Conclusions: GNBPVE is suffering from epidemiological changes. It is rare in the early period and is more frequently related to health care. HACEK prevalence is low. Large vegetations on echocardiography are common and in-hospital mortality remains high.

P57
INFECTIVE ENDOCARDITIS OF PROSTHETIC MITRAL VALVE, CAUSED BY *ACINETOBACTER BAUMANNII*

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Introduction: *Acinetobacter baumannii* is a causative agent of nosocomial infections; it is very difficult to identify and treat, which is a good explanation for its high lethality.
Aim: To introduce the case of a patient with infective endocarditis of a prosthetic mitral valve caused by *Acinetobacter baumannii*, who survived this infection.
The patient is a 65-year-old female. She came to the emergency room on April 10, 2012 with high fever, chills, dyspnea and clinical features of encephalopathy. Her anamnesis showed a surgical intervention of the mitral and aortic valves, one month ago. TEE revealed small hypoechogenic vegetations in the mitral valve. Three weeks after the hospitalization, the patient underwent another intervention, which consisted of another replacement of the mitral and aortic valves. The blood cultures were negative, while the cultures of the valves evidenced the growth of *Acinetobacter baumannii*. The bacteria was resistant to ampicillin, augmentin and imipenem. The patient was treated with imipenem in the beginning, but after the antibiogram she was treated with more effective antibiotics, such as piperacillin–tazobactam and ciprofloxacin. The patient had good response to this treatment (temperature normalized after 7 days, and TTE showed no

verrucas after 6 weeks of therapy). The patient is presently in good condition according to periodic clinical and imaging follow up.

P58

DIVERSITY OF VIRIDANS GROUP STREPTOCOCCI ISOLATED FROM PATIENTS WITH INFECTIVE ENDOCARDITIS IN CROATIA

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Background: Viridans group streptococci (VGS) are one of two leading pathogens causing native valve infective endocarditis (IE). Uniform penicillin susceptibility can no longer be assumed but VGS are still presumed to be susceptible to vancomycin.
Aim: The aim of this study was to examine the population structure of VGS isolates causing IE in Croatian patients and to investigate susceptibility of the isolates to the antibiotics most commonly used for treatment.
Methods: Patients with definite IE caused by VGS treated at University Hospital for Infectious Diseases Zagreb (UHID) from 2000 to 2012 were included. Medical records and microbiological data on phenotypic identification and antibiotic susceptibility of VGS isolates determined as minimal inhibitory concentration (MIC) by gradient diffusion (E-test) to penicillin, ceftriaxone and vancomycin were analyzed.
Results: Three hundred and two patients with IE were treated in UHID from 2000 to 2012. VGS caused IE in 59 patients aged 19 to 85 years. Two thirds of patients were men. Most of the patients had native valve endocarditis (49/59), 36 had IE of aortal valve and 3 had bicuspidal aortal valve.
Thirty-eight VGS isolates were identified to species level by phenotypization. At least 10 *Streptococcus* species were found belonging to four recently categorized groups: *S. mitis* (12), *S. oralis* (2), *S. sanguis* (8), *S. parasanguis* (1), *S. gordonii* (1) – *mitis* group, *S. anginosus* (2), *S. constellatus* (4), *S. intermedius* (4) – *anginosus* group, *S. mutans* (1) – *mutans* group, and *S. salivarius* (1) – *salivarius* group. Twenty-one other isolates were recorded as *S. viridans* (19), *Streptococcus* spp. (1) and streptococci (1).
Antibiotic sensitivity was available for 44 VGS isolates. All isolates were susceptible to penicillin (MIC 0.002–0.19 μg/mL). Penicillin MIC90 was 0.047 μg/mL. Ceftriaxone MIC were 0.002–0.25 μg/mL and MIC90 was 0.125 μg/mL. Twenty-three isolates were tested to vancomycin having MIC 0.25–2 μg/mL and vancomycin MIC90 0.75 μg/mL.
Conclusion: More than one third of IE cases (24/59) in the study were caused by streptococci of the *mitis* group and half of them by *Streptococcus mitis.* Antibiotic susceptibility to most common antibiotics used for IE treatment did not differ significantly in recording MICs between individual *Streptococcus* species or groups of streptococci. Few isolates with high MIC values to penicillin and to vancomycin point to the need of correct VGS identification and continuous surveillance on MICs.

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INFLUENZA A (H1N1) INFECTION AND PERICARDIAL EFFUSION IN A 50-YEAR-OLD WOMEN: A CASE REPORT

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Acute myopericarditis has infectious and non-infectious causes. However, viral infection is one of the most prevalent aetiological factors of pericarditis and the prevalence of cardiac involvement and myopericarditis caused by influenza infection is not yet known. There have already been several reports of H1N1 cardiac involvement in different age groups. They have suggested that the novel H1N1 influenza A virus is more often associated with severe cases of myopericarditis than previously encountered influenza strains.
We describe the development of pericardial effusion during swine Influenza A infection in a 50-year-old woman with no signs of cardiac tamponade and acute heart failure. Pericardial effusion was diagnosed by transthoracic echocardiography. Resolution of both symptoms and pericardial effusion occurred after treatment with oseltamivir and ibuprofen.
As we saw in our case, cardiac involvement in influenza is usually reported to occur during the first week after the onset of influenza symptoms. The pathogenesis of myopericarditis is not clear. Two main described mechanisms of myocyte damage are direct viral invasion and a host immune-mediated pathology, the former mechanism usually playing the main role in cases with early cardiac involvement.
Acute pericarditis and pericardial effusion are very rare complications of H1N1 influenza infection. However, the clinical course and response to medical treatment of acute pericarditis presented here showed no difference from acute pericarditis due to any other cause. This experience can be a reference for diagnosis and treatment of pericarditis and pericardial effusion complicated by novel influenza infection.

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DEVELOPMENT AND CHARACTERIZATION OF PORCINE MODELS OF NON-BACTERIAL AND STAPHYLOCOCCAL ENDOCARDITIS: HISTOPATHOLOGICAL ASPECTS

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Non-bacterial thrombotic endocarditis (NBTE) and, in particular, infective endocarditis (IE) are serious diseases. *Staphylococcus aureus* typically causes acute IE with a high embolization risk. Pigs are highly comparable to humans in numerous cardiovascular key-characteristics. Furthermore, the size of the pig allows for utilization of human diagnostics and treatment methods, e.g. diagnostic imaging and surgical procedures. Therefore, the pig was evaluated as a model for non-bacterial as well as *S. aureus* endocarditis, with special focus on histopathological manifestations.
Ten pigs underwent surgery with placement of an indwelling catheter in the left side of the heart. Six of the animals were non-inoculated in order to study the development of NBTE. The remaining four pigs were inoculated intravenously once (day 4 after surgery) or twice (days 4 and 11 after surgery) with 10^5–10^7 CFU/kg body weight (BW) of *S. aureus* strain S54F9. Clinical examination, echocardiography and bacterial blood cultures were used to diagnose and monitor the diseases. The animals were euthanized 2–15 days after surgery and tissues were sampled for histopathology. Endocardial lesions were examined in sections stained with HE, and immunohistochemically for *S. aureus* and myeloperoxidase.
The two pigs inoculated with one dose of 10^7 CFU *S. aureus*/kg BW developed clinical, echocardiographic and pathological signs of IE. NBTE was present in all other pigs, except one. *S. aureus* was cultured only from serial blood samples of the IE pigs. Histologically, lesions were comparable to human endocarditis, with numerous *S. aureus* bacteria present within the IE vegetations.
Staphylococcus aureus endocarditis was successfully established after intravenous inoculation of 10^7 CFU *S. aureus*/kg BW. The model parallels typical diagnostic and histopathological characteristics seen in the human disease. Furthermore, NBTE was induced in all but one of the pigs without IE. Thus, the porcine models can be valuable for future studies of the diseases.

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ACTIVITY OF DABIGATRAN ETEXILATE AND ABCIXIMAB IN THE PROPHYLAXIS OF EXPERIMENTAL ENDOCARDITIS DUE TO LOW-GRADE BACTEREMIA

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Background: Infective endocarditis (IE) could result from cumulative low-grade bacteremia following daily activities (*e.g.* tooth brushing) in the case of streptococci or from repeated bouts of bacterial discharges from a colonized site or i.v. device in the case of *Staphylococcus aureus*. In this context, the prophylaxis of IE with antibiotics would be compromised and other alternatives should be investigated. Platelet aggregation, induced via thrombin or the platelet fibrinogen receptor GPIIbIIIa, is strongly implicated in vegetation formation. We tested whether inhibition of thrombin with dabigatran etexilate or blocking GPIIbIIIa with abciximab could prevent streptococcal and *S. aureus* experimental endocarditis (EE) in rats using a model of continuous low-grade bacteremia (Veloso et al., IAI 2011).
Methods: Shortly after insertion of a catheter across the aortic valve, animals received over 48 h either i.p. dabigatran etexilate (DE; 10 mg/kg twice daily), i.v. abciximab (ABCX; administered every 24 h by a bolus of 0.25 mg/kg followed by a continuous infusion of 0.125 μg/kg/min) or saline (Controls). Rats were then inoculated i.v. with *Streptococcus gordonii* Challis (10^6 CFU) or *S. aureus* Newman (10^5 CFU) given by continuous low-dose infusion (0.0017 ml/min) over 10 h. Animals were killed 24 h later. Vegetation (veg) weight and infection rate were determined.
Results: See the table.

