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Abstracts from the 10th International Symposium on Modern Concepts in Endocarditis & Cardiovascular Infections

Epidemiology

001
THE ICE NETWORK: PAST, PRESENT AND FUTURE

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Background: Project networks provide opportunities for collaboration, research and knowledge. In 1999, the International Collaboration on Endocarditis Network was formed to support investigators in pursuing research on endocarditis. Today, ICE is a multi-center, multi-disciplinary international network of 64 sites in 28 countries. Its evolution spans from a merged database, to a prospective data collection registry, and finally to specific goal-directed studies.
Summary: *Phase I*: ICE's roots began in 1999 with the development of the merged database. Existing databases from seven centers from five countries were merged to form a combined dataset. Analysis was completed at DCRI and yielded data on 2200 patients with definite endocarditis leading to 12 manuscripts. This initial collaboration provided support for the network to expand.
Phase II: In 2000, the network launched the next phase: the ICE Prospective Cohort Study. More than 60 sites on 6 continents with >250 investigators collaborated to advance endocarditis research. Total patients enrolled was 5,593 with over 4500 definite cases reported. ICE PCS also collected 1-year follow up data. Some sites also participated in the echocardiography and microbiology substudies. Thirteen manuscripts on PCS are published. The prospective registry closed enrollment in December 2006 to analyze the dataset and future planning.
Phase III: Leaders in the ICE network approved plans to initiate the next phase of ICE: project specific collection. Focus would be placed on specific projects to answer questions based on the outcome of the PCS analysis.
ICE Network's infrastructure allows the ability to incorporate different projects with ease and transparency. New projects will include the base CRF and several "project-specific" pages will be developed as needed. Several projects were slated for initial development and launched in September 2008: Surgical Decision Making, Daptomycin Registry, and Coagulase-negative Staphylococcal Bacteremia Registry. Other projects under development include streptococcal IE, Outpatient Parenteral Antibiotic Therapy, and dental risk factors for IE.
Conclusion: Despite the limited resources and funding, ICE continues to be successful due to the commitment from all investigators. From the progression of a retrospective collection to a project specific network, the ICE has proven to be a successful program and model for future networks.

002
PUBLICATIONS: LESSONS LEARNED FROM THE ICE NETWORK

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Background: The International Collaboration on Endocarditis Network includes over 64 sites in 28 countries with over 250 investigators. Since the start in 1999, there were lessons learned in our publication processes.
Challenges: Authorship and publication recognition has been a challenge faced by the Coordinating Center. Members are not financially reimbursed for participation; tangible recognition is provided through authorship. While equity in authorship is the goal, it turned out more difficult than anticipated. Issues surfaced over time, authorship assignment and recognition, as well as project ownership and oversight. Complete authorship lists were created for publications at the start of the work. This presented problems as some projects lagged and others flourished. Disparity in site and investigator recognition became evident.
Change: Lessons were learned and change implemented. A publication advisor is assigned to each manuscript to assist progression from concept to completion. Leadership and mentorship of each publication is vital to its success. Manuscript groups were created to consist of first and last authors and investigators with interests in the topic. As the project matures, several factors are considered to create an authorship list:

1. The first author is given the opportunity to designate 4–5 authors from their institution or of their choosing.
2. Additional authors/sites will be selected based on site enrollment and participation, contribution of cases specific to the project, participation in analysis/writing, and investigator interest. While multiple abstracts on a particular topic from ICE are possible, abstracts on a single topic may be combined into one uniform manuscript. Therefore, recognition on abstracts should be limited.
3. All potential authors are sent to the site Principal Investigator for approval. The PI has the right of acceptance or refusal of the authorship list. The PI, at their discretion, may suggest an alternative investigator or data coordinator as an author.

Conclusion: The ICE Network updated its publication process due to lessons learned. From 2000–2009, ICE published over 25 peer-reviewed manuscripts. There have been ~140 unique investigators recognized on in these projects. All active ICE sites before 2007 have been recognized on a manuscript. With over 30 additional projects in the queue, the ICE Network's goal is to recognize all investigators on a manuscript.

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003

DEVELOPMENT AND ASSESSMENT OF A NEW EARLY SCORING SYSTEM USING NON-SPECIFIC CLINICAL SIGNS AND BIOLOGICAL RESULTS TO IDENTIFY CHILDREN AND ADULTS PATIENTS WITH HIGH PROBABILITY OF INFECTIVE ENDOCARDITIS (IE) ON ADMISSION

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Objectives: To assess if non-specific clinical signs or biological results can identify patients with high probability of IE to improve outcome.
Design: All patients tested for IE were included in a cohort and classified according to the modified Duke criteria. Patients with rejected endocarditis served as controls. Univariate and multivariate analyses were performed and a score was calculated by adding 1 when a variable independently associated with IE (excluding major Duke criteria) was present and 0 when the variable was absent. Scores were evaluated using the ROC curve method.
Results: IE was diagnosed in 402 of 2039 participants (19.7%). By multivariate analysis, PVD, fever, emboli, stroke, splenomegaly, finger clubbing, leukocytosis, and ESR > 50 were independently associated with IE. The rate of IE increased significantly from 4% (10/254) for a score of 0 to 83% (10/12) for a score of 6. The area under the ROC curve was 0.75.
Conclusions: This simple score can be used to identify in the emergency room or on admission patients with high probability of IE to speed up diagnosis, or initiate empirical antimicrobial therapy without replacing the modified Duke criteria

004

RECENT TRENDS IN THE EPIDEMIOLOGY OF INFECTIVE ENDOCARDITIS: A POPULATION-BASED STUDY IN OLMSTED COUNTY, MINNESOTA

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Background: The current epidemiology of infective endocarditis (IE) in the US has not been examined in a population-based setting. Therefore, we conducted a population-based IE surveillance study in Olmsted County, MN.
Methods: Utilizing resources of the Rochester Epidemiology Project, we identified all definite or probable IE cases by modified Duke Criteria in Olmsted County, MN adults from 2001 to 2006 (contemporary group) and compared the findings with those of IE cases from the same population diagnosed between 1970 and 2000 (historical group). Incidence rates were age-and sex-adjusted to the population of Whites in the United States in 2000 and reported as cases per 100,000 person-years.
Results: There were 107 cases of IE in Olmsted County from 1970 to 2000 and 40 cases between 2001 and 2006. Age- and sex-adjusted incidence rates were 7.8 (95% CI 5.4–10.3) in the contemporary group and 6.1 (95% CI 4.9–7.2) in the historical group. The age-adjusted IE incidence rate in females was higher in the contemporary group than in the historical group (6.7, 95% CI 3.7–9.7 and 2.7, 95% CI 1.7–3.7, respectively). The age-adjusted incidence rates in males were similar in both groups (9.1, 95% CI 5.0–13.2 in the contemporary group and 10.7, 95% CI 8.2–13.2 in the historical group). In contrast to the historical group findings, which demonstrated that viridans group streptococci were the predominant causes of IE (viridans group streptococci, 43.9%; *Staphylococcus aureus*, 26.6%; and coagulase-negative staphylococci, 6.5%); *S. aureus* was the most common pathogen in the contemporary group (*S. aureus*, 30%; viridans group streptococci, 27.5%; and coagulase-negative staphylococci, 20%). Importantly, 7.5% and 50% of cases in the contemporary group were either due to nosocomial or health care-associated exposure, respectively; no data regarding site of infection acquisition was obtained in the historical group. The 6-month mortality rates were similar in both groups (27.5% in the contemporary group and 26.2% in the historical group).
Conclusions: We observed important changes in the epidemiology of IE in Olmsted County. In the contemporary group, there was an increase in IE incidence in the female population. Moreover, *S. aureus* surpassed viridans group streptococci as the most common causative organism in IE. We hypothesize that the microbiologic shift could be due to an increased occurrence of health care-associated and nosocomial exposure in recent years. Trend analyses are pending to determine if the microbiologic shift is confirmed.

005

POPULATION BASED SURVEILLANCE OF INFECTIOUS ENDOCARDITIS IN A NORTH EST ITALIAN REGION

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Background: Epidemiology of IE is changing, but literature data are difficult to interpret and compare, due to different case-mix, data collection, selection biases. The present study was designed to collect ALL IE cases within a defined geographical area (Friuli-Venezia Giulia-Italy), to obtain up-to-date, complete epidemiological, clinical and microbiological data on IE on a population basis.
Methods: Surveillance study conducted in the whole Friuli-Venezia Giulia (population 1,200,000) in 2004–2008; for all patients with suspected/confirmed IE seen at one of the clinical centres of Friuli-Venezia Giulia (Italy) a warning alarm form was sent to the coordinating centre; in the following days, a standardized, detailed case-report-form was completed, including demographic, clinical (including predisposing conditions/risk factors), radiological, microbiological, laboratory data, therapeutical (including surgery) and outcome data.
Results: 238 cases were notified. Incidence was 4.95 cases/100,000/yr, and 15.3/100,000/yr in the population >65 years. Mean age was 67 years (SD 14), 35% were females; 32% were prosthetic valve IE; 46% had at least one hospital admission in the preceding 6 months. Eighty-one percent had a microbiological diagnosis; enterococci were 37%, *S. aureus* 21%, Viridans streptococci 19%, Coagulase-negative staphylococci 12%. Surgical repair was required in 39% (of whom 79% during antibiotic therapy). Deaths were 20%.
Conclusions: The changing epidemiology, microbiology, clinical picture, medical and surgical treatment strategies are well documented in this all-cases, whole-area, surveillance study. Incidence is 3-times higher in the elderly population. Of note, the most frequent isolates were enterococci, and not staphylococci and Viridans streptococci as frequently reported.

006

RISK FACTORS FOR INFECTIVE ENDOCARDITIS IN PATIENTS WITH *STAPHYLOCOCCUS AUREUS* BACTERIEMIA: A TEACHING HOSPITAL EXPERIENCE

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Objective: To determine the risk factors for infective endocarditis (IE) in patients with *Staphylococcus aureus* bacteremia (SAB).
Methods: All patients (pts) hospitalized in our teaching hospital and diagnosed with SAB in 2004 were identified from the microbiology laboratory files and their charts were retrospectively studied.
Results: 149 SAB were diagnosed in 145 pts [91M/58F, mean age = 63.9 (±17) yrs] hospitalized in medical (75, 50%), intensive care (44, 30%) and surgical (30, 20%) units. Comorbidities were diabetes (44, 30%), alcoholic cirrhosis (23, 16%), cancer (45, 31%), dialysis (24, 16%), bone prosthesis (15, 10%), valvular prosthesis (9, 6%), immunosuppression (8, 5%). Four (3%) pts were intravenous drug abusers (IVDA). No

comorbidity was known in 21 (15%) pts. Portal of entry was a vascular catheter in 99 SAB (66%), 95 SAB were nosocomial. Transthoracic (TTE) and transoesophageal (TOE) echocardiography were performed in 91 and 30 pts respectively: 44/75 (59%), 36/44 (82%) and 1/30 (3%) pts hospitalised respectively in medical wards, intensive care units and surgical wards. Septic localisations were searched by total body scanner in 61 SAB (41%). A focus of infection was found in 75 (50%). IE was diagnosed in 16 (11%), [12M/4F, mean age = 52.8 (±20.6) yrs], 7 in medical wards, 9 in intensive care units. The involved valve was mitral (6), aortic (4), tricuspid (4), and pace maker in 2. When comparing the 133 pts without IE and the 16 pts with IE, IVDA (1/133 vs 3/16 pts respectively) and valvular prosthesis (1/133 vs 4/16 pts respectively) were significantly associated to the IE risk. Death occurred in 29/133 (22%) versus 6/16 (37%) pts without or with IE (ns).
Conclusion: Comorbidities were frequent in pts as well as other foci of infection. IE was more frequent among pts with valvular prosthesis and IVDA. In this retrospective study, the proportion of IE diagnosed during SAB (11%) was probably underestimated, [nearly 30% in the literature when TTE and TOE are systematically performed], as only 60% of pts underwent echocardiography. Efforts should be made towards a more systematic use of echocardiography in SAB especially in surgical wards.

007

LOW PREVALENCE AND GOOD PROGNOSIS OF CULTURE-NEGATIVE INFECTIVE ENDOCARDITIS (CNIE) IN AN EUROPEAN TERTIARY-CARE HOSPITAL

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Background: The aim of this study was to describe the characteristics of CNIE and to determine whether CNIE had a poor prognosis as compared as the remaining episodes of infective endocarditis (IE).
Methods: Between January 2000 and December 2008 a prospective, observational cohort study was conducted at Vall d'Hebron Hospital, a 1200-bed tertiary-care teaching hospital, with all the medical and surgical departments, and a referral center for cardiac surgery, set in Barcelona, Spain. IE was classified as CNIE if both blood-stream cultures, serologies, and valve cultures – when appropriate – were negatives. Empiric antimicrobial treatment was established according to the most probable source of acquisition. Epidemiological, clinical and prognostic variables were recorded.
Results: During the period of study, 348 episodes IE were treated in our center. Of them, 18 (5.2%) fulfilled the CNIE criteria. In this subgroup of patients, the mean age was 58.6 years (SD 16.8), 13 (72.2%) were men, the mean Charlson index was 0.94 (SD 1.16), 15 (83.3%) were community-acquired, and the median time between symptoms onset and admission was 31 days (IQR 15–107). The aortic valve was the most frequently affected (11, 61.1%). Twelve patients (66.7%) presented a previously known predisposing valve condition (2 congenital, 5 prosthetic valves, and 5 others). Twelve patients (66.7%) received antibiotics previously to admission, mostly because of a presumed respiratory infection. As compared with the remaining cases of IE, CNIE patients were more frequently transferred from another facility (61.1% vs 13.5%, P = 0.034), underwent more surgeries (66.7% vs 37.3%, P = 0.018), presented slightly more complications (94.4% vs 82.4%, P = 0.215), and had a lower in-hospital mortality (11.1% vs 28.8%, P = 0.122). The cumulate one-year mortality in CNIE was 22.2%.
Conclusions: CNIE represented a small amount of total IE in our center. Despite the lack of an identifiable etiology and the need for an empiric antimicrobial treatment, CNIE showed a lower mortality as compared as the remaining cases of IE. IE should be discarded in every feverish patient bearing a predisposing valve condition.

008

INFECTIVE ENDOCARDITIS (IE) AT INSTITUTO NACIONAL DE CARDIOLOGIA, RIO DE JANEIRO, BRAZIL, FROM 1997 TO 2002

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Background: Few series describe IE in Brazil. There are differences in epidemiology from our country compared to that from Europe or the USA.
Methods: Retrospective analysis of cases between January 1997 and January 2002, using discharge codes. Probable and definite cases (Duke criteria) were included.
Results: 38 cases were included, 87% were clinically definite. Median age was 35 years. Prosthetic valve IE accounted for 27%. Nosocomial acquisition occured in 13% of all cases. 12/37 (32%) cases where information was available had rheumatic valvulopathy as predisposition. Blood cultures (BC) were positive in 67% of community-acquired IE, and viridans streptococci predominated (36%). BC were also positive in 87% of hospital-acquired cases; coagulase-negative staphylococci were responsible for 25% of these. Mitral valve involvement occurred in 51%. Surgery was indicated for 26 cases (68%). The most frequent surgical indications were valvular dysfunction (46%), acute mitral regurgitation (31%) and uncontrolled sepsis (23%). 46% of patients had more than one indication for surgery. Median duration of surgery was 250 minutes and median perfusion time 107. There was no correlation between these and death rate. All 4 cases of *S. aureus* had surgery and also had greater probability of post operative infectious complications compared to other operated patients with non *S. aureus* IE (p = 0.005). Overall mortality was 5/38 (13%).
Conclusions: Patients in this series were younger than those described in the literature, probably because of the large number of patients with rheumatic valvulopathy in Brazil. *S. aureus* was the agent with the most difficult clinical management and greater rate of complications.

009

CLINICAL AND EPIDEMIOLOGICAL PREDICTORS OF *STAPHYLOCOCCUS AUREUS*, VIRIDANS STREPTOCOCCAL, AND ENTEROCOCCAL NATIVE VALVE ENDOCARDITIS AT INITIAL CLINICAL EVALUATION

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Background: Only a small range of pathogens cause the majority of the cases of infective endocarditis. Staphylococci, streptococci and enterococci account for 85% of infective endocarditis (IE) cases in the literature. In Brazil, for patients with suspected IE, clinicians will draw blood cultures and either start empiric antibiotic therapy immediately or wait for the blood culture results without empiric antibiotic therapy, depending on what the suspected microorganism is.
The ability to predict the likely aetiological agent causing IE based on epidemiological characteristics and clinical manifestations at initial clinical evaluation in patients with native valve endocarditis (NVE) would be useful and has not been adequately addressed.
Methods: From 1978 to 2008, 391 cases of definite IE in 363 consecutive patients >18 years of age were admitted to our hospital.
Patients with definite cases of NVE caused by *Staphylococcus aureus* (*S. aureus*) who were admitted during the period April 1978 – May 2008 were compared with patients with definite cases of NVE caused by viridans group streptococci (Strep) and patients with NVE caused by *Enterococcus faecalis* (Entero).
Results: We extracted 154 definite cases of native valve endocarditis (NVE) due to *S. aureus* (66), Strep (64), and Entero (24) from 391 case of definite IE admitted between April 1, 1978 and May 31, 2008.

Blood cultures were positive in 67.5% of definite NVE cases. *S. aureus*, Strep, and Entero accounted for 74% of these cases of native valve endocarditis with positive blood culture.

Table 1. Epidemiological characteristics and clinical manifestations at initial clinical evaluation.

	S. aureus (%)	Strep (%)	Entero (%)	p value
Median age	36.5	42.8	56.1	<0.001
Duration of symptoms	17.3	76.6	41.2	<0.001
Health care-associated infection	31.9	50.0	00.0	<0.001
Hemodialysis	13.6	00.0	41.7	<0.001
Predisposing cardiac condition	27.3	75.0	45.8	<0.001
Intravascular source	12.1	00.0	29.2	<0.001
Peripheral stigma of IE	50.0	31.3	16.7	<0.016

Conclusions: We conclude that clinical and epidemiological characteristics can help predict the causative microorganism in some cases.