	S. gordonii Challis		*S. aureus* Newman	
	Veg. weight (mg)	Infected veg/total	Veg. weight (mg)	Infected veg/total
Control	22.5±1.9	17/21 (81%)	24.5±2.0	15/18 (83%)
DE	15.5±1.5*	7/10 (70%)	9.3±0.9*	2/8 (25%)*
ABCX	19.2±1.7	2/13 (15%)*	15.1±2.5*	1/8 (12.5%)*

*$P<0.05$ vs controls

Conclusions: Dabigatran etexilate prevented only *S. aureus* EE, and abciximab both *S. gordonii* and *S. aureus* EE, when implemented in a realistic rat model of low-grade bacteremia. These results suggest that anticoagulant and antiplatelet drugs could be effective in preventing IE following spontaneous low-grade bacteremia in humans.

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IMMUNIZATION OF RATS WITH *LACTOCOCCUS LACTIS* EXPRESSING CLUMPING FACTOR A PROTECTS FROM *STAPHYLOCOCCUS AUREUS* EXPERIMENTAL ENDOCARDITIS INDUCED BY LOW-GRADE BACTEREMIA

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Background: *Staphylococcus aureus* is a major cause of severe infections, including bacteremia, or infective endocarditis (IE). These result from more or less prolonged bacteria low-grade discharges from a colonized site or i.v. devices. *S. aureus* is also a major cause of community and health care associated bacteremia. Therefore, the development of an effective vaccine against *S. aureus* represents a clinical priority. A variety of *S. aureus* vaccine candidates have been tested in a number of animal models with some success, but all failed in clinical trials. The use of *L. lactis* as antigen delivery vehicle is a potential vaccination strategy against bacterial infections. Here we tested the efficacy of rat's immunization with recombinant *L. lactis* expressing *S. aureus* fibrinogen-binding protein A (ClfA), in the prevention of *S. aureus* experimental endocarditis (EE) due to low-grade bacteremia.
Methods: Four-week-old female Wistar rats were immunized i.p. with 10^8 CFU of UV-killed recombinant *L. lactis* expressing *S. aureus* ClfA (pIL253 plasmid). Recombinant lactococci were emulsified in Freund's adjuvant and injected on days 0, 14 and 28. Control groups received saline, the adjuvant alone or parent *L. lactis* pIL253. Catheter-induced aortic vegetations were produced on day 40. One day later, rats were inoculated i.v. with 10^4 CFU of *S. aureus* Newman, given by continuous low-dose infusion at a pace of 0.0017 ml/min over 10 h. The vegetation infection rates were determined 24 h later.
Results: While no or weak protection occurred in control animals receiving saline (3/9; 33%), adjuvant (2/5; 40%) or *L. lactis* pIL253 (2/8; 25%), immunization with *L. lactis* ClfA prevented *S. aureus* EE in 16/22 (72%) rats ($P<0.05$ vs saline and *L. lactis* pIL253).
Conclusions: The protection afforded by immunization with recombinant *L. lactis* expressing *S. aureus* ClfA suggests that this could be a promising approach to prevent *S. aureus* infections, including IE.

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HISTOPATHOLOGICAL FINDINGS IN CARDIAC VALVES SURGICALLY REMOVED FROM PATIENTS WITH INFECTIVE ENDOCARDITIS

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Objectives: To evaluate histopathological findings of cardiac valves surgically excised from patients with infective endocarditis relative to antimicrobial therapy and other clinical variables.
Methods: We studied 44 patients, 30 men and 14 women aged 10–76 (median 52.5) years. Thirty biopsies were of bioprosthetic valves and 25 of native valves. The infecting microorganisms were streptococci in 18 (41%), *Staphylococcus* spp. in 9 (20%), *Enterococcus* spp. in 3 (7%), Gram-negative rods in 2 (4%) and others in 6 (13%). In 6 patients the infecting microorganism was not identified in blood cultures. All histopathological sections were reviewed by the same pathologist. A semi-quantitative analysis was used.
Results: The mean of pre-operative antibiotic treatment was 19 days. Other findings are presented in Table 1.

Table 1: Histopathological valve findings relative to pre-operative antibiotic therapy (days)

	Antimicrobial therapy, n (%)	
	<30 days	⩾30 days
Presence of polymorphonuclear infiltrate	28/31 (90)	11/13 (84)
Predominance of polymorphonuclear infiltrate	16/31(51)	7/13 (53)
Presence of lymphomononuclear infiltrate	24/31 (77)	10/13 (77)
Presence of microorganism	14/31 (45)	8/13 (61)
Presence of fibrin	30/31 (96)	11/13 (84)
Relapses	2/31 (6)	2/13 (15)
Death	1/31 (3)	1/13 (7)

Conclusion: In patients with infective endocarditis treated for more than 30 days, histopathological sections of the excised valves may demonstrate bacteria and signs of acute inflammation.

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THE INTERACTION OF DNA- AND RNA-CONTAINING VIRUSES WITH CULTURES OF BONE MARROW MESENCHYMAL STEM CELLS AND CARDIOMYOCYTE PRECURSOR CELLS PREPARED FROM THESE CELLS

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It is known that viruses, particularly enteroviruses, are the etiological factors for cardiovascular disease development. Enterovirus infection brings on acute and chronic carditis, which can aggravate to dilated cardiomyopathy. It has been shown that enteroviruses could infect all major types of heart cells: cardiomyocytes (CMC), fibroblasts, endothelial cells and some others. Herpes viruses, particularly herpes simplex virus type 1 (HSV-1), could also affect the CMC, being a cause of cardiovascular disease. Mesenchymal stem cells (MSC) and

cardiomyocyte precursor cells derived from them by reprogramming are currently being investigated for efficacy in cell therapy for cardiovascular disease, but the information about the sensitivity of these cells to the virus is insufficient.

The purpose of this study was to explore the reproductive capacity of isolated human viruses (HSV-1 and ECHO 30) in cultures of mesenchymal stem cells and cardiomyocyte precursor cells derived from them by reprogramming using 5-azacytidine.

The infections caused by viruses (HSV-1 and ECHO 30) in cultures of murine bone marrow mesenchymal stem cells (phenotype $CD44^+$, $CD90^+$, $CD45^-$) were modeled. It was revealed that HSV-1 caused focal productive lytic infection in 10–20% of MSC and induced the formation of reactive oxygen species in the early stage of infection (4 hours). Viral DNA persistence in cultured MSCs for 7 days was found. Infection caused by ECHO 30 was characterized by the absence of pronounced cytopathology, by production of viral proteins in 10–12% of the cells, by viral DNA persistence for 7 days. Virus effects on the redox system of cells at the early stage of infection were not found. Cardiomyocyte precursor cells reduced sensitivity to HSV-1 and the absence of changes in it in respect of enterovirus ECHO 30 were revealed as compared to infected MSC.

The results can be used to develop monitoring and biosafety protocols for transplanted MSC derived from bone marrow, as well as to determine the prognosis in allogeneic and autologous transplantation of cells with these phenotype.

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AMPICILLIN PLUS GENTAMICIN OR AMPICILLIN PLUS DAPTOMYCIN FOR ENTEROCOCCAL INFECTIOUS ENDOCARDITIS: A RETROSPECTIVE COHORT STUDY

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Introduction: Enterococci are the third cause of infectious endocarditis (IE). The emergence of vancomycin-resistant (VRE) and high-level aminoglycoside resistant (HLAR) strains represents a challenge for clinicians. Aim of this study is to evaluate the effectiveness and safety of the association between ampicillin and gentamicin (AG) versus ampicillin plus daptomycin (AD), against enterococcal IE.

Methods: Retrospective cohort study. All patients diagnosed with enterococcal IE discharged from Ospedale di Circolo, Varese, Italy, from 2005 to 2012 were enrolled. We divided the patients into two groups: those treated with AG and those treated with AD.

Results: We included 24 patients, 12 for each group, with a mean age of 67 years (range 28–94), and male:female ratio of 2. In each group 50% of patients had prosthetic valves. The overall median duration of antibiotic treatment was 42 days. In both groups ampicillin dose was 2 g q4 h. In the AG group, 11/12 patients had *E. faecalis* IE (2 HLAR), and 1/12 had *E. durans* IE. Seven out of 12 (58.3%) patients underwent cardiac surgery. Gentamicin was administered at 5 mg/kg/day, for a median duration of 14 days (range 4–28). Two out of 12 patients (16.6%) developed acute renal failure and had to discontinue gentamicin. In the AD group, 11/12 patients had *E. faecalis* IE (5 HLAR), and 1/12 had *E. faecium*-HLAR IE. Six out of 12 patients underwent cardiac surgery. Daptomycin was administered at 8 mg/kg/day, for a median duration of 42 days (range 16–56). No patients in the AD group experienced side effects. At 6-month follow-up, in both groups, 11/12 patients were alive and no patient had relapses.

Conclusions: Our study showed that AG is as effective as AD for treating enterococcal IE. AD therapy seems to be better tolerated, and effective also against *E. faecium* HLAR-strains. Larger studies are needed to assess the role of ampicillin plus daptomycin against enterococcal IE.

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DAPTOMYCIN USE IN INFECTIVE ENDOCARDITIS AT A CARDIAC SURGERY REFERRAL HOSPITAL, 2009–2012, RIO DE JANEIRO, BRAZIL

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Background: Daptomycin is active against Gram-positive microorganisms, including those resistant to penicillins, cephalosporins and vancomycin. This makes it an important therapeutic option in cases of right-sided infective endocarditis (IE). It has become available in Brazil since 2009.

Methods: This is a prospective and consecutive cohort study in adults in a cardiac surgery referral hospital.

Results: Six patients with definite IE were treated with daptomycin in 2009–2012 at Instituto Nacional de Cardiologia. There were 5 males and 1 females. Mean age was 53.8±7.4 years. Clinical presentation was acute in 5 and subacute in 1 patient. Affected structures/microorganisms responsible were pacemaker (PM)/*S. aureus*, PM and mitral valve (MV)/MRSA, PM/*Propionibacterium acnes*, MV/*E. faecalis*, MV/*S. epidermidis*, and MV/not identified. Comorbidities were chronic renal failure in 3, diabetes in 1. All patients had fever, 3 had embolic phenomena and 2 had acute heart failure. All had transesophageal echocardiograms with vegetations. All had surgical indication. None of the patients had daptomycin as the antibiotic of first choice (4 had vancomycin, 2 of which associated with gentamicin, and 2 had cefazolin). Mean days of antibiotic use prior to daptomycin was 9. Indications for daptomycin use were lack of clinical response (1), worsening renal function (3), vancomycin MIC above 1.5 for *S. aureus* (1) and severe hypersensitivity to vancomycin (1). Mean daptomycin dose given was 7.3±1.9 mg/kg/day. Number of days used was 14.2±15.9 preoperatively and 24.8±9.4 days postoperatively. Association with rifampin was used in 3 patients and with gentamicin in 1. No creatine phosphokinase elevations were noted in the 4 patients in whom this was checked; hypomagnesemia was noted in 3 of 5 patients. One patient died in the same admission, with persistent sepsis (the patient with MRSA).

Conclusions: Daptomycin has been used successfully in Brazilian patients with IE, involving the right side (pacemakers and tricuspid valves) and the left side. However, more experience needs to be gained.

P67
24H-CEFUROXIME CAN BE SUFFICIENT FOR ANTIMICROBIAL PROPHYLAXIS IN CARDIAC SURGERY

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Introduction: Recent evidence points at a possible advantage of amtimicrobial prophylaxis prolongation up to 48 h post-operatively in cardiac surgery, but the issue is not resolved yet, because some studies have shown non-inferiority when 24 hours is used only, and the guidelines are not homogeneous.

Objective: To compare the incidence of post-operative infections in adult patients undergoing cardiac surgery who received 24 h of cefuroxime instead of 48 h of cefazolin as antimicrobial prophylaxis.

Methods: The study had two parts, a retrospective (12 months) and a prospective one (10 months). The retrospective group received a single dose of cefazolin 2 g before the surgical incision, with further doses of 2 g at 6-hour intervals by 48 hour. The prospective group received cefuroxime 1.5 g at induction and two further doses of 0.75 g at 8-hour intervals. 775 consecutive adult patients who underwent cardiac surgery were included, and demographic data, type of surgery and post-operative infection were compared.

Results: 446 patients received cefazolin and 329 cefuroxime. A total of 534 (69%) were male and the mean age was 58 years (14–86 years). No differences were found in frequency of diabetes (17.8%), obesity (4%), renal failure (4%), perfusion time and type of surgery (25% minimally invasive cardiothoracic). Twenty-four (7.29%) and 39 (8.74%) patients in the cefuroxime and cefazolin groups, respec-

Table (abstract P68): Clinical and microbiological data of the three MRSA infections

Case	Gender, age and underlying conditions	Type of infection	Date and site of first MRSA isolation	Susceptibility (MIC, μg/ml)	Date and site of second isolation	Susceptibility (MIC, μg/ml)	Antibiotic therapy (type, dosage and date)	Outcome
1	Female, 69 years old, underwent biological aortic valve replacement and mitral valve anuloplasty one month before	IE on mitral and biological aortic valves	02/04/12 BCs	Daptomycin (0.75) Vancomycin (1) Teicoplanin (⩽0.5) Gentamicin (0.5) Linezolid (1) Trimethoprim/ sulfamethoxazole (⩽10)	13/04/12 BCs	Daptomycin (4) Vancomycin (2) Teicoplanin (>8) Gentamicin (⩽1) Linezolid (2) Trimethoprim/ sulfamethoxazole (⩽1/19) Quinupristin/ Dalfopristin (⩽0.25)	– Teicoplanin (800 mg/day first 24hours, 400 mg/day second day, 200 mg/day from the third day) plus Gentamicin (80 mg Bid) for 7 days – Daptomycin (350 mg day) plus Rifampicin (600 mg day) for 15 days – Linezolid (600 mg bid) plus Gentamicin (160 mg day) for 9 days – Quinupristin/Dalfopristin for 14 days	BCs negative under treatment with Linezolid and later with Quinupristin/ Dalfopristin Non MRSA-IE related death
2	Female, 90 years old, COPD, CHF, biological aortic valve replacement 14 months before	IE on biological aortic valve	21/04/12 BCs	Daptomycin (0.5) Vancomycin (⩽0.5) Teicoplanin (⩽0.5) Gentamicin (⩽1) Linezolid (1) Trimethoprim/ sulfamethoxazole (⩽1/19)	29/04/12 BCs	Daptomycin (4) Vancomycin (⩽0.5) Teicoplanin (⩽5) Gentamicin (⩽0.5) Linezolid (2) Trimethoprim/ sulfamethoxazole (<10)	– Teicoplanin (400 mg/day first 24 hours, 200 mg/day from the second day) for 5 days – Vancomycin (1000 mg/day) until death	MRSA-IE related death after 13 days of treatment

BCs, blood cultures; CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; DS, daptomycin susceptible; IE, infective endocarditis; MRSA, methicillin resistant *Staphylocccus aureus;* SSI, surgical site infection.

tively, developed surgical site infections (p = 0.465). Deep sternal wound infections (DSWI) occurred in 9 (2.74%) in the cefuroxime group and in 13 (2.91%) in the cefazolin group (p = 0.76). No difference was found in global infections (15.8% vs 16.4%; p = 0.46). The most common pathogen isolated was MSSA in both groups.

Conclusions: This study revealed a similar incidence of postoperative infections in adult patients undergoing cardiac surgery receiving 24 h of cefuroxime compared to 48 h of cefazolin as antimicrobial prophylaxis.

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DAPTOMYCIN NON-SUSCEPTIBILITY IN PATIENTS PREVIOUSLY TREATED WITH GLYCOPEPTIDES FOR PROSTHETIC VALVE INFECTIVE ENDOCARDITIS

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Objective: To describe the clinical and microbiological features of two cases of prosthetic valve infective endocarditis (PV-IE) caused by methicillin-resistant *Staphylococcus aureus* (MRSA) in which daptomycin non-susceptibility (DNS) was detected.

Methods: Retrospective chart review of two patients with MRSA PV-IE in which DNS was detected by Vitek 2 system in the blood cultures (BCs) drawn during treatment, hospitalized in a large general hospital in Rome (Italy), over a 6-month period. The MRSA strains were sent to a reference laboratory for identification and susceptibility confirmation and for further molecular study.

Results: As shown in the Table, the study patients were two females older than 65 years with biologic aortic valve who developed a MRSA PV-IE 1 and 14 months after heart surgery, respectively. In both cases the MRSA strains were susceptible to daptomycin at the beginning of treatment. Teicoplanin was initially started in both cases but despite therapy BCs were still positive after 5 days of treatment, yielding a DNS-MRSA. In the first case the strain was further confirmed as vancomycin-intermediate *S. aureus* (VISA).

Conclusions: Clinicians should be aware of DNS occurrence in patients with severe MRSA infections, mainly in presence of prosthetic material and after exposure to glycopeptides.

P69
SUCCESSFUL TREATMENT OF *ABIOTROPHIA DEFECTIVA* ENDOCARDITIS WITH LINEZOLID

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Background: *Abiotrophia defectiva* is part of the normal flora of the oral cavity, the urogenital and intestinal tract. Infectious endocarditis (IE) due to *Abiotrophia* spp. is uncommon, and accounts for less than 4% of streptococcal IEs. Treatment protocol has not been fully established; the bacteriologic failure occurs in up to 40% despite *in vitro* sensitivity, with relapse rates up to 17%. The American Heart Association guidelines suggest a treatment consisting of penicillin or ampicillin plus aminoglycoside for four to six weeks.

Case report: A 50-year-old male presented with a 21-day history of fatigue, low grade fever, arthralgia and recurrent aphtae in the oral cavity. The day before admission, he became febrile up to 39°C with chills and rigors. Past medical history was unremarkable besides occasionally moderate neutropenia which was not evaluated further. Physical examination revealed a cardiac systolic murmur. Initial blood tests showed an elevated ESR of 84 mm/h, CRP 32 mg/L and a WBC of 3.7×10^9 (ANC 1.6×10^9). All of 6 blood cultures were positive for *Abiotrophia defectiva* [susceptible to vancomycin (MIC 1 μg/ml), rifampicin (MIC 0.004), teicoplanin (MIC 0.38) and clindamycin (MIC 0.19)]. TTE showed a mitral regurgitation without signs of vegetations. TEE revealed fluctuating vegetation (1 cm) on the posterior leaflet of mitral valve and a significant mitral valve prolapse with severe mitral insufficiency. The patient initially received ceftriaxone which was discontinued because of severe urticaria, and therapy with vancomycin, gentamicin and rifampicin was given. After a total of 15 days of therapy, neutropenia worsened (ANC 342×10^6) and renal impairment developed. Previous antimicrobial therapy was discontinued and linezolid was given to complete 6 weeks of therapy. The clinical course was unremarkable and control blood cultures were sterile. Elective mitral valve repair and later mitral valve replacement surgery were performed; no signs of endocarditis were noticed on affected valves. In the 5-year follow-up there was no relapse of IE.