010

EVOLUTION OF PROGNOSTIC FACTORS IN LEFT-SIDED ENDOCARDITIS: THE MULTICENTRIC GAEICV-SAEI STUDY

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Background: Analysis the risk factors of death in a large prospective cohort in two periods over more 20 years.
Methods: Multicentric cohort study of left-sided endocarditis from 1986 to 2007, in 7 hospitals of Andalucía (South of Spain). Definitive and probable case according modified Duke criteria was included. Patients was identified using microbiology blood culture registry, echocardiography laboratory and by consulting infectious diseases units. Demographic, clinical, microbiologic, echocardiographic, treatment and follow was entered in standardized database. We distingued two periods: from 1984 to 1995 and from 1996 to 2007. The main outcome measure was the in-hospital mortality. Univariate and multivariate analysis were performed by a logistic regression model.
Results: 866 cases was included, 208 cases in first period and 658 in second period. In-hospital mortality was 23.6% in the first period and 30.7% in the second period ($p = 0.048$). Independent risk factors for in-mortality was: severe cardiac failure (OR: 5.6 and 4.0), *Staphylococcus aureus* etiology (OR: 5.3 and 1.7), neurologic manifestations (OR: 3.0 and 1.7), prosthetic valve (OR: 2.8 and 1.6) Charlson index (OR: 1.3 and 1.1), septic shock (OR: 12.1 and 4.4), however periannular extension was observed only in second period (OR: 2.3). *Streptococcus* viridans group etiology (OR: 0.37) and early surgical treatment (OR: 0.5) was associated with better prognosis in last years.
Conclusion: Despite the improvement of medical care, in-hospital death of left-sided endocarditis is not decreasing. Prognostic factors were similar in both periods except periannular extension in the second. Surgical treatment and s. viridans group etiology was associated with better prognosis in last year.

011

INFECTIVE ENDOCARDITIS AT A TERTIARY CARE CENTRE IN LEBANON: CONTINUED PREDOMINANCE OF STREPTOCOCCAL INFECTION

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Background: Despite being a rare disease, infective endocarditis (IE) continues to cause significant morbidity and mortality. Previous data from the American University of Beirut Medical Center (AUBMC) had shown a predominance of streptococcal infections. As worldwide studies in developed countries show noteworthy increasing trends in *Staphylococcus aureus* endocarditis, it becomes ever vital to constantly inspect the local data for a similar change.
Methods: We conducted a retrospective review of all recorded IE cases in adult patients admitted between 2002 and 2008 to AUBMC. We then compared these cases to a historical cohort of 91 IE cases at AUBMC from 1986 to 2001.
Results: A total of 56 patients were diagnosed with IE between 2002 and 2008. The mean age was 61 years. Blood cultures were positive in 82% (46/56 patients) of the cases. The most commonly isolated organisms were *Streptococcus* spp. (37%), compared to 51% in the previous cohort. *Staphylococcus aureus* accounted for 11%. Only 1 isolate of *S. aureus* was methicillin-resistant. In contrast, in the historical cohort, 26% of cases were caused by *S. aureus*. Enterococci ranked closely behind staphylococci with 22% of the total cases, while in the previous cohort, the proportion of IE cases caused by enterococci was only 4%.
Conclusions: Compared to previous data published from AUBMC, the rates of both streptococcal and staphylococcal endocarditis have decreased while enterococcal endocarditis has increased. This study reconfirms that in Lebanon, a developing country, we continue to have a low predominance of staphylococci as etiologic agents in IE.

012

EVALUATION OF BACTEREMIA AND INFECTIVE ENDOCARDITIS (IE) IN A TERTIARY-CARE HOSPITAL

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Background: Sepsis and IE remain a challenge despite the medical progress. The aim of this study was to evaluate the cases of bacteremia in a 350-bed hospital in Sofia, Bulgaria.
Methods: A retrospective analysis was performed using definitions of the CDC and Duke's criteria. Blood-cultures were incubated in Bactec 9050, BD; microorganisms were identified by API, BioMerieux and Crystal, BD. Antimicrobial susceptibility was according to the CLSI.
Results: During the 3-year period, 335 patients had clinically significant bacteremia. Six of them, men, mean age 52, had left-sided acute IE (in 2 – of prosthetic valve) caused by *S. aureus* and *E. faecalis*. Patients were treated according to the AHA guidelines: they improved; 2 of them needed urgent surgery. Bacteremia was nosocomial in 48%. The majority of cases represented a secondary bacteremia, most often related to UTI or surgery, incl. in urology. Gram-negative microorganisms isolates were: 61 *E. coli*, 71 other *Enterobacteriaceae*, 58 non-fermenters. Top Gram-positive agents were: 57 *S. aureus*, 108 CoNS and 23 enterococci. VRE were not detected. Antimicrobial resistance showed a trend to increase: the rate of MRSA rose from 12% in 2006 to 50% in 2008, ESBL-producing *E. coli* rose from 18% to 25% and multi-drug resistant *P. aeruginosa* and *A. baumannii* emerged. The relative rate of patients with bacteremia and severe sepsis increased, too.
Conclusions: This study revealed epidemiology and differentiated types of bacteremia, together with an accent on increase in problem of antibiotic resistance, which is an obstacle in therapy.

013

PREDICTIVE FACTORS FOR CAUSATIVE PATHOGEN IN INFECTIVE ENDOCARDITIS IN DENMARK

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Background: Infective endocarditis (IE) from different causative pathogens differ with regards to prognosis. We looked at predictive factors for different pathogens in a series of 386 patients admitted to two Copenhagen tertiary centres from 2002 to 2008, including differences in patients with native valve (NVE) or prosthetic IE, stratified by time from surgery (<3 months = early PVE or ⩾3 months = late PVE).
Methods: The study population consisted of 439 patients, excluding IV drug users (N = 22), PM endocarditis (N = 20), and recurrent IE (N = 11). Data is presented as number (%) and differences were tested by $\chi 2$-test. Predictive factors for individual pathogens were analysed by multivariate logistic regression modelling.
Results: Median age (25th and 75th percentile) was 65 (56–75) and 113 (29%) were female. The prevalence of known risk factors for IE were: early PVE 18 (5%), late PVE 79 (20%), diabetes 34 (9%), history of cancer 38 (10%), renal dysfunction 57 (15%) and immunosuppression 36 (10%). Causative pathogen were Viridans group *Streptococcus* 120 (31%), *Staphylococcus aureus* 80 (21%), enterococci 66 (17%), Coagulase-negative staphylococci 32 (8%), other 44 (11%) and culture negative 44 (11%).
Viridans group *Streptococcus* IE was associated with NVE (OR = 3.8, 95% CI: 1.9–7.4) and was infrequent in patients with renal dysfunction (OR = 0.33, 0.13–0.79). *Enterococcus* IE was related to age (OR = 1.3, 1.2–1.5 per 5 years) and frequent in patients with renal dysfunction (OR = 4.2, 2.0–8.9). Coagulase-negative *Staphylococcus* IE was frequent in PVE (OR = 4.5, 2.0–10.1). Culture Negative IE was frequently associated with PVE (OR = 2.6, CI: 1.2–5.4) and younger age (OR = 0.8, 0.7–0.9). Rare pathogens, grouped as 'other' was associated with younger age (OR = 0.8, 0.7–0.9 per 5 years) and less frequent in patients with renal dysfunction (OR = 0.45, 0.23–0.90). No independent predictors of *Staphylococcus aureus* IE were identified (IV drug users excluded). No differences in the pathogens associated with early PVE and late PVE could be identified.
Conclusions: Viridans group streptococci are not common in patients with prosthetic heart valves, whereas coagulase-negative staphylococci and culture negative IE were more common in this group. *Enterococcus* IE are associated with increasing age. Considerable variation in the clinical appearance of IE and risk factors associated with causal pathogens underline the continuing diagnostic challenge of IE.

014

EARLY PROSTHETIC VALVE ENDOCARDITIS (E-PVE) IN A TERTIARY-CARE REFERRAL CARDIAC SURGERY HOSPITAL IN BRAZIL FROM 2006 TO 2008

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Background: The incidence of e-PVE is largely unpublished; its acquisition is mainly related to surgery and to intravenous line infections.
Methods: Prospective cohort study.
Results: There were 13 patients and 14 episodes of e-PVE in the study period. Only definite cases (modified Duke criteria) were included; 5 were pathologically proven. Mean incidence per number of patients submitted to valve replacement surgery (VRS) was 13/625 (2.1%); it was 5/192 (2.6%), 4/194 (2.1%) and 4/239 (2.0%) in 2006, 2007 and 2008 respectively. There were 9 male, 4 female. Mean age ± SD was 26.5±15.4 years. Causative organisms in 14 episodes were *Candida* 6 (*parapsilosis* 3, *albicans* 1, *tropicalis* 2), coagulase-negative staphylococci 4 (*S. epidermidis* 2, unknown 1, *viridans* 1), *Enterococcus faecalis* 1, *Enterobacter cloacae* 1. Involved structures were bioprosthesis – mitral (M) 3, aortic (A) 1, mitral and aortic (MA) 2; mechanical valves – M 3, A 1, MA 1, and pericardial patches in interventricular communications in 2 (1 with tricuspid valve involvement). Transesophageal echocardiograms showed major criteria in all cases. Complications were abscess (2/13), persistently positive blood cultures (5/13), cardiac failure (7/13) and emboli (9/13). Seven patients died; of these, 1 had surgery. Of the 6 who survived, 3 had surgery. In 8/13 cases IE occurred within 2 months of VRS.
Conclusion: Incidence of e-PVE at INC is within that described in the literature. However, cases may still be diagnosed for 2008. *Candida* predominated. No cases were caused by *S. aureus*, which may be due to routine pre-operative decolonization with mupirocin and chlorexidine.

015

LATE PROSTHETIC VALVE ENDOCARDITIS (L-PVE) AT A CARDIAC SURGERY REFERRAL HOSPITAL – YEARS 2006 TO 2008 – RIO DE JANEIRO, BRAZIL

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Background: PVE is increasing in Brazil, due to more patients being submitted to valve replacement surgery (VRS).
Methods: Prospective cohort study.
Results: There were 76 episodes of infective endocarditis (IE) in the study period; 50 (66%) involved native valves, 14 (18%) were early PVE, 12 (16%) were l-PVE. All l-PVE cases were clinically definite (modified Duke criteria), 4 were pathologically confirmed. Eight patients were male, 4 female. Mean age±SD was 42±22 years, median 38.5. Affected structures were bioprosthesis – mitral (M) 3, aortic (A) 3, mitral and aortic (MA) 1; mechanical M 3, MA 1, interventricular septum patch 1. Mean age of prosthesis was 9.6±4 years, median 9. 8/12 patients had VRS due to rheumatic valve damage. Organisms were *S. aureus* 4, *E. faecalis* 2, not identified 3 (all subacute presentations), viridans streptococcus 1, *Salmonella enteriditis* 1, *P. aeruginosa* 1. Only the last case was hospital-acquired (the patient was referred for surgery). All echocardiograms showed major criteria. Complications were abscess 3/12, heart failure 6, emboli 6. Six patients had surgery, and 5 survived. Six did not have surgery, and 3 died. Overall mortality was 4/12.
Conclusions: Despite the small number in this series, it is of note that only one patient acquired IE in hospital. The long median time of prosthesis insertion to IE confirms the literature data and our data on highest risk of endocarditis in the first year post VRS. Our patient cohort with l-PVE is younger, due to VRS being most often indicated for patients with rheumatic valvulopathy.

016

HEALTH CARE-ASSOCIATED INFECTIVE ENDOCARDITIS

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Background: Invasive medical technology has led to an increase in the incidence of health care-associated infective endocarditis (HAIE).
Methods: Prospective multicenter cohort study, conducted in 7 hospitals of the Andalusian Health Service, in Spain. Seven hundred

and ninety three cases of infective endocarditis (IE) were investigated. The aim of this study was to describe the characteristics of HAIE and to establish a comparison between health care and community-acquired episodes. HAIE was defined as either IE manifesting >48 hours after admission to the hospital or IE acquired in association with a significant invasive procedure performed during a stay and/or manipulation in a hospital setting within 6 months before diagnosis.

Results: HAIE accounted for 16% of 793 cases. Compared with community-acquired infection, patients with HAIE tended to be older (60.1 vs. 53.6; P = 0.0001) and had more co-morbidities (Charlson index, 3.3 vs. 1.8; P = 0.0001) and staphylococcal infections (58.3% vs. 24.8%). Intra-hospital mortality (44.9 vs. 24.2%) was higher in the HAIE group. Vascular manipulation constituted the main cause of bacteremia responsible for HAIE (63%). Septic shock (OR, 10.13; 95% CI, 3.18–32.12; P = 0.0001) and severe heart failure (OR, 2.79; 95% CI, 1.09–7.13; P = 0.03) were independent predictors of intra-hospital mortality in the HAIE cohort.

Conclusions: The present study demonstrates that HAIE attacks a fragile population and it is principally caused by microorganisms strongly related to vascular manipulations. Extremely careful management of vascular accesses is needed in order to minimize the risk of secondary bacteraemias.

017

INFECTIVE ENDOCARDITIS IN SPAIN: A PROSPECTIVE COHORT STUDY

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Introduction: Infective endocarditis (IE) is a relatively uncommon disease, so collaborative multicentric groups are desirable in order to obtain significant data in a relatively short period of time. The aim of this study was to describe the GAMES organization and to report the first collaborative data of infective endocarditis in Spain.

Material and Methods: GAMES includes 35 different-sized hospitals from Spain in which multidisciplinary teams prospectively collect consecutive episodes of IE in a pre-established protocol that includes risk factors, predisposing conditions, origin, clinical features, course, and outcome. Overall 150 health-care providers of different specialties are involved in the group, so far. Standard diagnostic criteria and definitions were used. Data collection started in January 2008. All completed reports are centralized in the coordinating center and entered in the data base by a single data manager who also reinforces the quality of the data.

Results: We report the results from the first 194 protocols completed in our database. Overall mean age was 66±16 years and 71% were men. Age-adjusted mean comorbidity index was 4±2.5. Regarding underlying conditions 42% had valvular disease, 23% diabetes mellitus, 20% COPD and 17% renal insufficiency. IE was community acquired in 129 (66.5%), nosocomial in 47 and health-care related in the remaining cases. Most IE were left-sided 85% (73 A, 66 M, 14 AM) and there were 7 pacemaker related infections. 71% IE affected a native valve. An etiological diagnosis was achieved in 92% of the cases. The leading causative organism was *S. aureus* 22.6% (7MRSA) followed by CNS 19%, *Enterococcus* 16.5%, and *S. bovis* 15%. A transesophageal echocardiogram was performed in 64% of the patients (78% vegetation, 25% aortic valve insufficiency, 18% intracardiac complication). A CNS event was detected in 21% of the patients and renal insufficiency in 43%. Surgery was performed in 39% of the cases (46% of the prosthetic valve IE). Euroscore was higher in operated patients who died (p < 0.001). OPAT was received by 7% of the patients. Overall in-hospital death was 21.6%. Mortality was higher in patients with endocarditis caused by *C. albicans* (2/3), *S. epidermidis* 48% or *S. aureus* 30%. Other factors associated to a higher mortality were: age-adjusted Charlon's index, cardiac insufficiency, indication for surgery, persistence of sepsis, intracardiac complications and renal failure.

Conclusion: It was possible to create an Spanish Collaboration on Endocarditis (GAMES). Preliminary 2008 results showed that staphylococcal endocarditis in older patients remains a major cause of mortality in Spain. Collaborative studies may help to better define the clinical picture of this severe and uncommon disease and to improve its management and outcome

018

NEW FEATURES IN THE ENDOCARDITIS WITH THE CHANGE OF MILLENNIUM

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Objective: To evaluate the characteristics of the IE and their possible variations in the 2 last decades.

Methods: Multicentric cohort study in 7 Andalusian hospitals of the episodes of left-sided IE from 1984 to 2007. The characteristics of the IE of the previous millennium (1983–1999) (GR-1) were compared with the present millennium (2000–2007) (GR-2).

Results: 877 cases of IE were included, 383 (44%) in GR-1 and 494 (56%) in GR-2. The average age (50 years vs 59; p = 0.002), the comorbidity (Charlson index 1.4 vs 2.5; p = 0.001) the number of concomitant diseases (49% vs 70%; p = 0.001), renal failure (22% vs 36%; p = 0.0001) and septic shock (10% vs 16%; p = 0.008) were significantly higher in GR-2. Conversely, previous cardiac predisposing factor for IE (73% vs 66.4%; p = 0.001) and embolic complications (45% vs 34%; p = 0.01 were more frequent in the GR-1. With respect to the diagnosis, the GR-2 had more frequently positive blood cultures (80% vs 85%; p = 0.01) and transesophageal echocardiography (TEE) (23% vs 57%; p < 0.001). GR-2 showed a decreased incidence of *Streptococcus* viridans group (23.5% vs 20%; p < 0.09), compensated by a larger proportion of IE due to *Enterococcus* spp. (9% vs 15%; p = 0.005), methicillin-resistant *Staphylococcus aureus* (0.5% vs 2.4%; p = 0.02), *Streptococcus bovis* (0.8 vs 6.3%; p = 0.005) and gram-negative bacteria (1.6% vs 3.6%; p = 0.04). The rate of early valve surgery was higher (35.5% vs 40%; p = 0.005) although no differences in-hospital mortality rate was observed neither in native valves (27% vs 27.5%.) nor in prosthetic (40% vs 43%; p = 0.53).

Conclusions: Considerable differences have been observed between the two periods, with a higher morbidity in the last period. This fact could explain the remaining high mortality despite the recent advances in diagnosis and treatment.