Conclusion: We presented a case of IE caused by *Abiotrophia defectiva* treated with linezolid, an unusual option for IE treatment. Our case report suggests that linezolid may be used in endocarditis caused by *Abiotrophia defectiva* in patients with limited treatment options.

P70
NEPHROTOXICITY DURING AMINOGLYCOSIDE THERAPY FOR ENDOCARDITIS

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Aminoglycosides are commonly used in the treatment of infective endocarditis (IE). Because of its nephrotoxic potential its place in the treatment arsenal is currently being debated. A cohort study of 128 consecutive patients with IE treated at Sahlgrenska University Hospital, Gothenburg 2007 through 2010 evaluated risk factors for kidney dysfunction during treatment and follow-up. A majority of the patients (93%) received combination therapy with tobramycin, 41% also received vancomycin. Kidney function was assessed by estimated glomerular filtration rate (eGFR), recorded prior to treatment, weekly during treatment, and 1 month, 3 months, and 1 year after IE treatment.

There was a mean decrease of eGFR from 88.4 to 78.0 mL/min (−11.8%) from start of tobramycin treatment to 1 week post-treatment. The decrease was accentuated 1 month post-treatment (−12.4%). A grad-

ual reversibility was recorded 3 months (−7.4%) and one year (−6.3%) post-treatment, respectively.
Age, total dose of tobramycin, cardiac surgery, concomitant treatment with potential renal toxic drugs, concomitant vancomycin treatment, and elevated serum tobramycin concentrations were associated with accentuated in-hospital decrease in eGFR.
Major risk factors for permanent decrease in kidney function were established after subgroup analyses of comparable groups. A total dose of >2500 mg tobramycin implicated a decreased reversibility of eGFR during 1-year F/U. Concomitant vancomycin + tobramycin therapy caused a 19% loss in eGFR while no reduction followed sequential vancomycin + tobramycin therapy. Patients with an intial eGFR <39 mL/min had the same decrease and reversibility of renal function as patients with eGFR ⩾40 mL/min. Patients with short-term therapy <10 days had no long-term decrease in renal function.
Conclusion: Total dose of >2500 mg tobramycin caused a decreased reversibility during 1-year F/U, while short-term therapy <10 days had no impact on long-term kidney function.

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DAPTOMYCIN IN CARDIOVASCULAR IMPLANTABLE ELECTRONIC DEVICE (CIED) ENDOCARDITIS

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Objectives: To evaluate the effectiveness of daptomycin in CIED endocarditis.
Methods: CIED endocarditis defined according to presence of vegetation on lead or valve with clinical and microbiological evidence or if modified Duke criteria for infective endocarditis met. Patients with CIED endocarditis between January 2010 and January 2013, and receiving daptomycin, were included.
Results: Four patients were included in the study. Mean age was 60.5 (45–69) and three of them were male. One patient had pacemaker endocarditis and three had ICD endocarditis. One patient had early CIED endocarditis, the others had late infections. Fever and fatigue were common symptoms. All of them underwent both transthoracic and transesophageal echocardiography that suggested CIED endocarditis. Vegetations were determined in all cases on the electrode leads and endocardial surfaces. Also in two patients oscillating vegetations were involved in tricuspid valve.
Blood cultures were positive in all of patients. The most common isolated microorganisms were staphylococci: MRCoNS (n = 2), MRSA (n = 1), *Streptococcus* spp. (n = 1). Lead culture was positive in only two which MRCoNS isolated.
In two of the cases hardware was removed with percutaneous lead extraction. In one patient with pulmonar emboli lead was extracted surgically.
Daptomycin was used in initial treatment in 1 patient with high creatinine levels, while treatment was subsequently modified to daptomycin in 3 patients because of persistence of infection in 2 patients and high MIC values in 1 patient. Daptomycin was used at a dosage of 6 mg/kg/day. Daptomycin-related side effects were not seen in any patients.
Clinical improvement was observed at 7.2±3.2 days. Microbiological eradication was observed in all cases at 11.1±3.6 days. Relapse was not seen in any patient. Duration of daptomycin treatment was 32 days. One patient died due to multi-organ failure.
Conclusion: Daptomycin has the potential to be an option in CIED endocarditis. Studies involving large sample sizes are needed.

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DAPTOMYCIN AS AN OPTION IN LEFT-SIDE INFECTIVE ENDOCARDITIS

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Objectives: To evaluate the effectiveness of daptomycin in left-side infective endocarditis (IE).
Methods: Patients with left-side IE according to modified Duke criteria between May 2010 and May 2012 and receiving daptomycin as monotherapy were included.
Results: Fourteen patients were included in the study. Mitral valve was involved in 10 and aortic valve in 4 patients. Eight patients had prosthetic valves. Cardiac abscess was detected in 5 patients. Blood cultures were positive in 13 patients. The most common isolated microorganisms were staphylococci. Early cardiac surgery was required in 5 cases due to congestive heart failure secondary to valvular dysfunction. Daptomycin was used in initial treatment in 4 patients with high MIC values or creatinine levels, while treatment was subsequently modified to daptomycin in 10 patients, because of persistence of infection in 7 patients, drug side-effects in 2 patients and high MIC values in 1 patient. In 10 patients daptomycin was used at a dosage of 6 mg/kg/day and in 4 patients 8 mg/kg/day. In 6 patients daptomycin-related side effects such as increase in serum CPK levels, peripheral neuropathy and myopathy were seen. Daptomycin was not stopped in none of these cases, and side effects returned to normal after the treatment. Clinical improvement was observed at 8.7±3.2 days. Microbiological eradication was observed in 12 cases at 11.1±3.6 days. Relapse was not seen in any patient. Duration of daptomycin treatment was 40.6±4.4 days. Four patients died due to multi-organ failure and heart failure. Ten patients were discharged healthy, with successful surgical treatment in two of them. The four patients in whom daptomycin was used at a dosage of 8 mg/kg/day recovered and no side effects were seen.
Conclusion: Daptomycin has the potential to be an option in left-side IE. Studies involving large sample sizes are needed for use of daptomycin in left-side IE.

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THE PROLONGED USE OF ONCE DAILY AMINOGLYCOSIDES IS SAFE AND EFFECTIVE IN THE TREATMENT OF ENTEROCOCCAL ENDOCARDITIS

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Background: For the treatment of enterococcal endocarditis, American and European guidelines recommend a 4-to-6 weeks combination of a cell wall active agent and an aminoglycoside in 2 or 3 equally divided daily doses. However, pharmacokinetic and pharmacodynamic considerations favour the once daily administration of aminoglycosides, as routinely done in our institution. We aimed to evaluate the safety and tolerability of this option.
Methods: Retrospective observational study of all adult patients with definite enterococcal endocarditis (modified Duke criteria) managed in our institution during the years 2000–2010. Cases were identified through our computerized database and data were collected from medical files and nurses reports through standardized questionnaire.
Results: We included 52 patients (median age 75 years, male/female ratio 3). Of these, 40 (77%) had predisposing heart disease, 38 (73%) presented at least one chronic comorbidity, and 29 (56%) had prosthetic valve endocarditis. *Enterococcus faecalis* was involved in 48 cases. Medical treatment mostly included i.v. amoxicillin (n = 48), and gentamicin (n = 51). Complete information on gentamicin administration was available for 39 patients: 28 (72%) received once daily gentamicin, for a mean duration of 29.5 days. Acute renal failure was documented in 26 patients (67%), moderate in most cases (n = 22), with a mean creatinine clearance decrease of 11%. Surgery

was performed in 16 patients (30%), mostly because of heart failure. Three patients relapsed. In-hospital and one-year mortality were, respectively, 4% and 15%.
Conclusion: The combination of amoxicillin and once daily gentamicin was safe and effective for the treatment of enterocccal endocarditis in a population of elderly patients with major comorbidities.

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IS TRIPLE THERAPY NECESSARY IN STAPHYLOCOCCAL PROSTHETIC VALVE ENDOCARDITIS?

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Objectives: Analysis of staphylococcal prosthetic valve endocarditis in an endocarditis series to know the impact of antimicrobial monotherapy, bitherapy or triple therapy.
Methods: Multicentric cohort of 1,240 consecutive episodes of left-sided infective endocarditis recruited from 8 centers in Spain.
Results: We found 109 staphylococcal prosthetic valve endocarditis: 29 *Staphylococcus aureus* (5% MRSA) and 80 coagulase-negative staphylococci (73% meticillin resistant).
Thirteen cases were treated with monotherapy (cloxacillin 4 cases and vancomycin 9 cases). 53 cases were treated with bitherapy (cloxacillin + gentamicin 14 cases, vancomycin + gentamicin 27 cases, cloxacillin + rifampicin 1 case, vancomycin + rifampicin 9 and other combinations 2 cases).
Relation between mortality and treatment: with monotherapy 84% of patients died (p = 0.031), with bitherapy 51% (n.s.) and with triple therapy 54% (n.s.).
Relation between acute renal failure and treatment: Patients with monotherapy had acute renal failure in 28%, with bitherapy in 37% and with triple therapy in 38%.
Conclusions: All clinical guidelines recommend triple therapy for staphylococcal prosthetic valve endocarditis (vancomycin/cloxacillin + gentamicin + rifampicin) but there are no studies that clearly support this. In this large series we found that bitherapy was similar to triple therapy in mortality, with similar rates of acute renal failure and probably with less drugs interactions.
Monotherapy would not be used in staphylococcal prosthetic valve endocarditis because it has more mortality than bitherapy and triple therapy.

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OUTCOME OF EARLY VALVE SURGERY COMPARED TO MEDICAL TREATMENT IN INFECTIVE ENDOCARDITIS COMPLICATED WITH EMBOLIC STROKE

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Background: The impact of early cardiac surgery after stroke in infective endocarditis (IE) remains controversial.
Methods: Data were obtained from the International Collaboration on Endocarditis – Prospective Cohort Study of 4,794 patients with definite IE who were admitted to 64 centers in 28 countries from June 2000 through December 2006. We examined in-hospital and 1-year mortalities in patients who underwent early valve surgery (ES) after stroke compared to only medically treated patients (MT).
Results: The ES group included 58 patients with emboli in whom valve replacement was performed within seven days after stroke. The MT group included 166 medically treated patients. Patients with hemorrhagic stroke were excluded. Patients in the ES group were significantly younger; more commonly infected with *S. aureus* and more often experienced paravalvular or intracardiac abscess complications. The in-hospital mortality was 28% (47/166) in the MT group and 22% (13/58) in the ES group, p = 0.491. The odds of hospital death were not significantly higher in the ES group after adjustment for age, *S. aureus* infection and congestive heart failure (OR = 0.943, 95% CI 0.425–2.023). Probability of six-month survival was also not significantly higher in the surgery group (0.0.516 vs. 0.544, p = 0.851, log-rank test).
Conclusion: In this observational study, early and 6-month outcome was the same in patients subdued to early valve replacement after embolic stroke as well as in only medically treated patients. Our results suggest that patients with non-hemorrhagic stroke should not be excluded from consideration for early valvular surgery. In addition, further studies are needed to clarify the factors that determine the choice and timing of surgical therapy among patients with IE.

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THE IMPACT OF VALVE SURGERY ON MORTALITY IN INFECTIVE ENDOCARDITIS COMPLICATED WITH EMBOLIC STROKE: A PROPENSITY SCORE ANALYSIS

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Background: The impact of cardiac surgery after stroke in infective endocarditis (IE) remains controversial despite the growing number of studies supporting the importance of valve replacement for patients' survival. We examined the impact of valve surgery after stroke on in-hospital and 1-year mortalities.
Methods: Data were obtained from the International Collaboration on Endocarditis – Prospective Cohort Study of 4,794 patients with definite IE who were admitted to 64 centers in 28 countries from June 2000 through December 2006. The treatment group included patients with embolic in whom valve replacement was performed after stroke (225 patients). The control group included medically treated patients (263 patients). Propensity score, which was the estimated probability that a patient would undergo surgery, was calculated for each patient. Patients undergoing surgery were matched on a 1-to-1 basis with patients treated medically on the basis of propensity score using a matching tolerance (caliper) of 0.05.
Results: After propensity score matching, 119 patients were included in each group. Demographic and clinical characteristics did not significantly differ between groups. In-hospital mortality was significantly higher in the medically treated group than in the surgery group. Overall, in the medically treated group 36 patients (30.3%) died, in the surgery group 16 (15.1%), p = 0.005. The odds of hospital death were almost three times higher in the medically treated group, OR = 2.806, 95% CI 1.900–4.227. The probability of one-year survival was also significantly higher in surgery group (0.788 vs. 0.567, p < 0.001, log-rank test).

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OUTCOME OF PATIENTS WITH INFECTIVE ENDOCARDITIS AND LIVER CIRRHOSIS: THE FATE OF OPERATED AND NON-OPERATED PATIENTS

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Objective: There are limited data on outcomes of patients with infective endocarditis (IE) and liver cirrhosis (LC). This study aims to evaluate the outcome of IE+LC patients with and without surgical treatment.
Methods: Consecutive patients with IE and LC from 1-1998 to 2-2011. Group assignment: G1 (surgical criteria-operated); G2 (surgical criteria-non operated); G3 (non-surgical criteria, non-operated). Modified Duke criteria used for IE. Child–Turcotte–Pugh and MELD scores for severity of LC. Mann–Whitney and Kruskal–Wallis tests

used for comparison of qualitative variables. Kaplan–Meier and Cox regression analyses of survival and hazard ratio of variables at 12 months. Logistic regression estimation for in-hospital and 12-month mortality. Significance set at 0.05.
Results: There were 610 cases of IE, 54 IE+LC. There were 37 patients with surgical criteria (22 G1 and 15 G2) and 17 without surgical criteria (G3). Overall in-hospital mortality was 28/54 (51.9%). Group mortality was 59% (G1), 60% (G2), 35% (G3). Most frequent causes of in-hospital mortality were: G1 multiorgan and liver failure (8/13), G2 heart failure and stroke (7/9), G3 liver failure (4/6). Predictors of in-hospital mortality were nosocomial acquisition, *S. aureus* infection, MELD score $\geqslant$15, presence of congestive heart failure and perivalvular abscess. At 12 months all G1 survivors with MELD score $\leqslant$19 are alive, 1 G2 died of liver failure and 2 G3 died of liver and unknown cause.
Conclusions: Patients with IE+LC are at high risk of mortality. There is survival benefit in G1 patients with Child A and MELD $\leqslant$19. In G2 and G3 patients results are concordant with the evolution of the disease.

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INVOLVEMENT OF THE SPLEEN IN INFECTIVE ENDOCARDITIS, AGGRESSIVE SURGICAL TREATMENT IS INDICATED IN SPLENIC ABSCESS

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Objective: Infective endocarditis (IE) is the most common predisposing cause of splenic abcsess with a not well defined but established incidence of 2–3%. A picture of abdominal pain, persistent fever or splenomegaly must lead to clinical suspicion. Unrecognized or delayed splenic abscess increases mortality. It is currently not well standardized what is the best timing for splenectomy when the patient requieres valvular surgery. This study aims to describe the patients with IE and spleen involvement requiring valvular surgery and splenectomy.
Methods: Consecutive patients with IE and splenic involvement from 1-1995 to 12-2012. Retrospective analysis of data stored in the prospective database. IE as per the Duke criteria. Identification of patients with splenic infarction or abscess diagnosed with imaging techniques or at postmortem examination. When required, splenectomy was performed in the same intervention after the valve procedure.
Results: There were 807 episodes of IE and 319 (40%) surgically treated. 8% presented with infarction and/or abscess. 7 patients (8.2%) required splenectomy. 6 (83%) were male. Mean age 53.4 (27–72). 6 had native valve IE with persistent fever and abdominal pain in all. Mean logistic EuroSCORE yielded 37.4% preoperative expected mortality (18.8–60.9%). There was mitral valve IE in 4, aortic in 2 and 1 multivalvular. Pathogens: *Enterococcus* spp. in 2, *S. aureus*, *S. bovis*, *S. gordonii* and *K. kingae* 1, culture negative 1. Abscess was diagnosed in 5 with CT. All patients required valve replacement. 3/7 died due to preoperative septic shock, postoperative liver failure and multiorgan failure. Mean follow-up of 4 survivors is 30.2 months (5–49) with no relapse. In all cases abscess was confirmed by pathological examination.
Conclusions: Clinical suspicion of splenic abscess is a must in IE patients with fever and abdominal pain. Splenectomy and valve intervention can be performed in the same operation.

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SPLENECTOMY IN ACTIVE INFECTIVE ENDOCARDITIS: SIMULTANEOUS OR TWO STAGE PROCEDURE?

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Background: Peripheral and central septic embolisation is a frequent complication in patients with active infective endocarditis (AIE), affecting most commonly organs like brain, kidneys and spleen. The recommendation whether splenectomy should be done immediately or within the same hospitalisation is not clearly stated. This study compares two possible strategies for splenectomy in AIE requiring surgery: either simultaneous during valve surgery (SV) or propounded surgery (AV).
Methods: Between October 1994 and December 2011 a total number of 1,532 patients were operated due to AIE. Of these, 77 were excluded due to isolated right-sided AIE. Of the remaining 1,431 patients 9.4% (n = 135) received splenectomy due to splenic abscess or infarction either simultaneously (n = 28) or as a two stage procedure (n = 107). Demographic data, intra- and post-operative parameters as well as long-term follow-up were collected and evaluated. Retrospective analyses were performed for morbidity, 30-day mortality, re-endocarditis and long-term follow-up.
Results: No differences could be found regarding demographic data between SV and AV groups except for age (respectively 64.2±10.4 years vs. 62.1±13.4 years; p = 0.042). There were no differences in co-morbidities except for arterial hypertension [SV group (n = 22) vs. AV group (n = 58), respectively; p = 0.019]. Intra-operative findings and post-operative parameters were similar for both groups. According to morbidity, 30-day mortality, re-endocarditis and long-time follow-up no advantage for either strategy was found.
Conclusions: Splenectomy due to septembolic complication in patients with active infective endocarditis can be done with comparable good early and late results either as a simultaneous or as a two stage procedure.