019

EPIDEMIOLOGIC TRENDS IN INFECTIVE ENDOCARDITIS OVER THE LAST THREE DECADES AT THE UNIVERSITY OF PERUGIA, INFECTIOUS DISEASES DEPARTMENT

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Background: Over the last years, changes in the epidemiology of infective endocarditis (IE) have been reported world wide. Here, we

sought to review all the IE cases seen at the University of Perugia, Infectious Diseases Department.
Methods: Both a four-year observational and a thirty-one year retrospective chart review of all infective endocarditis cases was performed. Potential retrospective cases were identified by discharge diagnosis. All included cases were classified according to the Duke Criteria.
Results: Overall, 130 (83.1% definite and 16.9% possible) cases in 128 patients were identified. Patient mean age was 59±18 years, 71.5% male and male to female ratio was 2.5:1. Mean age increased from 48 years in the first decade to 64 years in the last period. Ninety-six (73.8%) had non-prosthetic valve endocarditis (PVE), 34 (26.2%) PVE: 11 early PVE while 23 had late PVE. Regarding predisposing conditions, 43 patients (30%) had a previously diagnosed valvular disease, 3 (2.3%) patients had intra-cardiac devices and 5.4% had had a prior episode of infective endocarditis. Overall, 7 patients were intravenous drug users. Comparing the data from 1973 to May 2008 the number of IE cases increased from 10 (7.7%) to 86 (66.1%) and PVE from 1 (10%) to 27 (31.4%). In 112 (86%) cases a microorganism was identified. Streptococci were the most frequent bacteria isolated in non-PVE, while staphylococci were the most frequent microorganisms in PVE patients. Transthoracic echocardiography (TTE) detected vegetations in 55/99 (61%) of IE patients undergoing TTE. Transesophageal echocardiography (TEE) was positive in 74/79 (93.67%) patients. Almost 50% of patients had one (74.6%) or more (25.4%) embolic localizations and the most frequently sites involved were brain and spinal column. Seventeen patients were lost at follow-up, 94/113 (82.3%) were cured and 19/113 (16.8%) died.
Conclusions: This review is in agreement with: (1) infective endocarditis is being more frequently diagnosed, (2) its incidence is on the rise among the elderly, (3) Staphylococci are being more commonly identified, and (4) TTE markedly improves diagnosis.

020
INFECTIVE ENDOCARDITIS IN APPARENTLY NORMAL LEFT-SIDED NATIVE VALVE

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Aim: To study clinical, microbiological and prognostic characteristics of infective endocarditis (IE) in apparently normal left-sided native valves, and to determine differences with IE on pathologic native valves.
Methods: We analyzed 729 consecutive episodes of IE, 601 were left-sided and 357 were in native valves. The latter were our study group. They were prospectively recruited at four tertiary referral centers between 1996 and 2008. We established 2 groups: Group I (n = 149), IE in apparently normal native valves; Group II (n = 208), IE in pathologic native valves.
Results: In Group II, previous cardiac disease distribution was: rheumatic 28.6%, degenerative 31.9%, congenital 14.3%, mixoid 12.1%, hypertrophic cardiomyopathy 3.3%, previous IE 2.2%, and others 7.6%. Patients from Group I were younger (54±16 vs 61±16 years), and were more frequently intravenous drug users and alcohol abusers. Microbiologic profile: *S. Bovis* (8.7% vs 2.2%; p = 0.008) and *S. Aureus* (28.3% vs 16.5%, p = 0.011) were more common in Group I, whereas coagulase negative *Staphylococcus* (6.5% vs 13.7%) was more frequent in Group II. At admission, abdominal presentation was more common in patients from Group I. Vegetation detection rate was higher in Group I. Aortic location of the infection was more frequent in Group I. During hospitalization, heart failure (67.6% vs 56%, p 0.035), septic shock (22.1% vs 13.2%; p = 0.028), significant valvular regurgitation (89.9% vs 81.3%; p 0.032), and embolism in hepatosplenic axis (14.4% vs 6.6%, p 0.021) were more common in Group I. There was a trend toward a higher in-hospital mortality rate in Group I (35.5% vs 25.8%; p = 0.068). No differences were observed in the need of surgery.
Conclusions: Infective endocarditis in apparently normal left-sided native valves was more frequent in young patients, caused by virulent organisms (*S. aureus*) and associated to a higher proportion of complications than IE on pathologic native valves.

021
INFECTIVE ENDOCARDITIS IN YOUNG PATIENTS NON INTRAVENOUS DRUGS USERS

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Aim: To describe clinical, microbiological, echocardiographic and prognostic characteristics of episodes of infective endocarditis (IE) in patients under 40 years non intravenous drugs users (IVDU).
Methods: We analyzed 729 consecutive episodes of IE, 664 of which were IE in non IVDU patients. They were prospectively recruited at four tertiary referral centers between 1996 and 2008, and were classified in 2 groups: Group I (n = 79), episodes of IE in patients under 40 years, and Group II (n = 585), episodes of IE in patients older than 40 years.
Results: In Group I community acquired infections were more frequent. No differences in predisposing factors were observed between groups. Previous cardiac disease distribution was different among the two groups: congenital disease (25.4% vs 2.5%; p 0.001); prosthetic valves (19.7% vs 40.4%; p 0.001) and degenerative disease (2.8% vs 11.1%; p 0.029). In Group II previous comorbidity (chronic anemia, renal failure and chronic obstructive pulmonary disease) were observed more frequently. Infection location was similar in both groups, except high prevalence of tricuspid IE in Group I (10.4% vs 2.2%; p 0.001). There were no major differences in microbiological profile between groups. No differences were observed in vegetation detection rate, perianular complications, and valvular dysfunction. During hospitalization, septic shock (7.7% vs 15.9%; p = 0.05), heart failure (41.7% vs 56.8%; p = 0.015) and persistent infection (8.7 vs 24.8%; p = 0.016) were less frequent in Group I. No differences were observed in the need of cardiac surgery, but mortality was higher in Group II (15.3% vs 31.5%; p = 0.005).
Conclusions: Infective endocarditis in young patients non intravenous drugs users was associated with a lower incidence of complications and lower mortality.

022
INFECTIVE ENDOCARDITIS TREATMENT: EXPERIENCE IN LAST TEN YEARS

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Aim: To analyze changes in microbiological, echocardiographic, clinical and prognostic profile of infective endocarditis (IE) in the last 10 years.
Methods: We analyzed 729 consecutive episodes of IE. They were recruited prospectively at four tertiary referral centers between 1996 and 2008. They were classified into 2 groups: Group I (n = 363), episodes of IE registered between June 1996 and December 2001, and Group II (n = 366), episodes of IE registered between January 2002 and May 2008.
Results: In Group I patients were younger, 54 (16) vs 61 (16) years, and more frequently intravenous drugs users (IVDU) (12.7 vs 4.9%; p 0.001). Community acquired infections and previous cardiac disease (58% vs 71.6%; p 0.001) were more common in Group II. Prosthetic valve IE (28.5% vs 42.1%; p 0.001) was more frequent in Group II. Comorbidity was more common in Group II: diabetes (14.4% vs 23.1%,

p 0.002), chronic anemia (12.7 vs 21.5%; p 0.002), renal failure (5.8% vs 11.85, p 0.004), and neoplasm (5.3% vs 11%, p 0.005). In Group II, coagulase negative *Staphylococcus* (14.4% vs 20.8%, p = 0.029) was isolated more commonly. At admission, fever, constitutional syndrome, and pulmonary and rheumatologic presentations were more frequent in Group I, whereas in Group II cardiac and abdominal presentations were more common. During hospitalization, septic shock (12.7% vs 18.9%; p = 0.021) was observed more frequently in Group II. There were no differences in periannular complications, heart failure, valvular dysfunction, persistent infection and embolism. In Group II the need of cardiac surgery was higher than in Group I (49.3 vs 58.7%; p 0.011). No differences were observed in hospital mortality (28.1% vs 28%).
Conclusions: In the last years the incidence of infective endocarditis was higher in older patients with a higher degree of comorbidity. Prosthetic valve IE increased and IE in IVDU was less frequent. The need for cardiac surgery has also increased. Mortality remained similar.

023
CURRENT TRENDS IN INFECTIVE ENDOCARDITIS IN ITALY: REPORT ON 852 CASES FROM THE MULTICENTER, PROSPECTIVE SEI STUDY

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Background: Infective endocarditis (IE) is not an uncommon disease. The objective of this investigation is to describe the characteristics of an Italian multicenter cohort of patients with IE.
Patients and Methods: The SEI study (Studio Endocarditi Italiano) is a multicenter prospective observational study that collected data from 22 Italian referral hospitals on 947 cases of definite or possible IE (according to Duke's criteria), from January 2004 through November 2008.
Results: In our database, 852 (89.97%) patients had definite IE and 95 (10.03%) patients possible IE. 214 patients (25.12%) had a valvular prosthesis, 75 (8.80%) had had a previous IE and 281 (32.98%) had a congenital (72) or acquired (220) native valve predisposing condition. 819 strains were isolated from 773 patients (cases of culture negative IE were 9.27%). The most frequently isolated pathogen was *S. aureus* (201 patients, 24.54%), followed by viridans streptococci (157 patients, 19.17%) and coagulase negative staphylococci (123 patients, 15.02%). The most common complication was cardiac failure (338 patients, 39.67%), followed by peripheral embolism (274 cases, 32.15%), stroke (135 cases – embolic 100, hemorrhagic 26, unknown 9 –, 15.84%), arrhythmia (121 cases, 14.20%), cardiac abscess (106 cases, 12.44%) and TIA (26, 3.05%). Surgical treatment was performed in 406 patients (47.65%), 39.25% of prosthetic valve IE (PVIE) and 50.47% of native valve IE (NVIE) (p < 0.05, OR 0.63). Mortality was 16.20% (24.77% in PVIE and 13.32% in NVIE, p < 0.01, OR 2.14). Mortality in medically-surgically treated PVIE was 20.23%, while in only medically treated PVIE was 27.69% (p ns); mortality in surgically treated NVIE was 9.62% vs 17.01% in only medically treated NVIE (p < 0.05, OR 0.52).
Conclusions: *S. aureus* is the most frequently isolated pathogen in contemporary IE in Italy. In patients treated with combined medical-surgical therapy, if indicated, the mortality is lower, especially in NVIE. The microbiological and clinical features of Italian IE patients, as well as their rate of complications and their outcome match thoroughly with those observed in other recent multinational surveys.

024
A PROSPECTIVE STUDY OF INFECTIVE ENDOCARDITIS FROM A DEVELOPING COUNTRY – AIIMS INFECTIVE ENDOCARDITIS REGISTRY

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Introduction: The pattern of IE in the Western countries has changed considerably and India apparently has double burden of traditional and modern IE. There is relatively scarce data regarding the profile of IE in India.
Methods: Data was collected prospectively from 104 consecutive cases (mean age 25.02±17.6 years, range of 0.25–70 years) with a diagnosis of 'definite' IE as per the modified Duke's criteria.
Results: Congenital heart disease was the most common underlying heart disease [in 41 patients (39.4%)]. Native valve disease including rheumatic heart disease accounted for 29.8% (n = 31). Prosthetic valve disease (PVD) accounted for 20% cases (n = 24). Positive cultures were obtained in 43 cases (41%). The most common organisms isolated included streptococci (in 8 patients), *Staph. aureus* (in 7 patients), and *Acinetobacter* (in 7 patients). The reason for the low culture positivity was the high incidence of prior use of antibiotics (almost 51%). There were a total of 44 episodes of embolisation (42.3%). Overall 27 (26%) patients died during the hospital stay. Surgery for IE was done in only 16 cases of whom 12 patients survived. In a stepwise logistic regression analysis for predictors of mortality, a duration of fever of less than 30 days, underlying heart disease other than native valve disease, congestive heart failure, acute renal failure and septic shock were found to be predictors of mortality.
Conclusion: IE continues to have high morbidity and mortality rates despite advances in diagnostic and therapeutic modalities.

025
SURGICAL WOUND INFECTIONS AFTER MEDIAN STERNOTOMY: CLINICAL AND MICROBIOLOGIC RESULTS OF A LARGE MULTICENTRIC STUDY IN ITALY

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Objectives: Sternal wound infection (SWI) after median sternotomy is the most dreaded complication after cardiac surgery. When the deep tissues are involved, the mortality and costs are unacceptably high. Early diagnosis and adequate treatment are essential for reducing mortality and devastating sequelae. There is lack of consensus regarding the ideal operative treatment, surgical approach varying from simple drainage to extensive plastic procedures. We report the incidence of SWI, the clinical and microbiologic features and the current therapeutic approaches in a large series of patients.
Methods: Nineteen Italian divisions of Cardiac Surgery participated at this prospective, observational study. From October 2005 to July 2006, all the patients undergoing median sternotomy in the first week of every month were included and followed for 60 days after operation. For all the patients who developed SWI, clinical and microbiological data were collected, inserted in a common data base and analysed by a central supervisor.
Results: Overall, 49 out of 1668 patients developed SWI (2.93%). The mean age was 67.1 years, the mean ASA score was 3.28, the mean pre-operative hospitalisation was 6.84 days, 18.8% had non elective procedures, 93.4% had length of surgery >3 hours. The mean time between surgery and diagnosis of SWI was 18.4 days. Microbiologic cultures were performed in 31 patients (63.2%) and the causative microrganism was isolated in 28 patients. Eighty percent of isolates were staphylococci, of which 80% were oxacillin-resistant.

Twenty-two of the 49 SWIs (44.9%) involved the deep tissues (sternal bone in 15, mediastinum in 7). The mean time of onset of SWI was 17.8 days (in 45.4% of the patients after discharge). Wound discharge was present in 90.9% of the patients; sternal instability and fever were present respectively in 100% and 13.3% of osteomyelitis and in 57.1% and 100% of mediastinitis; 77.2% of the patients underwent surgical reoperation. The mean length of antibiotic therapy was 33.4 days. Mediastinal irrigation or vacuum aspiration were required in 86.3% of the patients. The mean time of hospitalisation was 49.8 days. Mortality for infection was 13.6%.
Conclusions: The rate of SWI was acceptably low. Most SWIs were due to oxacillin-resistant staphylococci. Deep involvement is frequent and usually requires reoperation, mediastinal irrigation or vacuum aspiration and prolonged hospitalisation. Mortality rate is relevant.

026
THE OUTCOME AND SURVIVAL WITH MEDICAL AND SURGICAL TREATMENT OF INFECTIVE ENDOCARDITIS IN UNIVERSITY MALAYA
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Background: Infective endocarditis (IE) is a challenging disease to treat because although it is relatively rare, it is still very lethal with mortality rates of up to 40% within one year of diagnosis. The current treatment of IE involves anti-microbial therapy and surgery. Being a heterogenous disease, it is difficult to prescribe one mode of treatment over the other without knowledge of current local practices and outcomes.
Materials and Methods: This was a retrospective study of 86 cases of IE in University Malaya Medical Centre, (UMMC) from January 2000 to December 2007. Patients were identified from hospital medical records and the modified Duke criteria were used to select confirmed cases of IE. Data on the patients' demographic characteristics, predisposing factors, clinical findings, complications, result of investigations, method of treatment and clinical outcome were extracted from the case notes. Data on 1-year survival was obtained from either phone interview with the patient or from the patient's medical case notes.
Results: From 2000 to 2007 there were a total of 86 cases of IE. Out of these, 63% were male and 37% female. At the index IE episode, the majority of patients had native valves except for 7% who had surgically repaired valves and 8% with valve replacements. *Staphylococcus aureus* was found to be the commonest causative agent (31%) followed by viridans group *Streptococcus* (27%). The most common complications recorded were systemic embolization (24%) followed by cerebrovascular events (21%). Ten patients (12%) had surgery at the index admission whilst 7 patients (8%) had surgery in the 1-year follow-up period. From the index admission 83% of patients were discharged alive whilst 17% had died including one patient who was treated surgically. In the one-year follow up period, another 6% of patients died whilst 5% were lost to follow up. All patients treated surgically in the follow-up period were still alive one year after the index admission.
Conclusions: This is the largest Malaysian study on infective endocarditis to date documenting clinical features, complications, treatment and outcome. Assuming patients lost to follow-up had died, the mortality rate of IE patients in this study is 28% which is comparable to the Western world. Patients treated surgically had a lower mortality rate (6%) compared to the medically treated patients (28%) although these numbers are still too small to reach statistical significance.

027
CHANGING PROFILE OF INFECTIVE ENDOCARDITIS: RESULTS OF THE COUNTY HOSPITAL IN SLOVAKIA
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Objective: The authors present two different series of patients (ps) with infective endocarditis (IE) hospitalized in the Hospital in Nitra, a local hospital with 800 beds that serves a population of 200,000 people.
Methods: The two series were separated, the first included ps seen from 1997 to 2001 (group I), and the second from 2004 to 2008 (group II).
Results: In the series we included 40 ps (I) and 60 ps (II) with native valve IE. The mean age of ps was 57 (I) and 48 (II). Blood cultures were negative in 25% (I) and 40% (II). The most frequently affected site was the aortic valve in 40% (I) and 57% (II), mitral valve 40% (I) and 33% (II). Bicuspid aortic valve was present in the 5% (I) and 33% (II). The most frequent isolated pathogens were: *Staphylococcus* 40% (I) and 28% (II), *S. aureus* 25% (I) and 17% (II), *Streptococcus* 17% (I), and 21% (II). Perivalvular complication (PC) demonstrated by echocardiography were 17% (I) and 33% (II). Nosocomial IE were identified in the 22% (I) and 25% (II). Overall mortality was 22% (I) and 10% (II), surgery was required in 30% (I) and 37% (II).
Conclusion: By comparing group I with group II, new trends were recorded: (1) the increase of percentage of IE in young patients with unknown bicuspid aortic valve, (2) the increase of number PC, (3) the increase of culture-negative IE.