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SURGERY FOR NATIVE INFECTIVE MITRAL VALVE ENDOCARDITIS: A CLEAR STATEMENT FOR MINIMALLY INVASIVE PROCEDURE

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Background: Isolated acute infective endocarditis (AIE) of the native mitral valve requiring surgery is a life-threatening disease. Whether conventional mitral valve surgery (conMV) via sternotomy or minimally invasive (micMV) surgery via lateral thoracotomy has to be preferred is not yet known.
Methods: Between 10/1994 and 12/2012 a total number of 1710 patients (pts) (69.9% male, age 62±15 years) were operated due to AIE at our institution. Isolated native mitral valve AIE was seen in 412 (24.1%) pts. Of these, 106 (25.7%) were operated minimally invasive including 5 pts with conversion to sternotomy. Preoperative, intra- and postoperative parameters were analysed comparing conMV vs. micMV. Cox regression, Kaplan–Meier curves were generated.
Results: Patients in the conMV group were significantly older (65.7±12.9 vs. 58.0±16.1 years; p < 0.001), were more often operated in low cardiac output (10.2% vs. 0.7%; p = 0.002) and showed therefore a lower ejection fraction (58.6±10.7% vs. 61.2±8.6%; p = 0.022). Logistic EuroScore was highly significantly higher in conMV (34.3±23.1 vs. 19.8±17.8; p < 0.001). Cardiopulmonary bypass time was significantly lower in conMV (104.9±44.0 min vs. 128.9±37.7 min; p < 0.001). However, in significantly more micMV pts mitral valve reconstruction was possible (33.0% vs. 3.9%; p < 0.001). In the postoperative period pts in the conMV group needed significantly longer ventilatory support (118.4±203.8 h vs. 58.6±148.4 h; p = 0.006), hemodialysis (20.4% vs. 13.2%; p = 0.001). ICU stay in days was significantly longer in the conMV group (7.4±13.1 vs. 3.2±6.4; p = 0.002) and also total length of stay (17.6±14.8 vs. 14.0±9.7; p = 0.023). Overall 30-day mortality was 15.4%, with significant difference between conMV and micMV (18.8% vs. 5.7%; p = 0.001). Kaplan–Meier survival curves showed highly significant statistical difference between conMV and micMV (log-Rank <0.001).
Conclusions: Isolated native mitral valve is often affected in AIE (24.1%). The kind of surgical procedure influences early and late outcome in these patients significantly with a preference for minimally invasive surgery; this should therefore whenever possible be preferred. Whether earlier time for surgery may improve outcome remains controversial and cannot be answered by our results.

However, it can suggest that hemodynamic status and extension of valve destruction may have an influence on surgical procedure.

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IMPACT OF VALVE SURGERY IN PATIENTS WITH INFECTIVE ENDOCARDITIS AND NEUROLOGICAL COMPLICATIONS

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Neurologic complications (NC) are a major cause of morbidity and mortality in patients (pts) with infective endocarditis (IE) and may prevent pts from receiving valve surgery.
Methods: Among 399 cases of Li definite left-sided IE collected during a one-year prospective population-based survey, 100 had at least one symptomatic neurological complication (SNC). NC included transient ischemic attack, ischemic stroke, cerebral hemorrhage, meningitis, brain abscess and intracranial mycotic aneurysm. A neuroimaging procedure was performed in 183 of the remaining pts, which diagnosed 35 asymptomatic (As) NC and was considered normal (NoNC) in 148 pts.
Results: Among pts with SNC, 40 episodes occurred after the beginning of IE antibiotic therapy (21 during the first 48 hours). Mechanical prosthetic IE (OR 3.4, p = 0.007), *S. aureus* IE (OR 1.8, p = 0.03) and mitral IE (OR 2.0, p = 0.008) were predictive of the occurrence of NC. Among the 135 NC pts, age, renal failure, septic shock and *S. aureus* as responsible micro-organism were predictive of in-hospital (33%) and 1-year mortality (38%). Furthermore, a symptomatic NC was also predictive of 1-year mortality. Rate of surgery was not different between pts with and without NC (52% vs 57%) but was significantly higher in AsNC than in SNC (77% vs 43%). In-hospital mortality was higher in pts with NC than in NoNC pts (33% vs 17%, p = 0.001) and in SNC than in AsNC (42% vs 9%, p = 0.0003). Among the 135 NC pts, 95 had a surgical indication (71%) which was performed in 70 (mortality 20%) and not performed in 25 (mortality 68%).
Conclusion: The presence of NC is associated with a poor prognosis when it is symptomatic. However, when NC is discovered on systematic neuroimaging, it is associated with a very high rate of surgery and a better prognosis than that of pts with SNC and even without NC, suggesting a protective role of surgery.

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EARLY PROSTHETIC VALVE INFECTIVE ENDOCARDITIS (EPVIE) IN A CARDIAC SURGERY REFERRAL HOSPITAL, 2006–2012, RIO DE JANEIRO, BRAZIL

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Background: EPVIE is a severe complication of valve replacement surgery. Little data from Brazilian hospitals is available on the subject.
Methods: Observational prospective case series study, from 2006–2012, of all adult patients with definite EPVIE operated at Instituto Nacional de Cardiologia.
Results: Nineteen patients (20 episodes) with EPVIE in a total of 151 patients (12.5%) with definite IE were included. There were 9 (47%) males and 10 (53%) females. Mean age was 44.3±18.1 years. The incidence of EPVIE by year by number of valve replacement surgeries was 4/192 (2.6%), 2/194 (2.1%), 6/239 (2.5%), 4/263 (1.5%), 1/225 (0.4%), 2/252 (0.7%) and 1/283 (0.3%) in the years 2006, 2007, 2008, 2009, 2010, 2011 and 2012 respectively. Acute presentation was seen in 18 (90%) episodes and subacute in 2 (10%). Of the 23 prosthetic valves affected, 14 (61%) were bioprosthetic and 9 (39%) were mechanical. Positions affected were mitral, 12 (53%), aortic, 10 (43%) and tricuspid, 1 (4%). EPVIE presented less than 2 months post-operatively in 13 (57%). Microorganisms found were *Enterococcus faecalis* 5 (25%), coagulase-negative staphylococci (CoNS) 4 (20%, *Staphylococcus epidermidis* 3), *Candida albicans* 1, *C. tropicalis* 1, and in 1 case (5%) each *C. diphtheriae*, *E. cloacae*, *P. aeruginosa*, *Salmonella enteritidis*, *E. cloacae* + *Enterococcus faecalis*, unknown; in 2 patients blood cultures were negative. Fever was present in 19/20 (95%), new valvular regurgitation in 7/17 (41.1%). Transesophageal echocardiograms were done in 18 cases; new valvular regurgitation was found in 12 (66.6%), vegetation(s) in 9 (50%), paravalvular leak in 6 (33.3%), dehiscence in 2 (11.1%), intracardiac abscess and valvular perforation in 1 (5.5%) each. Most frequent complications were: heart failure in 10 (50%), acute or worsening renal failure in 6 (30%) and embolization in 5 (25%). Antibiotic treatment only was given to 12 (60%) of patients; of these, 10 (83.4%) were discharged from hospital and 2 (16.6%) died; 8 patients (40%) had surgery for EPVIE, and of these, 3 (37.5%) died.
Conclusion: EPVIE in our series mostly affected younger patients and presentation was acute in 90% of cases. Sexes were equally affected. Incidence has been decreasing in our hospital, and is in accordance with the literature. Etiology involved Gram-positives, with CoNS and *E. faecalis* predominating, differently from the literature, where CoNS and *S. aureus* predominate. The absence of *S. aureus* in this series may be due to routine decolonization with nasal mupirocin and chlorhexidine in the pre-operative period. A mix of Gram-negatives and *Candida* were also present. Mortality was high, but comparable to the literature.

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TREATMENT OF ARDS DURING STAPHYLOCOCCAL ENDOCARDITIS WITH EXTRACORPOREAL MEMBRANOUS OXYGENATION (ECMO)

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Background: ECMO is not common in the treatment of endocarditis complications. A case is presented of complete recovery after staphylococcal endocarditis complicated with ARDS and septic meningitis in a 65-year-old female with no co-morbidities except arterial hypertension.
Case presentation: The patient was admitted to the hospital on the third day of fever, malaise and cough. On the 5th day of hospitalization she developed respiratory failure and was admitted into ICU. The first echocardiography showed mitral valve endocarditis, with no serious impairment of the valve function. Septic meningitis was also found. The next day after the admission into the ICU mechanical ventilation started because of the progressing hypoxemia. On the same day, because of the further deterioration, we started ECMO procedure and continued it for the next 48 hours. There were no complications of the ECMO treatment. After the weaning, cardiac surgery was performed because of the progression in the size of vegetation and abscess formation of the mitral annulus. The patient was medically treated with cloxacillin for the next 28 days. Sixteen months after the admission the patient was completely well, Karnofsky score 100%.
Conclusion: This case reports a rapid progression of the staphylococcal sepsis in the patient with no apparent risk factors and shows that initial complex critical care, including ECMO, might significantly improve patients' perspectives for full recovery.

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VALVULOPLASTY *VERSUS* VALVE REPLACEMENT IN MITRAL-VALVE INFECTIVE ENDOCARDITIS: AN OBSERVATIONAL STUDY

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Objectives: To determine the characteristics and prognosis of mitral-valve infective endocarditis (IE) according to the type of surgery performed: valvuloplasty (V) or prosthetic valve replacement (P).
Methods: Demographics and baseline characteristics, complications and outcome were obtained from the French 2008 cohort database of 497 Duke-definite left-sided IE. A total of 150 episodes of mitral valve only IE were studied and characteristics were compared according to the treatment (surgical *vs* medical) and, when surgery was performed, V *vs* P.
Results: Fifty-six patients (37%) underwent valve surgery: 18 V and 38 P. There were no differences in age and gender between the two groups. P patients had more morbid conditions (higher Charlson index, p = 0.02) but similar rate of severe cardiac complications. The microbiological profiles of the groups were not significantly different: streptococci (P 63%, V 56%), staphylococci (P 18%, V 33%).
In-hospital mortality was higher after prosthetic valve replacement (P 32%, V 6%, p = 0.04), but 1-year survival rates were not different (P 66%, V 72%, p = 0.07). After adjustment, 1-year survival of surgically treated mitral-valve IE (75%) was comparable to that of medically treated mitral-valve IE with no indication for surgery (76%, p = 0.89), but was better than survival of medically treated mitral-valve IE with indication for surgery (49%, p = 0.02).
Conclusion: Infective endocarditis is a severe disease with in-hospital mortality around 25%. One-year survival rates were similar after valvuloplasty or prosthetic valve surgery in this patient series.
Keywords: Infective Endocarditis, Mitral, Mortality, Surgery

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SORIN FREEDOM SOLO STENTLESS VALVE IN SURGICAL THERAPY OF AORTIC VALVE ENDOCARDITIS: INITIAL RESULTS AND MID-TERM FOLLOW UP

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Background: Despite significant improvement in antibiotic therapy, aortic valve endocarditis, with or without perivalvular abscess, still represents significant surgical challenge. Homograft implantation is the gold standard of surgical therapy, but new artificial valves attract more attention due to easier availability. We present our results in utilizing the Sorin Freedom SOLO stentless aortic valve in surgical management of aortic valve endocarditis.
Methods: From January 2009 until January 2013, seventeen male patients underwent aortic valve replacement due to aortic valve endocarditis utilizing the Sorin Freedom SOLO bioprosthesis made of bovine pericardium. Follow-up and postoperative echo data were collected in a prospective manner.
Results: There were 9 emergent surgeries (56%), 5 urgent (31%), and 2 elective (13%). Average age was 61.5±8.74 years (range 43–76) with median EuroSCORE 10, and logistic EuroSCORE mortality 23.09±20.09% (4.4–59.7%). One patient underwent concomitant mitral valve replacement, and four patients had annular abscesses which were closed with glutaraldehyde treated autologous pericardium. Average aortic cross-clamp time for isolated aortic valve replacement was 58.81±19.25 minutes (42–98), and for combined procedures (mitral valve replacement, closure of subannular abscess) 112.8±22.6 minutes (82–141). Median valve size was 25 mm (23–27). Follow-up was 18.98±14.49 months (0.1–43.86). Two patients died during hospital stay due to multi-organ failure, and one died during mid-term follow-up, for an overall mortality of 18%. Early mean postoperative transvalvular gradient was 11.22±4.36 mmHg (7–15.8), and medium-term gradient was 12.5±5.6 mmHg. During follow-up, there were neither structural valve deterioration of any kind nor prosthetic valve endocarditis.
Conclusion: Because of its specific implantation technique with single supra-annular suture line, and absence of any artificial material in its design, Sorin Freedom SOLO stentless bioprosthesis is a valuable tool in surgical management of aortic valve endocarditis. Although our initial results are encouraging, further follow-up is necessary.

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LONG-TERM RESULTS OF SURGICAL TREATMENT OF PATIENTS WITH VALVE INFECTIVE ENDOCARDITIS

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Long-term results of surgical treatment of patients with valve infective endocarditis (IE) were followed up in 332 patients. Follow-up was from 1 month to 25 years (mean 8.9+4.7 years).
The actuarial survival rate at the end of the first year was 83.7+4.1%, 5 years after surgery – 78.6+4.7% and by the end of the 10th year was 66.2+3.9%.
Early recurrence of IE affected 11.1% of patients, late – 16.2%. For early recurrence reoperated 7 of 30 patients were treated conservatively. In-hospital mortality in this group was 10% (3 patients). Late recurrence of IE was observed in 54 (16.2%) patients. Of these, 43 were reoperated, hospital mortality 6.9% (3 patients). Conservative therapy was given to 11, four of whom died.
Survival to 10 years, following surgery for lesions of the mitral, aortic, tricuspid, or mitral+aortic valve was 83.4%, 77.1%, 69.4% and 52.7%, respectively.
For the first year after surgery, 87.2% of patients survived with primary IE to 5 years – 81.3%, to 10 – 76.6%. In the group of patients with secondary IE to 1 year after surgery, 94.5% survived; to 5 years – 87%, to 10 – 85.5% of patients. In the group of patients with secondary IE, the first, fifth and tenth year of observation, survived 86.3%, 77.4%, 70.6%, respectively.
Likelihood of recurrence of IE in patients operated on in the remission of infection is minimal, and the first year after surgery is 7%. Relapse rate of IE in patients undergoing surgery in the active phase of IE, the first year after surgery is 17.2%.
By the fifth year of observation, the patients were operated in remission; freedom from recurrence of IE is 77.2%, while in the group operated in the active phase of IE, free of recurrence 71.4% of patients.

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TRANSAORTIC VALVE REPLACEMENT INFECTIVE ENDOCARDITIS, RISE OF A NEW ENTITY: CASE REPORT AND LITERATURE REVIEW

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Introduction: Transcatheter aortic valve implantation (TAVI) has developed in the last 10 years as a safe and technically feasible alternative to conventional surgical valve replacement in elder patients and in those with high surgical risk. However, it is not free of infectious complications, including endocarditis (IE).
Case report: A 90-year-old woman with TAVI placement 29 months earlier presented to the emergency room with fever and heart failure. Blood cultures grew *S. epidermidis* and daptomycin was started due to previous history of penicillin allergy. TTE performed due to persistent bacteremia showed ventriculo-auricular fistula without vegetations. Defervescence was achieved at day 8. She was discharged 2 weeks later on oral linezolid and died 13 days later due to septic shock.

Literature review: We found 26 cases of TAVI IE including ours. Mean age was 80.7 years (SD 7.4), 56% were males, mean logistic Euroscore at TAVI indication yielded 28.6% estimated mortality (IQR 23.4–40.3), 42.3% had chronic renal failure, 7.7% on hemodialysis, 46.2% had ischemic heart disease, 31% had chronic lung disease and 42.3% were immunosupressed (concomitant cancer, steroid therapy or transplant). TAVI approach was femoral in 65% and transapical in 35%. Twenty-three percent had a pacemaker. Prophylaxis for TAVI was reported in 35%. Twenty-one percent were late PVE, median time from TAVI to IE was 180 days (IQR 65–365) and 81% accomplished definitive diagnosis according to Duke modified criteria. Median follow-up was 47.5 days (IQR 29–317.5). 34.6% of cases were nosocomially acquired. HF occurred in 42.3% and embolic events in 19.2%. Most common agent was *Enterococcus* spp. (39%), followed by coagulase-negative staphylococci (19.2%). Median follow-up was 47.5 days (IQR 29–317.5). Mortality during follow-up was 32%. Twenty-seven percent received surgical treatment, with 14.3% mortality in this group.
Conclusions: IE on TAVI is not anecdotal. Its clinical picture resembles early PVE, but it is caused by different microorganisms, predominating enterococci. Around a third of patients are operated, which points to an inaccurate initial indication for TAVI. However, this issue merits further investigation.

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PROMPT SYSTEM EXTRACTION DECREASES MORTALITY IN PATIENTS WITH CARDIOVASCULAR IMPLANTABLE ELECTROPHYSIOLOGIC DEVICE INFECTION

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Background: Different management strategies of cardiovascular implantable electronic device (CIED) infections may impact patient outcomes. To date, limited prospective data have been evaluated to further characterize this influence on outcomes.
Methods: Data from the Multicenter Electrophysiologic Device Infection Cohort (MEDIC), a multinational cohort study of CIED infections, were utilized to evaluate the effects of host comorbidities, device characteristics, and management strategies, on patient outcomes.
Results: Of 434 patients who presented with CIED infections, 33 (7.6%) died during the index hospitalization. Mortality was 13.5% for 413 (95.1%) patients for whom follow-up data at 6 months were available. Increased risk of death was observed among patients who had more comorbid conditions, presented with emboli or leukocytosis, or had CIED-related endovascular infections. In multivariate analysis that adjusted for host- and device-related factors and clinical presentation, antimicrobial therapy involving beta-lactams (OR 0.32 [0.13, 0.80]) or vancomycin (OR 0.35 [0.15, 0.85]) when compared to other antimicrobials, was associated with lower mortality at 6 months. Major device removal complications were observed in 6.3% of patients and were associated with increased mortality during the hospitalization and at 6-month follow-up (ORs 10.62 [1.83, 61.60] and 6.09 [1.66, 22.40]). Despite these risks, mortality was three-fold lower during index hospitalization among patients who underwent device removal at initial presentation (OR 0.30 [0.09, 0.96]) as compared to those who had delayed or no device removal.
Conclusions: Outcomes in patients with CIED infections are influenced by specific underlying host factors, CIED characteristics, clinical presentation, and approach to therapy. Despite the increased mortality risk associated with complicated device removal, this risk is uncommon and overall outcomes are improved with complete and timely device removal.