028
INVESTIGATION OF BLOOD CULTURE NEGATIVE ENDOCARDITIS IN A TERTIARY CARE CENTRE IN TUNISIA
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Microbiological profile of infective endocarditis (IE) has been well reported in developed countries. However, in developing countries, most studies reported high proportions of blood culture negative endocarditis (BCNE), up to 50%. We conducted a prospective study in our hospital in 2008, in order to determine etiological profile of IE in our region.
Data on all cases of IE hospitalized in the university hospitals of Sfax (2nd town of Tunisia) between 1st January 2008 and 31 December 2008, were prospectively evaluated. Sera from patients with BCNE were tested in a micro-immunofluorescence assay for Chlamydophila pneumonaie, Bartonella and Coxiella burnetii antigens. Removed cardiac valves, when available, were tested in a broad range 16Sr_DNA PCR amplification and sequencing.
We included 33 cases of putative IE. Twenty six cases were definite IE. With 20 cases of native valve endocarditis and 6 cases of prosthetic valve endocarditis. The mean age of patients was 42.7 years.
When considering the results of blood cultures, an etiological agent was detected in 9 cases (34.6%) with viridans streptococci in 5 cases, *S. aureus* in two cases and Enterobacteria in two cases. Serology showed positive results in 5 cases with 4 cases positive for Bartonella and 1 case with chronic Q fever. PCR on valves was positive in 6 cases allowing the diagnosis of two additional cases of IE due to viridans streptococci. Considering all methods of diagnosis, the etiological agent was identified in 18 cases (70%). Among the remaining eight cases, prior antibiotic therapy was noted in five cases.
BCNE poses a major problem in our institutions. We have demonstrated in a prior retrospective study that the proportion of Bartonella endocarditis is at least 10%. In this prospective survey, in spite of the low number of patients, we showed that serology coupled to molecular biology could improve the diagnosis of BCNE and so that better antibiotic treatment.

029

CLINICAL PROFILE OF 272 CONSECUTIVE CASES OF INFECTIVE ENDOCARDITIS

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Infective endocarditis is still considered a severe cardiac disease: although uncommon (annual incidence 1.7–6.2 cases per 100,000 population), endocarditis constitutes a potentially life-threatening disease (mortality rate 20–25%), with increasing incidence.

From 1992 to 2008 we identified 272 consecutive cases of I.E., 13 cases per year in the first 9 years, and an annual rate of 21 cases per year in the last 8 years. The age ranged from 6 to 82 years with increasing incidence among elderly in the last 8 years.

In the last 8 years I.E. was more frequent among elderly patients: we have now 75% of patients over 61 y. versus 57% in the first period.

Vegetations were visualized in 75% of NV, in 17% PV, in 8% of observed intracardiac catheters.

Endocarditis associated with intracardiac catheters had an important increase in the last 8 years; from 3% in the first 9 years to 9% in the last period.

Predisposing factors in our patients were degenerative valve lesions (40%), congenital heart disease (17%), end stage kidney failure (13%), immunosuppression (8%), IV drug use (4%).

The infective organisms were identified in 63% patients with decisive predominance of gram positive (streptococci and staphylococci), especially among patients over 60.

Predisposing conditions were more evident in elders (90% versus 40%).

Complications were more frequent in older patients; 20% of patients had thromboembolic events; among these patients 50% had provable large size mobile vegetations (>10 mm); in 28% severe valvular regurgitation was documented; in 11% abscesses and pseudoaneurism were displayed; 12% had valvular dehiscence.

Preoperative abscesses were more frequently observed after 1999 (5% versus 17% after 1999), when we started performing TEE to all endocarditis patients; TEE is more sensitive in detecting intracardiac complications.

Antibiotic therapy was effective in 65%, with 9% in hospital mortality rate; 35% underwent surgery, with 3.7% operative mortality in NVE versus 30% in PVE.

Surgery was performed promptly as aggressive treatment of I.E. (less than 14 d.) in 24% of cases, when rapid onset of valvular destruction was documented, despite efficacy of antimicrobial therapy against highly susceptible strains.

Between 1992 and 2008, 39 patients were admitted with right sided IE with 14% increase in the last 3 y., due to escalation of population with risk factors: Tesio catheters, intracavitary devices (PM-CD), IVDA, immunocompromised.

30% of our patients with right side IE had Tesio catheters for HD; the main clinical presentation was persistent fever in all patients, with pleuropolmonary manifestations in 17%; staphylococcus epidermidis was the causative agent in 60% of patients.

Albeit effectiveness of prolonged antibiotherapy the removal of infected material was the only method to cure definitively intracavitary device associated endocarditis.

Etiology

030

STREPTOCOCCUS BOVIS (SB) FECAL CARRIAGE (SBFC) AND COLONIC TUMORS IN FRANCE: AN UPDATE

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Background: Colonic tumors are associated with a higher rate of SbFC and an increased risk of Sb bacteremia/endocarditis. The aims of this study were to re-assess the SbFC rate in patients undergoing a colonoscopy and the link between SbFC and the frequency and type of colonic lesions, in a country where the frequency of Sb endocarditis has increased significantly.
Methods: We enrolled 268 adult patients who underwent colonoscopy for whatever reason. The following data were collected: demographics, history of colonic tumor, indication for colonoscopy, and colonoscopy/pathology diagnosis. The latter was distributed into 3 classes: normal, tumoral lesion (adenoma/carcinoma), and non-tumoral anomaly. Before colonoscopy, stool samples were collected, frozen and centralized. After thawing, several dilutions were plated onto a semi-selective agar medium. All Gram positive, catalase and PYR negative colonies were identified using the API 20 Strep system (bioMérieux) and by sodA gene sequencing.
Results: After exclusion of 9 patients (missing data), 259 cases (131 men, mean age 59.5 years, range 22–90), were analyzed. 52 patients had tumoral lesions (48 adenomas, 4 carcinomas). The SbFC rate was 4.6% (12/259). Species distribution was: *S. infantarius* subsp. *coli* (n = 9), *S. gallolyticus* subsp. *pasteurianus* (n = 2), and *S. gallolyticus* subsp. *gallolyticus* (n = 1). SbFC was more frequent in patients with history of tumor (10.5% vs. 3.0%, p = 0.03) but not in patients with current tumor (6.1% vs. 4.3, p = 0.7).
Conclusions: SbFC rate was lower than anticipated. However it was found to be higher in patients with history of colonic tumor, but not in patients with current tumor.

031

CURRENT FEATURES OF INFECTIVE ENDOCARDITIS WITH MICROBIOLOGICALLY-NEGATIVE BLOOD CULTURES

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Background: The onset of infective endocarditis (IE) is characterised by fever that often triggers the administration of empirical antibiotics. This practice may jeopardize the subsequent isolation of the causative pathogen. Blood culture-negative IE (CNIE) accounts for about 10% of cases in the largest series, but very few studies have analysed this patient subgroup. We studied the large ICE cohort to delineate risk factors, clinical features, course and outcome of CNIE.
Patients and Methods: Consecutive cases of definite IE were evaluated. Patients with CNIE were compared with culture positive IE (CPIE) cases. The statistical significance of the differences was evaluated through the chi-square or the Wilcoxon tests for categorical and continuous variables, respectively.
Results: 438 patients (9.6% of the ICE cohort) had definite CNIE. They were younger than the 4101 CPIE patients (55.1 vs 60.3 years; p < 0.0001) and more likely to be hospitalised later than one month from onset or transferred from another facility to the enrolling centre (p < 0.0001 for both). Among CNIE patients, there were more cases of prosthetic valve IE (23.9% vs 20.8% of CPIE; p = 0.015) and fewer patients with IVDU or diabetes. Clinical manifestations did not differ between the two groups except for fever, which was less often observed in CNIE patients. Blood cultures were obtained less often in CNIE patients but serologic and molecular tests were more extensively applied. CNIE more commonly involved the aortic valve (vegetations 50.6% vs 36.6%, regurgitation 45.4% vs 29%; p < 0.0001) and resulted in heart failure (44.3% vs 29.6%; p < 0.0001). Although the two groups did not differ for other major IE complications, including embolism, intracardiac abscesses and arrhythmias, higher rates of surgery were recorded in CNIE (71% vs 48%; p < 0.0001). Importantly, CNIE and CPIE had similar mortality (16.9% vs 18.6%; p = 0.413).
Conclusions: CNIE represents a major subgroup of IE despite advances in microbiological techniques. Negativity of cultures may also be linked to a longer pre-hospitalization course and greater use of antibiotics before blood cultures. CNIE more frequently involves the aortic valve and results in heart failure and valve surgery. However, it does not carry an increased mortality. Further analyses are warranted to evaluate the possible relationship between timing of antibiotics and initial blood cultures as well as individual antibiotic regimes and survival in this subgroup.

032

STREPTOCOCCUS BOVIS IN THE ITALIAN ENDOCARDITIS STUDY (SEI): COMPARISON WITH VIRIDANS GROUP STREPTOCOCCI AND ENTEROCOCCI

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Streptococcus bovis (Sb) is increasingly recognized as a cause of infective endocarditis (IE) in the mediterranean area. The clinical and epidemiological features of Sb IE have been evaluated in single center studies in Italy. The aim of this work was to evaluate the features of Sb IE in a larger cohort prospectively collected in our country. From January 2004 to December 2008, 852 cases of definite IE were enrolled in 22 Italian centers using a standard case report form. Of these, 400 were caused by streptococci/enterococci, including 178 (44.5%) viridans group streptococci (VGS) cases, 126 (31.5%) enterococci (ET) cases and 102 (25.5%) Sb cases. The clinical and epidemiological features of Sb IE were studied and compared with those of IE caused by VGS and ET spp.
The most important findings are summarized in the table.

	S. bovis	VGS	ET spp.	P value
Number of patients	102	178	126	
Age, mean ± SD	66±11.2	56.8±16.6	65±14.8	NS
Males (%)	74.5	70.7	69.8	NS
Diabetes, %	17.6	9.5	26	0.0001
Advanced cirrhosis, %	10.8	12.9	14.2	NS
Cancer, %	14.7	7.9	21.4	<0.005
Native valve IE, %	86	85.9	69	<0.05
Multivalve involvement, %	26.5	12.4	7.9	0.0001
Surgical treatment, %	50	47.8	44.4	NS
Emboli, %	34.3	24.2	22	<0.015
Vertebral discitis, %	5	5	1.6	NS
In-hospital mortality, %	5	5	17.5	0.0001

Conclusions: Patients with Sb IE, as well as ET IE, were older than patients with VGS IE. In this cohort, we did not observe an association

between Sb IE and advanced liver disease. Sb IE was more often complicated by embolic events. This may be due, at least in part, to the higher frequency of multivalvular involvement by Sb IE. In-hospital mortality was lower in Sb IE and VGS IE as compared with the ET group. Sb IE confirms to be a major cause of streptococcal, community acquired, native valve IE in Italy.

033

NOSOCOMIAL VS COMMUNITY-ACQUIRED ENTEROCOCCAL ENDOCARDITIS IN GREECE: CURRENT EPIDEMIOLOGICAL TRENDS

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Objectives: Enterococcal endocarditis has recently emerged as the leading cause of nosocomial infective endocarditis (NIE) in the Greek hospitals. Epidemiological trends of the disease are currently analyzed.
Patients and Methods: A comparative analysis between NIE and community-acquired IE (CIE) caused by enterococci was performed within a merged data base of enterococcal IE cases by the Hellenic Endocarditis study group registry (2000–2004) and new recorded cases (2004–2008) in Attikon University Hospital. Demographics, IE predisposition, susceptibility to antibiotics, IE complications, prosthetic valve IE (PVE), congestive heart failure (CHF), surgery for IE and in-hospital mortality were recorded.
Results: Forty-four cases of enterococcal IE were assessed, (NIE n = 15, 34%). There was no difference regarding age (mean + SD) for NIE (63.2 + 11.5) vs 65.4+12.5 for CIE) and gender (p = 0.2) as well as IE predisposition (p = 0.5). However, comorbidities, empirical prior to IE diagnosis administration of antibiotics and embolic events were more prominent in the NIE than in the CIE group [(86.6% vs 51.7%, p = 0.04), (80% vs 48.3%, p = 0.05), (53.3% vs 20.7%, p = 0.04) respectively]. Enterococcal IE was nosocomially acquired in half of patients with cancer. (n = 3). *E. faecalis* (n = 29), *E. faecium* (n = 3) and non-typable/other enterococci (n = 12) were distributed in both groups. Two VRE cases were recorded; one following valve surgery for staphylococcal IE. Resistance to gentamicin was detected more in NIE than in CIE cases (72.2% vs 36.4%, p = 0.07). PVE and surgery for IE did not significantly differ between NIE and CIE [(20% vs 27.5%, p = 0.5) and 20% vs 31%, p = 0.5) respectively]. Death rates (n = 10, 22.7%), were similar in NIE and CIE (p = 0.7).Overall CHF was detected in 62% of patients. However, CHF was present in 80% of patients who died (n = 8), most of them (n = 6) without surgery for IE. Reasons for no surgery were related to poor underlying conditions of those patients. On the contrary, 10 patients with CHF survived, but 90% underwent urgent valve replacement.
Conclusions: Enterococcal IE predominates males and the elderly and is quite often nosocomially acquired. Increased rates of comorbidities, antibiotic administration prior to IE diagnosis and emerging antimicrobial resistance of enterococci might be a challenge for the treatment of enterococcal NIE.

034

PREVALENCE OF GASTRO-INTESTINAL DISEASE, BOWEL CARCINOMA AND INFECTIVE ENDOCARDITIS IN A PATIENT POPULATION WITH *STREPTOCOCCUS GALLOLYTICUS* BACTERAEMIA

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The association between *Streptococcus gallolyticus* (previously *Streptococcus bovis*) bacteraemia and colonic neoplasia, gastrointestinal disease, and Infective Endocarditis (IE) is well described in small studies in the literature. Recent re-classifiction of *Streptococcus bovis* as *Streptococcus gallolyticus* and changing laboratory diagnostic methodologies may alter recognition of this important clinical association. The aim of this study was to identify the prevalence of colonic neoplasia, gastrointestinal disease and IE and the follow-up of cohort patients diagnosed with *Streptococcus gallolyticus* bacteraemia over a twelve-year period in a hospital based population in Ireland.
The Microbiology computer system was reviewed for all blood cultures reported positive for "*Streptococcus bovis*", "Group D *Streptococcus*" or "*Streptococcus gallolyticus*" from January 1st 1996 through to December 31st 2007. Cases were listed and medical notes were reviewed for the cause of bacteraemia, IE and prevalence of colonic neoplasia and gastrointestinal disease, and case follow-up was recorded.
Streptococcus gallolyticus bacteraemia was identified in 14 cases. Hepatobiliary disease was present in 5 (35%) cases. Intestinal and extra-intestinal neoplasia was present in 9 (62%) cases. Infective Endocarditis was present in 4 (28%) cases. Four of 14 (28%) cases had colonoscopy performed.
A strong association between *Streptococcus gallolyticus* and both hepatobiliary disease and carcinoma of the colon was identified in this cohort. The need for follow-up screening should be highlighted. The renaming of *Streptococcus bovis* as *Streptococcus gallolyticus* needs to be re-highlighted so that it is not "lost in translation".

035

ENTEROCOCCAL ENDOCARDITIS IN THE SOUTH OF SPAIN: A MULTICENTER IN DEPTH STUDY OF 99 CASES

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Background: There are few multicenter studies providing an in depth analysis of enterococcal endocarditis (EE).
Methods: A description of the features of the 99 cases (native: 74, prosthetic: 25) of left-sided EE of the Andalusian Cardiovascular Infections Study Group database, with emphasis on the comparison with left-sided non-enterococcal endocarditis (nEE).
Results: Enterococci produced 99 of 877 episodes of left-sided endocarditis (11%). Compared with nEE, EE was more frequently seen in patients greater than 65 years old (47% vs 28% p < 0.0005), with chronic diseases (75% vs 55% p < 0.001), calcified valves (19% vs 10% p < 0.05), previous urinary (30% vs 2% p < 0.00001) or abdominal (10% vs 3% p < 0.01) foci, and produced a higher rate of relapses (6% vs 2% p < 0.05). EE produced less peripheral vascular or skin manifestations (14% vs 27% p < 0.05) and less immunological phenomena (10% vs 24% p < 0.01).
Thirty-nine percent of patients with EE underwent valve surgery during hospitalization. Mortality during hospitalization of EE (29%) was intermediate between viridans group streptococci endocarditis (VGSE; 11%) and *Staphylococcus aureus* endocarditis (SAE; 49%)
In EE, patients treated with the combination of a penicillin or vancomycin plus an aminoglycoside (n = 78) and those treated with ampicillin plus ceftriaxone (n = 11) had the same mortality during hospitalization (25% vs 18%; p = 0.59).
High-level resistance to gentamicin was detected in 5 of 38 episodes of EE (13%).
Conclusions: EE appears with well-defined characteristics, its relapse rate is higher than in nEE, and its mortality is intermediate between VGSE and SAE. Ampicillin plus ceftriaxone combination was as effective as the combination of a penicillin or vancomycin plus aminoglycoside. High-level resistance to gentamicin is still uncommon in enterococci causing endocarditis in Spain.

036

CHANGING TRENDS IN ENTEROCOCCAL BACTERAEMIA

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Background: The incidence of enterococcal bacteraemia (EB) is increasing. We ought to appraise the incidence and clinical characteristics of EB in the current decade.
Methods: From 2001–2008, all adults with EB were included. Data on demographics, co-morbidities, severity (Charlson and Pitt scores), and clinical characteristics were obtained. Two periods were compared: 2001–2004 (P1) and 2005–2008 (P2).
Results: There were 100 EB out of 3060 (3.3%) total bacteraemias. Median age was 71.5 y (range, 21–97), 65% were males; 27% were seen in P1 and 73% in P2 (p = 0.0006, CI 0.036–0.01) that represented 2% and 4.2% of all bacteraemias, respectively. 54% were due to *E. faecalis* and 23% to *E. faecium*. EB had a community-onset (C-O) in 56% of cases, polymicrobial in 32%. Nosocomial EB was due to urinary-tract-infection (UTI) (39.5%), unknown-origin (U-O) 16.3% and 11.6% catheter-related. In C-O cases, 37% were UTI, 32% were biliary tract infection and 16% U-O. Endocarditis was diagnosed in 4% cases, all of C-O. 8% presented shock. LOS was 18 days and mortality 24%, 5/24 (21%) patients died within <72 h. Charlson score was 2.13 vs 3.38 (p = 0.027), respectively. There were no significant differences between both periods in terms of origin of EB, severity, LOS or mortality.
Conclusions: The incidence of EB has doubled in the last 4 years in our hospital. A higher presence of co-morbidities in admitted patients could probably explain this finding. Enterococcal endocarditis remains a C-O entity. EB is rarely associated with shock or severity and it presents with a high late mortality rate.

037

***STAPHYLOCOCCUS AUREUS* PROSTHETIC VALVE ENDOCARDITIS**

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Objective: To know the variables related with the mortality and the surgery impact in the staphylococcus aureus prosthetic valves (SAPE).
Methods: Multicentric cohort study of 877 left sided endocarditis from 1986 to 2007 in 7 hospital of Andalucía (South of Spain), 215 were prosthetic valve endocarditis and 25 (2.8%) were SAPE. We analyzed the variables using SPSS 13.0.
Results: 11 cases (44%) were early prosthetic valve IE. Mean age 57±12 years and Charlson index 1.76±2.2. Complications developed in 21 patients (84%): Heart failure in 17 (68%), renal failure 10 (40%), septic shock 8 (32%). The global mortality ratio was 68%.
Surgery was performed in 15 patients (60%): 13 without delay with 46% of mortality and 2 with delay (100% of mortality). Surgery was not performed in 10 patients: 7 of them for bad clinical situation (6 of them died: 85% mortality), 2 were proposed but surgery was deferred 6 month (0% death) and in 1 patient surgery wasn't considered and she was cured with antibiotics alone.
We considered heart complications like heart failure and/or heart block: When heart complications are present and surgery is performed the mortality is lower (50%) than when heart complications do not appear and sepsis is the indication for surgery (100% death).
Conclusions:

- SAPE is a aggressive entity with high complication index (84%), high mortality (68%) and high surgery prescription (88%).
- In the mortality analysis only Euroscore >9 (13.14% logistic Euroscore) was statistically significant.
- SAPE has high mortality in spite of correct decisions: Patiens without surgery for bad clinical situation and patiens with delayed surgery have higher mortality. Surgery has better results when performed for cardiac complications and worse results when it is indicated by another cause like sepsis.

038

MORTALITY PREDICTORS IN *STAPHYLOCOCCUS AUREUS* INFECTIVE ENDOCARDITIS

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Background: To describe epidemiological, clinical, echocardiocardiographic and prognostic characteristics of *Staphylococcus aureus* (SA) infective endocarditis (IE). We compared patients who died with those who survived. Mortality predictors were obtained.
Methods: We analyzed 725 consecutive episodes of IE, 169 of which were caused by *Staphyloccus aureus* (SA). They were recruited prospectively at four tertiary referral centers between 1996 and 2008. We established 2 groups: Group I (n = 64), patients died during hospitalization, and Group II (n = 105), patients who survived.
Results: Among 169 episodes of IE caused by SA, 64 (37.9%) died during hospitalization. There was no differences in sex, but age was significantly higher in Group I (57±16 vs 51±17; p = 0.011). No differences were found in previous cardiac diseases. Prosthetic valves were more frequent in Group I [21 (61.8%) vs 13 (38.2%); p = 0.002]. There were no significant differences neither in predisposing factors nor in comorbidity. Neurologic [21 (32.8%) vs 18 (17.3%); p = 0.021] and cardiologic [30 (46.9%) vs 30 (28.8%); p = 0.022] presentations were more common in Group I. At admission, a higher prevalence of heart failure, renal failure, septic shock, intracranial bleeding and confusional syndrome was observed in Group I. Echocardiographic findings of IE were found in 59 out of 64 patients (92.2%) who died during hospitalization. In Group I, the most common location of the infection was the aortic valve (22 cases). There were no significant differences neither in the prevalence of periannular complications nor in the degree of valvular dysfunction. During evolution, heart failure, cardiogenic shock, persistent signs of infection, CNS septic embolism, and renal failure were more frequent in Group I. Mortality predictors found in multivariate analysis were: septic shock (OR 7.34, 95% CI 2.91–18.50; p = 0.001), heart failure (OR 5.71, 95% CI 2.33–14.00; p = 0.001), CNS embolism (OR 3.65, 95% CI 1.29–10.35; p = 0.015), periannular complications (OR 2.79, 95% CI 1.01–7.71; p = 0.048), and age (OR 1.030, 95% CI 1.002–1.060 p = 0.035). Cardiac surgery worked as a protective factor of mortality (OR 0.110, 95% CI 0.042–0.310 p = 0.001), either emergency surgery (OR 0.12, 95% CI 0.04–0.39 p = 0.001) as well as that undertaken before the end of antibiotic therapy (OR 0.08, 95% CI 0.02–0.30 p = 0.001).
Conclusions: Heart failure, septic shock, CNS embolism, periannular complications and age were found to be prognostic.

039

RARE ETIOLOGIES IN INFECTIVE ENDOCARDITIS – REPORT FROM A 9-YEAR STUDY IN A UNIVERSITY HOSPITAL OF INFECTIOUS DISEASES

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Introduction: The etiologic diagnosis of infective endocarditis (IE) is easily made but fastidious organisms or bacterium rarely associated with IE are difficult to be diagnosed and treated.
Objectives: The aim of the study was to identify the etiology, outcome and risk factors of IE focusing on IE due to rare microorganisms.

Methods: We performed a retrospective study comprising 260 consecutive episodes of IE admitted in the University Hospital of Infectious Diseases Cluj-Napoca, Romania, during 2000–2008. The diagnosis of IE was established according to the modified Duke Criteria.
Results: The range of age was 7–89 years, median 52.5 years, male:female ratio 1.55. The etiology was established in 60% of cases: staphylococci (35%), oral streptococci (25%), *Enterococcus faecalis* (17%), Gram-negative rods (11.6%). There were 13 cases of IE caused by rare microorganisms: *Streptococcus pneumoniae* (5), *Candida parapsilosis* (2), *Streptococcus agalactiae* (2), *Globicatella sanguinis*, *Abiotrophia defectiva*, *Corynebacterium* spp., *Flavobacterium* spp. (one case each). All cases occurred in adults of more than 45 years (except one) with mitral (6), aortic (5), mitral-aortic (1) and tricuspid valve (1) involvement. Both fungal IE developed on prosthetic valves: one occurring immediately after reintervention for paraprosthetic leaks in a 69-year male, the other in a 54-year female previously treated with trimethroprin-sulfamethoxazole for *Stenotrophomonas maltophilia* IE. Both survived under antifungal therapy, surgical intervention was postponed due to complications. The five cases of pneumococcal native valve IE occurred in patients with cardiac risk factors who underwent dental procedures and/or respiratory infections. The evolution was good under medical treatment except for a 70-year female who developed embolism but survived. Unusual onset of IE due to *Corinebacterium* spp. with artery thrombosis and severe evolution (double valve destruction) requiring valve replacement was found in a 47-year male without predisposing factors. The cases due to *Abiotrophia* and *Globicatella* occurred in adult males with dental infections and previous heart disease, the evolution was marked by atrial fibrillation and heart failure. The other cases had a favorable outcome under medical treatment.
Conclusion: Unusual etiologies shoud be considered in patients with previous IE, prosthetic valves, underlying diseases having other risk factors, mainly dental procedures.

040
PROPIONIBACTERIUM ACNES PROSTHETIC VALVE ENDOCARDITIS: REPORT OF TWO CASES

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Propionibacterium acnes is an anaerobic, non-spore forming, slow-growing, gram-positive bacillus, and is often part of the normal flora of human skin. However, it can rarely cause serious infections. We describe 2 cases of P. acnes prosthetic valve IE.
Case 1. A 75-year-old man, with a mitral bioprosthesis implanted 5 years before and multiple comorbidities, was admitted in July 2007 for persistent fever. Trans-thoracic echocardiogram (TTE) showed vegetations on the mitral valve but this finding was not confirmed by the trans-esophageal echocardiogram (TEE). The blood cultures (BC) came back negative and since the patient became afebrile he was discharged home 8 days after admission. Four months later the patient was readmitted because of persistently high fever; 6 BC were drawn and piperacillin/tazobactam was empirically started. A few days later the patient was afebrile but was kept on antimicrobial treatment; 3 weeks after admission *P. acnes* grew from 3 BC. Piperacillin-tazobactam was stopped and ampicillin was started concomitantly. A repeat TTE showed vegetations on the prosthetic valve. However, surgery was not feasible because of the very poor overall clinical condition. The patient died 1 month later for multiorgan failure.
Case 2. A 53-year-old man, with an aortic mechanical prosthesis implanted 7 years earlier, was admitted with an history of high fever lasting 1 month. TTE and BC performed on admission were negative with the exception of one positive for P. acnes, originally interpreted as a contamination. A repeat TTE and TEE, performed 14 days after admission showed vegetation-like images and a partial detachment of the prosthetic valve. The patient underwent aortic valve replacement and was empirically started with vancomycin and meropenem. The histologic examination of the explanted valve was consistent with IE and the culture was positive for *P. acnes*. Vancomycin and meropenem were stopped and a 6 week course of ceftriaxone was started. The patient is currently 2 months after completing the treatment and no clinical and microbiologic evidence of relapse has been documented.
P. acnes and other slow-growing anaerobic bacteria are often considered as contaminants. In both our cases the diagnosis was late because BC were always negative when closed after the standard period of 5 days of incubation. Whenever there is a strong suspicion of IE it is mandatory to extend the BC incubation period in order to identify slow growing bacteria.

Pathogenesis

041

INFECTIVE ENDOCARDITIS ON CARDIAC RHYTHM MANAGEMENT DEVICES: PRELIMINARY STUDY ON THE POSSIBLE PATHOGENIC ROLE OF INHERITED THROMBOPHILIAS

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Background: During the last decades, growing rates of cardiac rhythm management device (CRMD) implants and, as a consequence, infections, have been observed. The pathogenesis of infective endocarditis (IE) on CRMD comprises a two-step process: 1. formation of a non-bacterial clot; 2. bacterial seeding on the clot during bacteremia. Despite high rates of spontaneous bacteremia, though, only a limited proportion of CRMD carriers develop IE. Inherited thrombophilias are common causes of thrombosis within the venous compartment but no study has evaluated the potential role of these alterations in the pathogenesis of CRMD IE.
Aim: In this study, we analyzed the prevalence of some inherited thrombophilias in a series of CRMD IE.
Patients and Controls: From Jan 2004 through Dec 2008, 245 cases of infective endocarditis were seen at our centre. 10% of IE cases were on CRMD. The index cohort for this study was therefore made of 25 CRMD IE patients. As controls, we used a large cohort of historical blood donors from the same geographical area.
Methods: All patients underwent blood cultures and echocardiography (including a transesophageal study in most cases). Blood samples were obtained under informed consent and genomic DNA was extracted with a spin-column method. DNA samples were subjected to PCR-RFLP analysis to seek for the following polymorphisms: factor V G1691A (FV Leiden), prothrombin 3′UTR G20210A, methylenetetrahydrofolate reductase C677T and platelet glycoprotein IIIa C1565T (HPA-1).
Results: Patients median age was 66 years and 72% were males. All patients showed vegetations on CRMD leads with an average maximum length of 2.3 cm. Blood cultures grew gram-positive cocci in most cases.
The allelic frequencies in CRMD IE patients and controls were as follows: FV G1691A 8% vs 2%; FII G20210A 4% vs 2%; MTHFR C677T 52% vs 44%; GPIIIa C1565T 16% vs 12%. At least one mutation was found in all cases. Two different mutations were found in 12% of cases and three different mutations in 4%.
Interpretation: These preliminary data suggest that inherited thrombophilias are common among carriers of CRMD endocarditis. Their prevalence may be higher than expected in the general population, although at present the small number of subjects studied does not allow us to draw any conclusion. Further studies are surely necessary to ascertain the potential role of inherited thrombophilias in the pathogenesis of CRMD endocarditis.

042

THE EFFECT OF STAPHYLOCOCCAL DERIVED CELL WALL COMPONENTS ON THE ENDOTHELIAL GAP JUNCTION NETWORK

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Background: Traditionally regarded as a cause of prosthetic valve endocarditis, coagulase-negative staphylococci (CoNS) are increasingly being associated with both community- and hospital-acquired native valve endocarditis. Gram-positive cell wall components such as peptidoglycan (PGN) and lipoteichoic acid (LTA) are proinflammatory and have been shown to modify connexin expression and gap-junction communication in astrocytes. Gap-junctions establish direct intercellular channels between neighbouring cells and are formed by hexagonal organization of proteins called connexins. It is unknown whether the proinflammatory milieu that ensues during CoNS infection is capable of altering gap-junction communication and expression in endothelial cells during endocarditis.
Methods: Using ELISA, ATP assay, semi-quantitative PCR analysis and western blotting, a model brain endothelial cell line (bEnd5 cells) was assessed for the effect of exposure to CoNS PGN and LTA on hemichannel and gap-junction activity.
Results: Following challenge of the cells for up to 24 h with PGN and LTA an associated increased in production of IL-6 was observed indicating an inflammatory response. Semi-quantitative PCR analysis and western blotting revealed no difference in Cx43 expression profiles or phosphorylation status following 24 h exposure. By contrast, short term exposure to PGN resulted in a rapid activation of hemichannel activity, assessed via the release of ATP into the media. This occurred within 15 minutes of exposure and could be blocked by connexin mimetic peptides, lanthanum and carbenoxolone.
Conclusions: We propose that CoNS cell wall components have a localized effect on gap-junctions and hemichannels which initiate intercellular signalling cascades that may have profound pathophysiological consequences.

043

EFFECT OF SUB-INHIBITORY CONCENTRATIONS OF ANTIBIOTIC ON THE ABILITY OF VIRIDANS GROUP STREPTOCOCCI TO BIND HUMAN PLASMINOGEN

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Background: Viridans group streptococci (VGS) are the second leading cause of infective endocarditis (IE), presenting a high level of morbidity and mortality, despite antibiotic treatment. The ability of these organisms to bind plasminogen and its subsequent activation into plasmin has been suggested as a contributing factor to the pathogenesis of streptococcal endocarditis, by increasing the proteolytic activity of the bacterial cell surface leading to a decreased stability of the vegetation and possible embolization. Penicillin and vancomycin are commonly used in the management of VGS endocarditis. Evidence suggests that the penetration of these drugs into an established vegetation may result in the exposure of the biofilm-forming cells to sub-lethal antimicrobial concentrations which can alter the expression of virulence-associated genes.
Methods: Twenty-two IE and 9 non-IE VGS isolates were examined for their ability to bind plasminogen. Determination of plasminogen binding was performed through quantification of plasmin, using the colorimetric substrate D-Val-Leu-Lys p-nitroanilide. The influence of sub-inhibitory concentrations of penicillin and vancomycin (1/8× and 1/4× MIC) on the ability to bind plasminogen was evaluated for selected strains.
Results: All members of the VGS assessed were able to bind plasminogen. Although the adhesion capability of these organisms to plasminogen appears inherent, they bind with differing affinities and independent of the initial site of isolation. Phenotypic tests demonstrated that penicillin and vancomycin at sub-MICs increased the ability of selected isolates to bind plasminogen.
Conclusion: This data suggests that the sub-optimal antimicrobial therapy may contribute to embolic events in this group of IE patients.

044

GENETIC PREDISPOSITION TO INFECTIVE ENDOCARDITIS

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Background: In view of the high prevalence of cardiac risk factors and the frequent occurrence of bacteremias, the incidence of

endocarditis is unexpectedly low. Animal studies have demonstrated that a hypocoagulable state is protective for endocarditis. Aside from abnormalities of coagulation, disturbances in pro-inflammatory conditions likely play a role in vegetation formation. The objective of this study was to determine whether genetic polymorphisms that cause a procoagulant state or provoke a proinflammatory condition in humans predispose to endocarditis.

Methods: Gene polymorphisms or polymorphic regions in the genes of factor V Leiden, prothrombin, tissue factor, interleukin-1α, interleukin-1 receptor antagonist, and fractalkine receptor (CX3CR1) were determined in patients with left-sided native valve endocarditis and compared to controls. Patients were derived from a multicenter cohort study of left-sided native valve endocarditis performed in the Netherlands. We obtained blood samples for SNP genotyping from 110 of the 123 patients that composed the endocarditis cohort, and we were able to isolate DNA from 105 of them. To determine the population frequency of alleles and genotype distribution of polymorphisms in the genes of factor V Leiden, prothrombin, TF, IL-1α, IL-1ra and CX3CR1, historic controls were used. We searched for studies in which the distribution of the selected polymorphisms were determined in Dutch or other European control subjects, and when not available, we used historic controls from outside Europe.

Results: The interleukin-1α gene allele A1 was present in 145/204 alleles (71.1%) of the patients and in 78/120 alleles (65%) of the controls, while allele A2 was present in 11/204 (5.4%) and 28/120 (23.3%), respectively ($P < 0.001$). Minor differences were observed in the genotype distribution of the tissue factor gene. The genotype distributions of the factor V Leiden, prothrombin polymorphism, interleukin-1 receptor antagonist polymorphism and fractalkine receptor polymorphisms were similar in patients and controls.

Conclusions: The association between endocarditis and interleukin-1α polymorphism may point to two mechanisms increasing the propensity to endocarditis. First, through regulation of the local pro-inflammatory and procoagulant response. Second, IL-1A polymorphism affects the severity of periodontal disease and damaged oral mucosa forms a port d'entrée for the viridans streptococci to enter the bloodstream.

In Vitro/Animal Studies

045

COMBINATION OF DAPTOMYCIN WITH AMPICILLIN PREVENTS THE EMERGENCE OF DAPTOMYCIN-RESISTANT ENTEROCOCCI IN VITRO: AN ALTERNATIVE TREATMENT FOR MULTI-RESISTANT ENTEROCOCCUS ENDOCARDITIS?