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HEART TRANSPLANTATION FOR COMPLICATED INFECTIVE ENDOCARDITIS

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Introduction: Infective endocarditis is currently medically or surgically treated. Heart transplantation has been exceptionally proposed in isolated case reports. Herein we describe 4 cases of severe endocarditis in which conventional valve replacement was not effective enough to cure the patients.
Case descriptions: A 24-year-old man underwent urgent aortic valve replacement for a *Staphylococcus aureus* endocarditis which recurred 3 weeks later, requiring iterative surgery and temporary mechanical circulatory support. Because of absence of myocardial recovery and after sterilisation of lesions, the patient was registered on the high emergency list for heart transplantation, which was performed 6 weeks after his first operation.
A 54-year-old man underwent urgent aortic valve replacement for a *Streptococcus pneumoniae* endocarditis. After 2 reoperations for infectious recurrences with severe damage to the basis of the heart, the only solution was high emergency heart transplantation 2 months after the primary surgery.
A 53-year-old man with a *Streptococcus agalactiae* aortic valve endocarditis underwent 2 valve replacements before undergoing heart transplantation for acute heart failure one month after his first operation.
A 35-year-old man was operated 3 times for a complicated multivalvular *Streptococcus pneumoniae* endocarditis, and underwent heart transplantation 5 months after initial surgery for end-stage congestive cardiac failure.
Results: Early postoperative course was uneventful in all cases after heart transplantation. Post transplantation hospital length of stay was respectively 47 days, 34 days, 30 days, 68 days. Survival is respectively 6 years, 2 years, 6 months, 5 months.
Conclusion: High emergency heart transplantation can be indicated in rare and specific cases of endocarditis after failure of valve surgery. In this series we confirm the high destructive potential of *Staphylococcus aureus* and *Streptococcus pneumoniae*, needing complete infected tissue eradication.

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THE ROLE OF SURGERY IN INFECITVE ENDOCARDITIS – SIGNIFICANT IMPACT ON PROGNOSIS OF STAPHYLOCOCCAL ENDOCARDITIS

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Objectives: In recent years surgical treatment of infective endocarditis has become a mainstay in treatment of infective endocarditis. The objective of our study was to evaluate the frequency of surgery and the impact of surgery on the outcome of infective endocarditis in our population of patients.
Material and Methods: All patients treated at the Department of Infectious Diseases in Ljubljana, Slovenia, in the years 1984–2011 were prospectively studied. The patients were included according to

Duke Criteria. Clinical, microbiological and echocardiographic data were collected.
Results: In the years 1984 to 2011 there were 675 episodes of endocarditis – 240 female, 435 male with median age 59 years. In 494 (73%) native valve was affected, in 180 (27%) endocarditis occurred on prosthetic valves including pacemakers. *Staphylococcus aureus* was the leading cause of disease in 28%, followed by viridans streptococci in 24%. Cultures were negative in 14%. Overall, 28% of patients were operated while still receiving antimicrobial therapy (in active phase); postoperative mortality was 16.8%. In non-operated patients the mortality was 22.7%; the difference was not statistically significant. Overall in-hospital mortality was 20.6%. Patients with staphylococcal endocarditis were more often operated than patients with viridans endocarditis ($p < 0.02$), patients with early postoperative prosthetic valve endocarditis were treated surgically more often than others. Comparing two time periods (before the year 2000 and after) the frequency of surgical procedures increased from 14.5% to 37.6%, the mortality decreased from 23.6% to 19.2%. Most importantly, the mortality of *S. aureus* endocarditis decreased from 40.7% to 23.3%.
Conclusions: Our results demonstrate the significance of surgical intervention in treating patients with infective endocarditis, especially in patients with *S. aureus* endocarditis.

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MINIMALLY INVASIVE SURGERY: AN INNOVATIVE TREATMENT FOR INFECTIVE ENDOCARDITIS

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Introduction: Despite diagnostic and therapeutic advances, infective endocarditis (IE) remains a serious disease with high in-patient mortality. Surgery is an important part of treatment and early intervention is advocated. Minimally invasive valve replacement has proven good results but its role in IE has not been proven. We present a series of 9 patients with IE treated by a minimally invasive surgical approach.
Methods: The medical records of patients who underwent minimally invasive valve surgery at our center between November 2010 and February 2013 were reviewed.
Results: Of the 234 minimally invasive valve surgeries performed, 9 patients had IE. A total of 6 were male (66%) and the mean age was 48 years (29–77 years). Seven patients had positive blood cultures. *Streptococcus* was the most frequent pathogen (5/7), one patient had *Candida albicans* and another *Arcanobacterium haemolyticum*. The most frequent indications for surgery were severe valve regurgitation (4/9) and recurrent embolisms (3/9). The mean time from the decision to operate to the procedure was 3 days. Six patients underwent only mitral valve replacement, 2 only aortic valve replacement, one had mitral and aortic valve replacement and 3 had a combined procedure (mitral or aortic valve replacement plus tricuspid repair and mitral valve replacement and atrial fibrillation ablation). Mean cardiopulmonary bypass and aortic cross-clamp were 121 and 87 minutes, respectively. The mean stay in the intensive care unit was 3.7 days and in-hospital was 12 days. Two patients required blood transfusions during or after surgery. Mean follow-up was 6 months (1–13 months). None of the patients has died.
Conclusion: Patients with infective endocarditis can undergo minimally invasive valve surgery with or without additional procedures with acceptable short-term results. More studies are needed to show if this type of surgery should be the preferred approach for valve endocarditis.

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DAPTOMYCIN (D) IN LEFT-SIDED INFECTIVE ENDOCARDITIS (LSIE)

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Background: Daptomycin is a cyclic lipopeptide antibiotic highly active against Gram-positive bacteria. It is recommended for use in cases of right-sided IE endocarditis. There have been few studies regarding the use of daptomycin in the LSIE.
Objective: The aim of this study was to evaluate the effectiveness of daptomycin in LSIE (native and prosthetic valve).
Materials and Methods: Prospective, observational cohort study of consecutive cases of LSIE according to modified Duke Criteria, in adult patients (pts).
Results: From 1/2009 to 12/2010, 45 pts were treated with D; 26 had LSIE (57.8%; 2 pts were excluded because they received <5 doses of D). Of the 24 pts evaluated: male 50%; age 60.95 (median; SD = ±17.4). IE definite 19/24 (79.2%). Native valve IE 10 (41.6%), prosthetic valve IE 14 (58.3%). Microbiology: *Enterococcus faecalis* 11, MSSA 2, MRSA 2, CoNS 2, *Gemella* spp. 1, *S. agalactiae* 1, *St. viridans* 1 and polymicrobial 2 (1 MRSA+MSSA, and 1 *E. faecalis* + *Escherichia coli*). Twenty-two pts (84.6%) were treated with high doses ($\geqslant$8 mg/kg); treatment duration 23.5 days (median; range 5–42 days). D was a second-line treatment in 18/24 pts (75%) and vancomycin was the more frequent antibiotic used at first. Seven pts underwent valvular surgery during the acute phase of the disease. Clinical success rate 22/24 (91.7%) pts; there were 2 deaths (8.3%): 1 during hospitalization and 1 during the follow-up period (not related to IE). Adverse effects: 2 pts. Follow-up: 15 months (median; range 3–28 months). Seventeen pts (70.8%) received D in an outpatient parenteral antimicrobial therapy (OPAT) modality (median: 19.11 days; range 7–40).
Comments: Daptomycin can be used successfully in left-sided native and prosthetic valve IE, caused by Gram-positive bacteria, with no significant side effects even at high doses (>8 mg/k/d). Clinical success was high in this difficult-to-treat population. Also, D is an appropriate option to OPAT.

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HAEMOPHILUS SPECIES ENDOCARDITIS: A CASE REPORT

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A review of fifteen population-based epidemiologic studies of infective endocarditis (IE) found that crude incidence rates ranged from 1.4 to 6.2 per 100,000. The HACEK group is responsible for approximately 3% of all IE cases. *Haemophilus* species account for 0.8% to 1.3% of all cases of IE.
The case of a patient who presented with *Haemophilus* species endocarditis is reported. A 56-year-old Caucasian man was admitted to our Department with history of fever and shaking chills lasting five days. His past medical history revealed that at the age of six he had suffered an episode of arthritis. He was taking a prescription drug for hypertension. Physical examination revealed a grade 3/6 holosystolic murmur consistent with mitral regurgitation. Laboratory investigation demonstrated a white blood cell count of 12.4×10^9/L (81% neutrophils). On the fourth day of hospital stay in blood cultures collected on admission *Haemophilus* species was identified as the pathogen. Transthoracic echocardiography (TTE) performed ten days after admission failed to reveal any vegetation. Transesophageal echocardiography (TEE) performed on the twenty-fourth day of hospital stay demonstrated oval formation measuring 9×12 mm on the atrial side of the anterior mitral valve leaflet which could correspond to fibroelastoma or partially organized vegetation. The patient had moderate mitral regurgitation. He received a four-week course of ceftriaxone with good clinical response. The patient was discharged home and follow-up echocardiography planned one month after discharge.
Once more, as shown in our case report, it is necessary to point out the importance of performing TEE even with negative initial TTE when there is high clinical suspicion of IE. As reported in several studies, for the detection of vegetation, TEE has a sensitivity of 90–100%, whereas that of TTE ranges from 40% to 63%.

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