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Background: Endocarditis due to multi-resistant enterococci is a major therapeutic concern. Daptomycin (DAP) is a lipopeptide antibiotic with bactericidal activity against vancomycin-resistant (Van-R) and high-level aminoglycoside-R enterococci in vitro. DAP is currently licensed for the treatment of bacteremia and right-sided endocarditis due to *Staphylococcus aureus*. DAP, however, is not approved for *Enterococcus faecium* or Van-R enterococcal infections. Indeed, clinical failures associated with selection of resistant strains, although rare, have been described in patients with enterococcal endocarditis treated with DAP alone. One strategy to prevent resistance emergence is the use of antibiotics in combination. We evaluated the potential ability of ampicillin (AMP), gentamicin (GEN) or rifampicin (RIF) to synergize with DAP and to prevent the selection of DAP-R enterococci in vitro.
Methods: Five *E. faecalis* (4 Van-susceptible and 1 Van-R) and 5 *E. faecium* (3 Van-susceptible and 2 Van-R) were tested for antibiotic synergism by time-kill assay. Of these, two *E. faecalis* and 2 *E. faecium* were used for resistance studies. Spontaneous DAP resistance was checked by plating $\geqslant 10^8$ CFU on agar+50 mg/l calcium and increasing DAP concentrations. Bacteria were also serially exposed in broth+50 mg/l calcium to two-fold increasing concentrations of DAP alone or in combination with a fixed amount ($0.25 \times$ MIC) of the second agent for 7 days. The MIC was examined after each cycle.
Results: Baseline DAP MICs were 0.25–2 mg/l. Combining DAP with AMP or GEN acted in synergy in 70% and 100% isolates, respectively. Combining DAP with RIF was indifferent. Spontaneous DAP-R mutants (growth on >4 mg/l) on plates inoculated with 10^8 CFU were not found. On the other hand, sequential exposure of enterococci to DAP alone led to the enrichment of resistant mutants (MIC > 4 mg/l) within 3–4 cycles of exposure. Addition of AMP prevented or delayed the selection of DAP-R enterococci. Addition of GEN or RIF had no effect.
Conclusions: DAP-resistant enterococci did not emerge spontaneously and were only obtained by serial passage on the drug. Combining DAP with AMP prevented the selection of DAP-R isolates. This combination has the potential to overcome the issues encountered when DAP was used alone for the treatment of *E. faecium* or Van-R enteroccocal infections such as endocarditis. Further investigations, particularly animal studies, are needed to confirm the benefit of these findings.

046

EFFICACY OF DAPTOMYCIN IN MONOTHERAPY OR COMBINED WITH RIFAMPICIN IN A RABBIT MODEL OF EXPERIMENTAL ENDOCARDITIS DUE TO *E. FAECIUM*

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Background: Enterococci are an important cause of endocarditis. Increasing rates of resistance to antibiotics traditionally used to treat these infections, raises the need for alternative regimens. The aim of this study was to evaluate the effectiveness of daptomycin alone or in combination with rifampicin in *E. faecium* experimental endocarditis.
Methods: The rabbit model of left sided endocarditis was used. On day 2 (catheterization on day 0), animals were inoculated with a clinical strain of *E. faecium* and were randomly assigned to control (no treatment) and A (daptomycin monotherapy) and B (daptomycin plus rifampicin) treatment groups. Antibiotic regimens were initiated on day 4 and lasted for five days. On day 9, animals were sacrificed and vegetations were aseptically removed and cultured quantitatively. Sensitivity tests before inoculation revealed: Ampicillin MIC: $\geqslant$32 mg/L (R), Vancomycin $\leqslant$1 (S), Gentamicin High Level syn-S, Daptomycin =4 (S), Rifampicin 8 (R). Doses employed were: Daptomycin 14 mg/kg o.d I.V and Rifampicin 30 mg/kg o.d I.V.
Results: The study results are summarised in the table.

Treatment group	Log_{10} CFU/g, Mean$\pm$SD	No. of animals
C (Controls)	8.80$\pm$0.49	7
A (Daptomycin)	5.39$\pm$1.00	11
B (Daptomycin+Rifampicin)	4.72$\pm$1.15	9

Statistical comparisons (Mann-Whitney test): A vs C: p = 0.001; B vs C: p = 0.001; A vs B: p = 0.305.

Conclusions: In the rabbit model of left sided endocarditis due to *E. faecium* treatment with daptomycin in a dosing regimen corresponding to human 6 mg/kg/d reduced significantly bacterial vegetation counts. Adjunct of rifampicin didn't enhance the efficacy in a statistically significant manner.

047

DAPTOMYCIN IN THE TREATMENT OF EXPERIMENTAL ENDOCARDITIS (EE) DUE TO METHICILLIN-RESISTANT *STAPHYLOCOCCUS EPIDERMIDIS* (MRSE)

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Background: Daptomycin (DAP) is a lipopeptide antibiotic with potent activity against Gram positive cocci approved by the FDA for the treatment of complicated skin infections as well as *S. aureus* bacteremia and right-sided infective endocarditis. There is little information about its activity in vivo in front of MRSE infections. The aim of this study is to value the effect of DAP in therapy of MRSE aortic EE in rabbits.
Methods: 48 h after formation of catheter-induced aortic valve vegetations, an inoculum of 5×10^9 cfu/mL of MRSE (MRSE-375) strain was injected intravenously. 48 h post-infection the animals were treated for two days with DAP (6 mg/Kg iv qd) or Vancomycin (VAN) (1 g iv q12 h) given with a computer-controlled infusion pump system simulating human serum kinetics. Treated rabbits were sacrificed after 48 h of therapy.
Results: For MRSE-375 strain, DAP and VAN MIC/MBCs were 2/8; 2/32 mg/L respectively. Peak and trough levels for DAP and VAN were: 86 and 15 mg/L, and 52 and 10 mg/L respectively. Therapy with DAP was more effective than VAN in sterilizing the vegetations (9/15 [60%]) Vs. (3/16 [19%]) (p = 0.02). The reduction of density of microorganisms in this strain did not show differences between DAP or VAN (0 [0–4.1] log10 cfu/g veg Vs. 2[2–2] log10 cfu/g veg) (p = 0.17).
Conclusions: After two days of therapy, DAP showed a significantly higher effectiveness in sterilizing vegetations than VAN in the treatment of MRSE EE.

048

EXPERIMENTAL MODEL OF INFECTIVE ENDOCARDITIS (IE) ON LABORATORY ANIMALS

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Research of IE in laboratory animals (rats) was induced by injury of the aortic valve. Catheterization of carotid artery and intravenous injection of *Staphylococcus aureus* in different concentration of microorganisms was performed.

Different series were accompanied by stress and immunosuppression. The research was performed to reveal the most significant factors in IE etiology and pathogenesis. Techniques of D.Durack (1972) and V.Teplyakov and co-authors (1991) were used. IE was reproduced in 1 year-old scrub male rats.

Experiment series: first – the reproduction of noninfective endocarditis by catheterization of the carotid artery; in series 2–5 besides the catheterization, the injection of *Staphylococcus aureus* (strain ATCC6538P) in concentration 10^4, 10^6, 10^8 microorganisms in 1 ml was made. Moreover in the third series animals were subjected to immunosuppression (intravenous injection of Prednisolone in extrapolated medium therapeutic dose). In the forth series animals exposed to immobilization stress, in the fifth – cold stress. In the sixth series valve endothelium was not injured, animals received *Staphylococcus aureus* in concentration 10^9 microorganisms intramuscularly in the femoral muscle sphacelous by calcium chloride.

Animals were killed after 7–10 days of infection. Microscopic examination of aortic valve, spleen, kidneys, adrenals was performed. When blood culture and valve culture were taken out, the cultures were plated out on blood and egg-yolk-salt agar.

In the second series 2 of 15 animals developed IE; in the third – 3 of 15; in the forth – 4 of 11, spontaneous death occurred. In the fifth series there were 4 spontaneous deaths of 13 animals, IE was in 9 cases. In the sixth series 4 of 12 animal developed primary IE (without noninfective endocarditis), in addition there was hematosepsis, peritonitis, purulent pleurisy, pericarditis and spontaneous death in 6 cases. Along with *Staphylococcus aureus*, *Staphylococcus albus*, *Proteus*, *Escherichia coli* were sifted out. Thus the concentration of microorganisms along with immobilization and cold stress played the most important role in the development of experimental IE. Prednisolone immunosuppresion played a less important role.

Frail Patients

049

HOW MANAGEMENT-BASED APPROACH OF INFECTIOUS ENDOCARDITIS (IE) TREATMENT LED TO A DRAMATIC FALL IN MORTALITY

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Despite improvements in medical and surgical therapy, IE is still associated with severe prognosis and remains a diagnostic and therapeutic challenge.
Aims: To evaluate the impact of standardized diagnostic and therapeutic protocols on the outcome of IE and to correlate the outcome of IE with the compliance to our management-based protocol.
Methods: A multidisciplinary task force defined and applied a simplified protocol for IE management including a sampling strategy, the use of 4 antimicrobials only, a standardized duration of treatment, standardized surgical indications, and one year follow-up. Because our protocol was based on a local consensus by physicians and surgeons, it was impossible to randomize the study. To evaluate our protocol we performed a prospective cohort study including all patients treated for IE at our institution to compare the outcome of IE patients before and after implementation of the protocol.
Results: The study was divided in 2 periods: period 1 (1991–2001), before implementation of the therapeutic protocol and period 2 (2002–2006) after implementation of our protocol. The risk of dying at the hospital was 2.1 times higher during period 1 when 12.7% of 173 IE patients died versus 4.4% of 160 IE patients during period 2. During period 2, there was a better compliance in antimicrobial therapy, a higher rate of pacemaker ablation, and fewer cases of renal failure. Deaths by embolic events and multiple organ failure syndromes (MOFS) decreased significantly during period 2.
Conclusion: The creation of a multidisciplinary task force improved significantly the management of IE and subsequently improved the outcome of IE leading to the lowest mortality rate reported yet in literature.

050

FEATURES OF INFECTIVE ENDOCARDITIS IN PERSONS ON CHRONIC HEMODIALYSIS. RESULTS FROM THE PROSPECTIVE, OBSERVATIONAL SEI STUDY (ITALIAN STUDY ON ENDOCARDITIS)

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Background: Hemodialysis (HD) is a well known risk factor for infective endocarditis (IE). Studies focusing on the features of IE in HD patients have been limited by their descriptive nature, retrospective and monocentric design. Moreover, HDIE patient data have commonly been compared with those from heterogeneous and much larger cohorts of concurrent patients or not compared at all. Accordingly, we performed this study to assess the actual features of HDIE by comparing these patients with a matched cohort of controls enrolled within the multicenter, prospective, observational SEI study.
Patients and Methods: Among 852 definite IE patients admitted between January 2004 and December 2008 in 22 enrolling centres throughout Italy, 20 (2.3%) were on chronic HD. These patients were compared with 60 IE patients not on HD matched with a 1:3 ratio for age, sex, type of IE (native vs prosthetic) and location of infection (right vs left heart).
Results: HDIE patients had higher rates of diabetes (45% vs 20%; $p = 0.05$) and were more often on immunosuppressive drugs (25% vs 3.3%; $p = 0.01$). Previous hospitalization rates were higher for HDIE although the overall number of prior invasive procedures did not differ between groups. HDIE patients showed a higher rate of aortic valve involvement but no other distinctive clinical feature. HDIE was caused more often by staphylococci (65% vs 33%) and less often by streptococci or enterococci ($p = 0.05$). Complications such as heart failure, arrhythmias and myocardial abscesses occurred more often in HDIE patients, who also showed a higher in-hospital mortality rate (25% vs 12%; $p < 0.05$).
Conclusions: Using a matched case-control design, we found that HDIE patients have increased rates of comorbid conditions, complications and death. A large proportion of HDIE is caused by staphylococci. Reducing the incidence of IE in HD patients by correct adherence to infection control protocols seems crucial to decrease mortality in these patients.

051

INFECTIVE ENDOCARDITIS IN PATIENTS ON HEMODIALYSIS

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Background: Infective endocarditis (IE) is one of most serious infectious complications in patients submitted to hemodialysis.
Objective: To describe the epidemiological characteristics, clinical manifestations and outcome of the EI in patients submitted to hemodialysis in the Hospital Universitário Clementino Fraga Filho (HUCFF).
Methodology: Descriptive analysis of 28 consecutive episodes of IE in 28 patients submitted to hemodialysis admitted during the period between April 1978 to May 2008 in the HUCFF.
Results: Twenty-eight definitive cases of IE in patients in hemodialysis were identified from 391case of definite IE. The mean age of these patients was 45.8years (range 21–75 years); men and women were equally affected.
Severe comorbidities included chronic renal failure (100%), diabetes (14.3%), chronic liver disease (14.3%) and systemic lupus erythematosus (3.5%).
Twenty-eight patients were on long-term hemodialysis. Vascular access for hemodialysis was a short term venous catheter in 64.2% and an arteriovenous fistula in 35.7%. IE was found on native valves in 89.3% and on prosthetic valves in 10.7% of cases. Mitral valves were involved in 53.6%, aortic valves in 39.2%, tricuspid valve in 3.6% and right atrium in 3.6% of these episodes.
Blood cultures were positive in 85.7% of the cases. The causative agents were *Enterococcus faecalis* in 35.7%, *Staphylococcus aureus* in 32.1%, coagulase-negative staphylococci in 10.7%, *Pseudomonas aeruginosa* in 3.6% and *Trichosporon* sp. in 3.6%.
Valve replacement was performed in 42.9% of the cases. Intra-hospital mortality was 50%.
Conclusion: IE in patients submitted to hemodialysis is a serious complication with a high lethality.

052

INFECTIOUS ENDOCARDITIS (IE) IN PATIENTS WITH CIRRHOSIS OF THE LIVER (LC): MODEL OF INFECTION IN THE FRAIL PATIENT

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Background: IE is, more that in the past, an infection of the chronically ill, fragile patient. We hypothesized that patients with LC have a higher risk of acquiring IE within the hospital, surgery is frequently refused and have a gloomy prognosis.
Methods: Review of medical records of patients with IE complicating CL from a series of 286 consecutive cases of IE seen during 10 years. Patients with chronic hepatitis without hepatic dysfunction or portal hypertension were excluded. A control group was used for comparison

(2 per each case; the immediate preceding and immediate following a case patient were chosen).
Results: LC was found in 27 out of 286 cases of IE (9.4%). Alcoholism and virus C and B were the main causes of LC. Patients with LC were younger than controls (58.6 y vs 67.3 y). Differences in predisposing valve disease or valve involvement were not observed. Non-viridans streptococci (OR = 4.9; CI 95 1.4–16.6; $p < 0.05$) and specifically β-hemolytic streptococci (OR = 12; CI 95 1.3–109; $p < 0.05$) were causative agents of IE more frequently in patients with LC than in controls. IE was hospital-acquired in 37% of patients with LC and in 12.9% of controls (OR = 3.9; CI 95 1.3–12; $p < 0.05$). Venous cath, Foley cath, parenteral nutrition, colonoscopy, liver biopsy and Sengstaken-Blakemore balloon were the sources of nosocomial IE in patients with LC. Surgery seemed indicated in 16 cases (59.2%) and in 23 controls (42.5%). While valve replacement was attained in 19 (82.6%) of controls, it was performed in only 4 (25%) of patients with LC (OR = 0.07; CI 95 0.01–0.33; $p < 0.05$). Mortality of IE in patients with LC was significantly higher than in controls (48% vs 20%; OR = 3.6; CI 95 1.3–9.9; $p < 0.05$).
Conclusion: LC is a common underlying disease in patients with IE that is frequently caused by "virulent" microorganisms. They have a serious hazard of acquiring IE while hospitalized for invasive diagnostic and therapeutic procedures. Being considered bad surgical candidates, valve replacement is denied or refused and mortality is high.

053
INFECTIVE ENDOCARDITIS IN PATIENTS WITH CHRONIC LIVER DISEASE

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Background and Objective: Although patients with cirrhosis have an increased susceptibility for bacterial infections, endocarditis complicating cirrhosis has been reported only infrequently. To evaluate the clinical and microbiological features of infective endocarditis in patients with chronic liver disease we studied 48 episodes of endocarditis in 44 patients.
Methods: We retrospectively studied all cases of bacterial endocarditis that occurred from January 1985 to December 2006 in our hospital.
Results: 44 patients (33 males) were identified; mean age was 52.21 yr (range 23–85 yr). Bacterial organisms included *Staphylococcus aureus* (37.5%), coagulase-negative (14.6%), S. viridans (8.3%), non viridans Strep. (18.8%), *Enterococcus* (8.3%), Polymicrobial (8.3%). Child-Pugh classes were: A in 25 patients, B in 14 and C in 9. Distribution of heart valves: affected were mitral valve (14), aorta (10), both mitral and aortic valves (8), tricuspid (12), pacemakers (1) and not known (3). The overall in-hospital mortality was 33.3%. 14 patients were operated on and mortality rate in these patients was 50% (28.6%[n = 2] in class A, 100% [n = 1] in class B and 66.7%[n = 4] in class C). The rate of major complications was 77%.
Conclusions: Infective endocarditis in patients with chronic liver disease is due to *Staphylococcus aureus* in most of the cases. The global mortality is high in patients with cirrhosis although patients with Child-Pugh class A cirrhosis tolerate cardiac surgery satisfactorily. Patients with more advanced cirrhosis should be evaluated individually before being operated on.

054
CLINICAL CHARACTERISTICS AND OUTCOME OF INFECTIVE ENDOCARDITIS IN ELDERLY PATIENTS TREATED AT A SINGLE INSTITUTION IN SPAIN

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Background: Despite recent multicentric studies, it is controversial that infective endocarditis (IE) in the elderly has a worse prognosis. Some clinical, etiological, diagnostic and therapeutic issues are also in discussion.
Objectives: To evaluate the different features and prognosis of IE at a single institution in elderly patients.
Methods: We prospectively registered patients with definite criteria of IE admitted to a general teaching hospital during a ten-year period. We compared the epidemiological, clinical, echocardiographic, and microbiological data of two groups of patients: age ⩾70 years (A) and age <70 y (B).
Results: 305 episodes of IE were included: 91 (A) and 214 (B). The incidence of IE in the elderly was higher (10.1 vs 3.2/100.000 population/y). Male/female ratio was lower in older patients (1.67/2.75). In group B 82 episodes (38.3%) were in intravenous drugs users (IVDU). Group A patients significantly had more cardiovascular diseases, diabetes, cancer, urological, respiratory and neurological diseases, and less hepatobiliary illnesses. Despite this, Charlson Index in the elderly was similar to group B (2.96/3.04), though significantly higher than in non-IVDU young patients (2.40). Nosocomial (24%/15.4%) and prosthetic IE (34%/17%) were more frequent in group A. The location of IE was: mitral (36%/23%), aortic (31%/20%), tricuspid (7%/32%), and non-valvular (14.3%/12.1%). Aetiology: *S. aureus* (23%/45%); *Enterococcus* (22%/4%), *S.* coagulase-negative (14%/13%), *S. bovis* (6%/1%), and culture-negative (7.7%/7.9%). Clinical manifestations were similar except for an increased incidence of neurological symptoms in A (36%/24%). Time until diagnosis was significantly longer in the elderly (14.2/7.3), despite an increased use of transesophagic echocardiogram in this population (85%/59%). No statistically significant differences were found in the proportion of surgery indication (55%/45.6%) or in the performance of surgery (30.7%/30.3%). In-hospital mortality was higher in group A (48%/28%). Independent prognostic factors in the multivariate analysis were: nosocomial IE (OR 7.81), stroke (OR 3.57), renal failure (OR 3.19), heart failure (2.94), age older than 70 (2.61), and Charlson index (OR 1.38).
Conclusions: Nowadays IE in the elderly has become an emerging epidemic, as it once used to be in intravenous drugs users. Outcome is more adverse, only partially explained by their higher comorbidity and cumulative adverse prognostic factors.

055
INFECTIVE ENDOCARDITIS IN OCTOGENARIAN PATIENTS

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Background: The proportion of elderly people among patients with infective endocarditis has increased notably in the last decades. Accurate information on the full scope and specific features of endocarditis in the aged population is necessary. The aim of the study was to asses the specific clinical features and outcome of infective endocarditis (IE) in octogenarians as compared with younger patients.
Methods and results: 618 consecutive episodes of endocarditis were distributed in three groups of age: group I (⩽64 years): 350 episodes, group II (65–79 years): 234 episodes, group III (>79 years): 34 episodes. Episodes were recruited prospectively at four tertiary referral centers between 1996 and 2006. Octogenarians with IE were more frequently male patients with community-onset infections, mitral valve involvement, diabetes and chronic anemia. Fever and new heart murmurs were less common in this most aged population. Heart failure, when present, had a tendency to be less severe. Streptococci were the most common isolated microorganisms. Vegetation detection rate by transesophageal echocardiography was lower in octogenarians ($p < 0.002$). Octogenarians presented a shorter hospitalization length, needed surgery less frequently (group I: 58.3%, group II: 53.8%, group III: 17.6%; $p < 0.001$) and showed a lower overall mortality (group I: 24.6%, group II: 35.9%, group III: 20.6%; $p < 0.007$). Mortality

in operated patients was not higher in elderly (groups II-III) than in younger patients. Age was not a predictor of in-hospital mortality according to multivariable analysis.
Conclusions: Age per se, is not a predictor of in-hospital mortality in IE. Endocarditis in octogenarians has a more insidious and benign clinical course. The likelihood of transesophageal echocardiography for the detection of vegetations is lower in octogenarians. Surgery in elderly patients with IE is a good alternative to medical treatment.

056
INFECTIVE ENDOCARDITIS IN ELDERLY PATIENTS OVER 65 YEARS

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Introduction: Increasing medium life span and the impact of interventional medicine in individuals over 65 years is reflected in the morbidity and the etiology of infective endocarditis (IE) in this group of age.
Objectives: The evaluation of the epidemiological, bacteriologic features and the most encountered complications of IE in patients over 65 years.
Methods: From 1998 to 2008, 270 consecutive episodes of definite IE, according to modified Duke criteria, admitted in the University Hospital of Infectious Diseases Cluj-Napoca were retrospectively rewieved. We compared 62 episodes of IE in patients over 65 years with 208 IE in patients under this age. The data base and statistical analysis were done in EPIINFO6 software.
Results: Among 270 episodes of IE, 62 (23%) occurred in patients over 65 years, median 68 years (range of age 65–89 years), the sex ratio M/F was 1.3/1. A prosthetic valve IE was identified in 26% of patients over 65 years. Within the 62 cases of IE in the elderly, 34% were considered nosocomial infections. Case-fatality rate did not differ in the two subgroups (6.4% vs 6.7%). Invasive procedures or genitourinary diseases were significantly associated with IE in patients over 65 years in comparison with those of less than 65 years ($p = 0.001$, OR = 6.68, CI [2.8–16]). Other possible causes of bacteremia were gastrointestinal invasive procedures or chronic digestive diseases (11%). The etiology was dominated by Gram-positive cocci (83%): *Enterococcus* spp. 32%, staphylococci 24%, oral streptococci 17% and other streptococci 12%. We found a significant correlation between IE in patients over 65 years and enterococcal etiology ($p = 0.002$, OR = 3.68, CI [1.4–9.5]). There were no significant associations between the comparison subgroups with clinical manifestations, major complications, in-hospital mortality, the need of surgical treatment.
Conclusions: Within our IE episodes, the elderly patients represent a major subgroup and nosocomial IE was found in one third. Significant correlations were found for genitourinary invasive procedures and the enterococcal etiology. These findings are most useful in the management of IE.

057
THE FREQUENCY AND FEATURES OF INFECTIVE ENDOCARDITIS IN NEWBORN AND INFANTS WITH SEVERE SEPSIS

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Background: Patient with sepsis is the special "risk group" of development Infective Endocarditis (IE) due bacteriemia, endothelium damaging, thrombinemia, more invasive manipulation and immunological immature.
Methods: 732 case of severe sepsis: 373 patient (pts) have survived and 449 pts who was died. All child had not congenital heart disease and was in age from few days till 12 month, study period went from Jan. 1988 till Dec. 2008. Duration and kind of bacteremia was taken into account. The diagnosis of IE was strictly defined according to modified Duke criteria, in the population of patients who died, the gross morphology, histological assay and post-mortem microbiological investigation was realized.
Results: The main reasons of the death in septic patient included infective shock and multiple organ failure (MOF) and IE as a main reason of the death not once was recorded. The frequency IE in surviving from sepsis population was 0.8% (3 pts). It was acute (2 pts) and subacute (1 pt) IE; causative pathogens were *S. aureus* (2 pts), *E. faecalis* + *C. albicans* (1 pt) with multivalvular damaging. Surgical intervention in 100% was needed. In population who died IE wasn't so clear before death and was special post-mortem discovery in 7 case (1.6%).
In 5 of 7 cases there was distinct prevalence of myocardium and pericardium damaging: multiple abscess and purulent pericarditis. In all cases there was multivalvular damaging with little size of vegetations; the mitral valve was more affected, than aortal, tricuspid insufficiency was permanent. Causative pathogen of IE in this group was *S. aureus* (3 pts), *S. pyogenes* + *C. albicans* (2 pts), *P. aeruginosae* (1 pt), *P. mirabilis* (1 pt).
Conclusion: Despite our expectation due existing multiple risk factors for IE in newborn and infants with severe sepsis IE still rare disease in this population. The myocardium and pericardium involvement in inflammation sometimes more strongly vs endocardium. In surviving population IE is very severe disease with high necessity of surgeon intervention.

PM/AICD/Vascular Prosthesis Infections

058
CLINICAL CHARACTERISTICS AND OUTCOME OF A CONSECUTIVE SERIES OF PATIENTS WITH VASCULAR PROSTHESIS INFECTION: A SINGLE CENTER REPORT

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Background: The growing number of vascular prosthesis implants has been paralleled by an alarming increase of prosthesis infection rates. Besides single case reports, there are no sizeable case series describing the current etiology, clinical course and complications of vascular prosthesis infection. Moreover, many patients show severe comorbidities that preclude or make surgical removal of the prosthesis a high risk procedure. For these patients, a long-term suppressive treatment might be a valid therapeutic option. In this report, we describe our recent experience with vascular prosthesis infections.
Methods and Results: From Jan 04 to Dec 08, 11 pts with vascular prosthesis infection (7 abdominal aorta, 2 ascending aorta, 2 common iliac artery) were admitted to our referral centre for cardiovascular infections. Median age was 71 y. (37–81), all were males. The median time from implant to onset was 3 y. (0.2–21). 72% had ischemic heart disease, 18% dilated cardiomiopathy. CV risk factors were: hypertension 91%; diabetes 18%; impaired fasting glucose 27%; dyslipidemia 36%; obesity 18%.
Cultures were positive in 9 pts (81%), the infection was polymicrobial in 5. Blood cultures were positive in 90% cases. Culture of explanted material showed the same bacteremic pathogen in 75% of operated pts. Gram-positive organisms were grown in all pts, gram-negatives were also found in 4 of them, a multi-drug resistant organism in 2 cases. Diagnosis was corroborated by a positive leucocyte or PET scan in 40% and 20% of cases, respectively. Multislice CT or GI-endoscopy disclosed aorto-enteric fistulas in 4/9 intra-abdominal infections. The therapeutic approach was conservative with targeted, long-term suppressive antibiotic treatment in 6 (55%) cases, mostly due to high operative risk owing to pre-existing heart disease. None of these pts died during a median follow up of 24 mo (9–48). Antibiotics have been given for a median of 24 mo (range 6–48). Urgent/elective surgery was performed in 5 patients, 2 of whom (40%) died shortly thereafter. The other 3 patients have received antibiotics for 6 months post-operatively, and are considered cured.
Conclusions: Vascular prosthetic infections are potentially lethal illnesses believed to require prosthesis removal for cure. Our experience during the last 5 years suggests that a satisfactory outcome can be obtained with a conservative treatment in those patients who cannot tolerate surgery. In more than half of our patients, a sine die targeted antibiotic therapy was able to control the disease progression. When antibiotics fail to control sepsis or there is impending rupture of the prosthesis, the high risk surgical option seems justified. Indeed, combined medical and surgical therapy remains the only curative option.

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MICROBIOLOGICAL EPIDEMIOLOGY FROM 2000 TO 2008 OF INFECTIONS RELATED TO PACE-MAKERS (PM) AND INDWELLING CARDIAC DEFIBRILLATOR (ICD) OBSERVED IN 628 ITALIAN PATIENTS

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Background: The Cardiology Unit at Cisanello Hospital in Pisa is the Italian reference centre for non invasive, transvenous removal of PM or ICD. The aim of the study is to review microbiological findings of PM and ICD infections observed at this Unit in 8 years period (2000–2008).
Materials and Methods: Retrospective observational study on consecutive patients. All patients with clinically documented PM or ICD infections were enrolled in the study to define the aetiology of the infections. Catheter leads and/or the infected material from the pocket upon removal were cultured in aerobic and anaerobic media.
Results: In the study period PM and ICD leads and generators were removed transvenously from 843 patients. Positive microbiological results were obtained from 628 patients (74.4%) and 807 different microorganisms were isolated due to polymicrobial infections; therefore we had negative culture in 215 patients. Staphylococci were the most frequently isolated pathogens (676/807, 83.7%). The coagulase-negative staphylococci (CNS) resulted the first pathogen (550) followed by *S. aureus* (126), methicillin-resistant (MR) strains, among staphylococci, were 190/676 (28%), MR strains were almost all CNS and the rate of MR were stable over time. Gram negative rods and fungi are relatively rare. Other microorganism such as *Propionibacterium* spp., enterococci and *Corynebacterium* spp. are relatively rare. Overall susceptibility were also studied; the classes of antibiotic with good activity were newer quinolones (moxifloxacin and levofloxacin) followed by aminoglycosides and glycopeptides.

Table 1: overall results of the study

	Years					
	2000–2001	2002–2003	2004–2005	2006–2007	2008	Total
Patients	121	228	263	219	101	843
Microorganisms	132	180	248	177	70	807
CNS	93 (70%)	117 (66%)	170 (69%)	116 (65%)	54 (77%)	550 (68%)
S. aureus	19 (15%)	35 (20%)	40 (16%)	23 (13%)	9 (13%)	126 (16%)
Gram negative	16 (12%)	14 (7%)	5 (2%)	17 (10%)	4 (6%)	56 (7%)
Yeast/mold	–	4 (2%)	7 (3%)	4 (2%)	–	15 (2%)
Other	4 (3%)	10 (5%)	26 (10%)	17 (10%)	3 (4%)	60 (7%)

Conclusions: In our experience PM and ICD infections were mainly caused by staphylococci, especially CNS, other microorganisms (Gram-negative rods, other Gram-positive and fungi) were also documented in few cases. The epidemiology of PM/ICD infections are stable over time. The knowledge of the epidemiology of these infections and the susceptibility to antibiotics might be useful for clinicians to start an adequate empiric antibiotic therapy.

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TRICHOSPORON BEIGELII PACEMAKER (PM) INFECTIVE ENDOCARDITIS (IE) WITH FATAL OUTCOME

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Background: *Trichosporon* IE has been reported since the 1990's, mainly in association with valve prosthesis. We describe the 1st case of *Trichosporon* IE related to a PM.
Methods- Case report: A 68-year-old female, with a 6 year old PM, presented progressive dyspnoea, non-productive cough, daily fever, malaise and diarrhea 1 week before admission. She referred pneumonia 3 months previously, and had had intermittent fevers since. She had fever (38–40°C), heart rate, 64 bpm; blood pressure, 158/49 mmHg. Lab tests showed haemoglobin of 9.9 mg/dl, platelet count of 61,000/mm^3, 18,790 WBC, 24% band forms. Chest radiograph showed alveolar infiltrate on the right lung base. TTE showed a vegetation attached to the PM lead measuring 4.5 cm × 2.5 cm.

Peripheral blood cultures (BC) were drawn and therapy was started with vancomycin (V) 2 g/day, fluconazol (F) 400 mg/day and oral rifampin (R) 600 mg/day. After 2 days, 2 of 4 BC showed yeasts. After 5 days treatment, she was still febrile and had leukocytosis. V and R were stopped, F dose was increased. BC collected 5 days after the 1st sets were positive; F was changed to amphotericin. Platelets fell to 26,000. On day 12 of admission she presented cardiac arrest, presumably due to massive pulmonary embolism. The yeast was identified as *T. beigelii*.

Conclusion: This patient is the first case of *Trichosporon* PM IE. Unfortunately, her surgery was delayed due to lack of platelets and she died the day prior to the scheduled PM removal.

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GHOST OF INFECTED LEADS: A NEW CRITRION OF CARDIAC DEVICE-RELATED INFECTIVE ENDOCARDITIS

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Background: CDE is a rare but serious complication of permanent pacemakers (PPM) and implantable cardiovertor defibrillators (ICD). Its diagnosis is difficult and mainly based on data collected before material removal.

Objectives: We sought to determine the incidence, the diagnostic value and the outcome of an intracardiac mass sometimes detected by echocardiogaphy after removal of PPM and ICD. We hypothesized that these "ghosts" of leads could be associated with the diagnosis of cardiac device-related infective endocarditis (CDE).

Methods: The preoperative clinical, microbiological and echocardiographic conditions, the indication and the type of removal technique were analysed in a retrospective cohort including all consecutive patients who underwent percutaneous lead removal. Three groups were formed according to the final diagnosis: CDE, local device infection (LDI), and other indications. Incidence of ghost was compared between the three groups. All predefined clinical and technical factors were studied for their association with ghosts. All patients who had a ghost underwent a clinical and echocardiographic follow-up.

Results: Four hundred and fifty-six leads were removed from 212 patients (88 for CDE, 59 for LDI, and 65 for other indications) Ghosts were noticed in 17 patients with a global incidence of 8%. A significant association was found with CDE compared to other diagnosis (OR = 7.63, 95% CI, 2.12–27.45, p = 0.001). At three months, 2 patients died because of a sudden death, 2 underwent surgery and one had a pulmonary embolism.

Conclusions: Ghost is a post operative entity that might help to diagnose CDE but which can be complicated by sudden death and pulmonary embolism.

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TRANSVENOUS PACEMAKER LEAD REMOVAL IN PATIENTS WITH PACEMAKER INFECTIVE ENDOCARDITIS

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Background: The aim of this study was to investigate whether transvenous lead removal is safe and effective in patients with pacemaker or defibrillators leads endocarditis.

Methods: From 1989 to 2008, a total of 50 patients underwent pacemaker or ICD lead removal for endocarditis. We removed percutaneously 94 leads in these patients. Transvenous lead removal was performed in all of them and was found to be effective in 47 (92.2%). In 16 of these patients, transesophageal echocardiography (TEE) verified vegetations greater than 1 cm in size ranging from 0.5 to 5.7 cm.

Results: The interval from the lead implantation to diagnosis of endocarditis was 76.18 SD 61.55 months (range 0.23 to 242.89). Endocarditis appeared after pacemaker implantation, early (<1 year) in 13 patients and late (⩾1 year) in 27 patients. Perioperative mortality was 6% (3 patients); all of them underwent primary ECC removal had severe endocarditis and died after long treatment because of severe sepsis. 1 patient with large vegetation had major pulmonary embolism requiring sternotomy and cardiopulmonary bypass with good result. The major pathogens causing pacemaker endocarditis were *Staphylococcus epidermidis* (n = 22) and *S. aureus* (n = 19). All patients were treated with prolonged antibiotic regimens before and after electrode removal with a mean of 26.67 days (SD 8.05) after removal.

Conclusions: This study demonstrates that transvenous lead removal is a safe and highly effective procedure for the removal of infected pacemaker and ICD leads, even in patients with large vegetations.

Diagnosis: Micro

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MOLECULAR DIAGNOSIS OF INFECTIVE ENDOCARDITIS (IE) BY REAL-TIME BROAD-RANGE POLYMERASE CHAIN REACTION (PCR)

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Background: Microbiological diagnosis of infective endocarditis is somewhat difficult in patients with negative blood cultures due to either prior antimicrobial therapy or the presence of difficult-to-culture microorganisms.
Objective: To evaluate the utility of a new diagnostic technique for the diagnosis of IE.
Methods: Seventeen valves (13 natives and 4 prosthetic) from patients with definite/possible IE operated in three hospitals of our group were analyzed. Real-time broad-range PCR of a sample from each case was performed in a reference center and histological studies and conventional cultures were done in each hospital. We included as controls five samples (3 natives and 2 prosthetic valves) from patients undergoing valve replacement because of valvular dysfunction without IE.
Results: PCR was negative in all controls, although in one sample tissue culture was positive (contaminant microorganism). In 10 patients with repeated positive blood cultures and diagnostic echocardiography, PCR was positive according with isolated blood specimens although tissue cultures were always negative. Five samples from other patients with diagnostic echocardiography but negative blood cultures had positive PCR to different microorganisms that were considered the etiologic agents of IE, and histological examination was characteristic of IE. Finally, two patients with negative blood cultures and non diagnostic echocardiography rendered a negative PCR with negative histological studies, although prolonged valve culture was positive to microorganisms that were finally judged as contaminants.
Conclusions: Universal real-time PCR is a sensitive and specific tool in the etiological diagnosis of patients with IE and cardiac surgery.

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EVALUATION OF REAL-TIME BROAD RANGE PCR ASSAY FOR RAPID DETECTION OF EUBACTERIAL 16S RRNA IN HEART VALVE TISSUE

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Background: Prompt and accurate detection of causative agent of infective endocarditis (IE) is essential for patients' treatment. Unlike identification of bacteria by culture that may take several days and may be influenced by antibiotic therapy, results of 16S rRNA real-time PCR followed by direct sequencing are available within 24 hours. The aim of this study was to develop fast, sensitive and efficient molecular diagnostic tool for universal detection of wide range of bacteria.
Methods: Bacterial DNA was extracted from 46 samples of human heart valve tissue using lysozyme, lysostaphine and proteinase K pretreatment and QIAamp DNA Blood Mini Kit (Qiagen). PCR reagents were decontaminated by 8-Methoxypsoralen in combination with ultraviolet A radiation to eliminate background bacterial DNA. A noncompetitive internal amplification control was designed and coamplified simultaneously with the target 16S rRNA sequence to overcome false negative results. Sensitivity was determined by performing real-time PCR reactions with ten fold dilution series of plasmid DNA in buffer in triplicates. The limit for a detectable concentration was a cycle treshold (CT) value of 3 CT lower than the mean CT value from the control of isolation process.
Results: Negative controls and controls of PCR preparation remained negative approving successful decontamination. Efficiency of PCR was 81% with dynamic range from 1.10^2 to 1.10^8 copies in buffer per reaction. Positive and negative results were shown in 39 and 7 samples, respectively, which was in 100% concordance with results of a routinely used conventional broad-range PCR.
Conclusions: Broad-range real-time PCR followed by direct sequencing allowed us to detect a wide range of bacterial species and showed the detection limit of 1.10^2 copies per reaction. In comparison with the conventional broad-range PCR it was faster, less laborious and avoiding ethidium bromide agarose gels staining, while a sensitivity was kept at least the same. A validation of this method for detection of IE pathogens in blood is going to be our next step.

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COMPARATIVE STUDY OF TWO BLOOD CULTURE SYSTEMS: BACTEC™ VERSUS BACT/ALERT® 3D – AN EXPERIENCE OF THE MICROBIOLOGIC LABORATORY OF EAST TALLINN CENTRAL HOSPITAL, ESTONIA

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Background: The detection and identification of microorganisms in a patient's blood is essential in the diagnosis and treatment of the etiologic agents of sepsis, septic endocarditis and other septic conditions with unknown aetiology, remaining an important function of the microbiology laboratory. Due to increased number of incoming blood cultures the laboratory had to expand the possibilities of blood culturing and to replace available BACTEC™ devices with more capacious BacT/ALERT® 3D systems. Having some experience in working with both diagnostic systems we decided to compare them on sensitivity indicators. Two blood culture systems were evaluated: BACTEC™ 9050 (BD Diagnostics) and BacT/ALERT® 3D (bioMerieux).
The **aim** of the study was to compare two blood culture systems on sensitivity indicators and reveal differences in their ability to recover the significant isolates from the blood samples. The following indicators were calculated during the 9 month time interval: number of total blood sets, number of positive sets, time of detecting of positive signals separately for different media, bacterial spectrum of isolates and contamination rate.
Results: During the period of study the number of blood samples, positivity rate and the spectrum of isolated microorganisms was similar. However, study revealed significant advantage of anaerobic media over aerobic in positivity rate during first 8 hours of incubation in both systems. The comparison revealed the difference in contamination rate and in positivity during first 24 hours between systems, especially in context of prevalent isolates. Also, study showed evident difference in growth of aerobic microorganisms in aerobic and anaerobic media for both systems. Moreover, the differences in growth of fungi in aerobic and mycotic media between investigated systems were revealed.
Conclusions: Both methods have evident advantages and imperfections and comply with the needs of clinical microbiologic laboratory, but following comparative studies are needed.

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THE ROLE OF THE MICROBIOLOGY DEPARTMENT IN THE ALERT FOR DETECTION OF INFECTIVE ENDOCARDITIS (IE)

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Introduction: Early recognition of IE is improved if physicians of different specialities work together in a coordinated way and alert each other in certain situations that predispose or suggest IE. The contribution of the Microbiology laboratory to such alerting system has not been studied.

Objective: Measure the contribution of the Microbiology Department to the list of suspected cases of IE. Assess the yield of transesophageal Echocardiography (TEE) requested systematically in patients with bloodstream infections (BSI) caused by certain microorganisms.

Material and Methods: The GAME study group may respond to echocardiographic, clinical or microbiological alerts. A microbiological alert is activated when the Microbiology department detects a BSI with *S. aureus*, *Streptococcus* spp., *Enterococcus* spp., CNS in patients with endovascular prosthetic material, HACEK or *Candida* spp. This information is transmitted to a specialized nurse and physician who evaluates the clinical condition of the patient, assess the presence of risk factors for IE and recommend and facilitate the echocardiography request.

Results: During the two years of the study (2007–2008), IE was suspected in 1291 patients (alerts). Of them, 1121 (86.3%) had an origin in the Microbiology Department due to BSI caused by: *S. aureus* (317; 28%), CNS (347; 31%), *Enterococcus* spp. (219; 19.5%), *Streptococcus* spp. (128; 11.4%), *Candida* spp. (103; 9%) and 7 others. There were 94 polymicrobial infections (8%). An echocardiogram was finally performed in 667 patients (59.5%) and was transesophageal in 314 (47%). Microbiological alert confirmed 64 IE episodes (73.5% our 87 cases). The efficacy of TTE and TEE in microbiological alerts was 7%/29% for *S. aureus*, 2%/5% for CNS, 6%/21% for *Enterococcus* spp., 8%/19% for *Streptococcus* spp. and 7%/26% for *Candida* spp. BSIs.

Conclusions: Microbiology Departments may contribute very substantially to the alerts of IE and certain BSIs are good surrogate markers for it. TEE when feasible, has a relatively high yield in patients with BSI caused by certain microorganisms.

Diagnosis: Echo

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EVALUATION OF THE SYSTOLIC HEART MURMUR IN A ROUTINE PEDIATRIC EXAMINATION

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Background: 20–40% of asymptomatic children are diagnosed with heart murmur. The aim of this study is the investigation of the heart murmur, diagnosed in a typical pediatric examination.
Methods: 216 children were examined, 112 boys (56%) and 104 girls (48%), 1 month – 17 years old (average age 8.1±4.1 years old). All of the children underwent a clinical examination, electrocardiogram, chest X-RAY and sonograph 2D + colored Doppler by a pediatrician-cardiologist.
Results: 10 (4.6%) of the children of our study were diagnosed with anatomic or functional heart failure: (a) 2 with slight aorta deficiency, (b) 2 with ventricular septal defect, (c) 2 with left cardiac hypertrophy (athletes), (d) 2 with slight mitral valve prolapse, no deficiency, (e) 1 with "silent Botallo" treated with occlusion with the "umbrella" technique, (f) 1 with slight pulmonary stenosis. These children were diagnosed: (a) with cardiomegaly (2 of them with ventricular septal defect), as it was shown by the chest X-RAY, (b) with left ventricular hypertrophy (4 of them with ventricular septal defect and left ventricular hypertrophy), as it was shown by the electrocardiogram. Chest X-RAY and electrocardiogram was normal for the rest of the children (6/10). 206 children (95.4%) had normal chest X-RAYS, electrocardiogram and sonograph.
Conclusions: The 1st–2nd degree systolic heart murmur diagnosed in a typical pediatric examination in asymptomatic children, with normal electrocardiogram and chest X-RAY, is in percentage >95% an "innocent" heart murmur.

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TRANSTHORACIC ECHOCARDIOGRAPHY FOR THE DIAGNOSIS OF INFECTIVE ENDOCARDITIS

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Background: In the 1990's the medical literature has reported the major sensitivity of transesophageal echocardiography (TEE) compared with transthoracic echocardiography (TTE), while both the techniques have a high specificity. Important technical improvements have raised the quality of TTE images, a easier and less invasive diagnostic exam to be performed.
Aim: To evaluate the diagnostic utility of high quality TTE compared with TEE in the contemporary real clinical practice.
Methods: Italian registry of IE (RIEI) prospectively collects data on new cases of IE in Italy, by an Internet accessible database. Sixteen centres are participating, and variables are related to epidemiological, clinical, instrumental, prognostic, and therapeutic aspects of IE (1). Cases are consecutively enrolled. The quality and reliability of data are controlled by a central operator. Among the collected variables, data are available on TTE and TEE and the echo exam that was initially diagnostic.
Results: Data are available on 267 patients with a definite IE (mean age 60±15 years, 152 males). The following echo exams have been performed: 252 TTE, 187 TEE. TTE has been performed in 68 cases of the available 246 dates (28%) before the admission, in 45 cases (18%) on the day of admission, and during hospitalization in the remaining 133 cases (54%) after 7±12 days.
TEE has been performed in 33 cases (18%) before the admission, in 20 cases (11%) on the day of admission, and during hospitalization in the remaining 132 cases (71%) after 11±14 days. TEE is performed less than TTE before the admission ($p = 0.021$), more during admission ($0 = 0.0001$), and significantly later ($P = 0.01$; $t = -2.518$).
TTE had a diagnostic sensitivity of 58% (70% with native valve), 21% were uncertain, 19% negative. TEE had a diagnostic sensitivity of 94%, 4% were uncertain, 2% negative. TTE was diagnostic in 58% of cases, while TEE was diagnostic in the remaining 42% of cases.
Conclusions: In the real world good quality TTE has a relevant role for the first diagnostic evaluation of IE, being easily available, with a good diagnostic sensitivity. TEE has a wide use, is done later to increase diagnostic sensitivity, especially with prosthetic valves, devices, and when there is a suspicion of complications.

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COMPUTED TOMOGRAPHY AS A TOOL FOR DIAGNOSING AORTIC ROOT ABSCESS IN PROSTHETIC VALVE ENDOCARDITIS. A CASE REPORT

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Introduction: Development of a valve ring abscess is a serious complication of infective endocarditis and often difficult to diagnose, especially in presence of a prosthetic valve. Recent development of a multidetector ECG-triggered myocardial CT scan might offer new possibilities to establish an abscess diagnosis. Here we present a case where transesophageal echocardiography (TEE) showed no signs of aortic root abscess, whereas an abscess was visible using multidetector computed tomography (MDCT).
Case description: A 59-year-old man with a bioprosthetic aortic valve since six years was admitted with several days of fever. He had a history of progressive renal failure and had been treated with hemodialysis since four months.
Multiple blood cultures were positive for *Staphylococcus aureus*. Initial TEE showed no signs of vegetation or abscess. Three days later a new TEE revealed vegetations on the bioprosthetic aortic valve, but no signs of aortic root abscess. However, MDCT performed the same day demonstrated contrast leakage into a mass, measuring approximately 1 cm in diameter, just below the aortic valve suggestive of aortic root abscess. The leakage was visible exclusively in the systolic phase. The patient was accepted for surgery the same day, where a valvular ring abscess was clearly visible around the bioprosthetic aortic valve confirming the radiological finds.
Discussion: TEE is the tool of choice today to diagnose complications of infective endocarditis but unspecific findings, as thickening of the aortic root, occurs frequently. There is a need for better imaging modalities in order to diagnose abscesses associated with endocarditis. MDCT may prove to be a useful complement.

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DEVELOPMENT OF CRITERIA FOR THE INDICATION OF TRANSESOPHAGEAL ECHOCARDIOGRAPHY IN *STAPHYLOCOCCUS AUREUS* BACTEREMIA

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Background: Infective endocarditis (IE) represents a severe complication in patients with *Staphylococcus aureus* bacteremia (SAB) and is associated with a poor outcome. Therefore it has been suggested that transesophageal echocardiography (TEE) needs to be performed in every patient with SAB. However, in some clinical scenarios IE is unlikely to occur, but rules where echocardiography is dispensable are lacking.
Methods: Included in this study were 406 consecutive patients with SAB enrolled in the prospective INSTINCT study from January 2006 to December 2008 at the Cologne and Freiburg University hospitals. Patients with and without endocarditis were analyzed for predisposing factors, clinical features, diagnostic measures, and outcome. The diagnosis of IE was based on the Duke criteria and patients were followed closely for the development of IE during a 3 months follow-up period. Criteria for performing TEE were defined as: community acquired SAB, prosthetic heart valve, vascular implant, hemodialysis, injection drug use, prolonged bacteremia (>3 days), spondylodiscitis, and osteomyelitis. The suitability of the criteria set was assessed retrospectively.
Results: In 10.3% (42) of patients with SAB, a diagnosis of IE was made during hospitalization. Further two patients (0.5%) developed IE during the follow-up period, both patients had community-acquired SAB but TEE performed during hospitalization was unremarkable. The mitral valve (41%) and aortic valve (38%) were most commonly affected; 14% of cases were prosthetic valve infections. Of all patients with SAB, 290 (71%) fulfilled one or more criteria for echocardiography, mainly community acquisition (49%), prolonged bacteremia (41%), occurrence of a vascular implant (14%) and hemodialysis (8%). All patients with a final diagnosis of *S. aureus* IE fulfilled at least one criterion for performing TEE (sensitivity: 100%). Among patients not fulfilling any of the criteria for performing TEE, none developed IE during hospitalization and follow-up (negative predictive value: 100%). The positive predictive value of TEE increased from 10.3% to 14.4% when using the criteria set. Thus the number of echocardiographic evaluations could be safely decreased by about 30%.
Conclusion: We developed a simple criteria set for patients with *S. aureus* bacteremia, that allows to safely reduce the number of echocardiographic evaluations for infective endocarditis by about 30%.

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SIZE OF VEGETATIONS AND RELATION TO EMBOLIC EVENTS, MANAGEMENT AND OUTCOME IN INFECTIVE ENDOCARDITIS. THE COPENHAGEN EXPERIENCE

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Background: Size and mobility of vegetations are known risk factors of embolic events in infective endocarditis (IE). The present study investigated the prognostic impact of size ad mobility of vegetations risk of embolic events prior to admission, need for surgery and in-hospital mortality in Denmark.
Methods: Consecutive patients admitted for IE in two Copenhagen tertiary centres from 2002 to 2008 with left heart valve IE were studied, N = 375. Vegetation size was measured as maximal length. Data is presented as median (25th and 75th percentile) or number (%), differences tested by t-test, χ2-test or logistic regression.
Results: Patients studied were 64 (56–75) years of age and 108 (31%) were female. IE was associated with the aortic valve in 190 (51%), the mitral valve in 127 (34%) or both in 58 (15%), vegetation were present in 261 (70%) of which 131 (50%) were highly mobile. An abscess was diagnosed in 35 (10%) and prosthetic valve IE was found in 95 (25%).
Embolic events at time of admission were diagnosed in 111 (30%) of the patients, and were more common in patients with *Staphylococcus aureus* (SA) IE [OR = 2.8 (1.4–5.3)]: Vegetation size or mobility were not related to presence of embolic events, OR = 1.0, p = 0.92 and OR = 1.1, p = 0.71, respectively. IE affecting the mitral valve tended to be associated with increased risk of emboli [OR = 1.4 (0.8–2.7)].
Surgical management of IE was performed in 204 patients (55%), and were more prevalent in patients with larger vegetation size [OR = 1.05 (1.00–1.10) per mm], native valve IE [OR = 6.1 (2.7–14)], abscess [OR = 5.4 (1.7–17)], SA IE [OR = 3.0 (1.4–6.4)] and younger age [OR = 1.26 (1.13–1.41)]. Mobility of the vegetation was not associated with surgical management of IE.
Fifty-eight patients (16%) died during admission, and in-hospital mortality was associated with vegetation size [OR = 1.09 (1.03–1.16) per mm], embolic event [OR = 3.7 (1.6–8.5)], increasing age [OR = 1.4 (1.1–1.6) per 5 years] and SA IE [OR = 2.8 (1.1–1.6)]. A trend towards increased mortality was seen in patients with mobile vegetations [OR = 1.9 (0.8–4.3)]. Mortality in native and prosthetic valve IE was not different.
Conclusions: Vegetation length was not associated with embolic events in the present population, but as in most clinical situations echocardiography was performed after the embolic events had occurred. However, vegetation size was a significant predictor of need for surgery and increased in-hospital mortality.

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VEGETATION LENGTH OR AREA: WHICH IS THE BETTER PREDICTOR OF OUTCOME IN INFECTIVE ENDOCARDITIS?

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Background: Vegetations in infective endocarditis (IE) are complex structures, but are frequently described by its maximal length only. The present study compared the predictive power of measuring of vegetations by length or area with regards to risk of embolic events, need for surgery and in-hospital mortality.
Methods: Consecutive patients admitted for IE in two Copenhagen tertiary centres from 2002 to 2008 with left heart valve IE were studied, N = 375. Size of vegetation is presented as maximal length or area (length $\times$ width). Data is presented as median (25th and 75th percentile) or number (%), differences tested by t-test, χ2-test or logistic regression. Predictive information by c-statistics (area under the curve, AUC) was compared.
Results: Patients studied were 64 (56–75) years of age, 108 (31%) were female and 95 (25%) had prosthetic valve IE (PVE). Site of IE was the aortic valve in 190 (51%), the mitral valve in 127 (34%) or both in 58 (15%). An abscess was diagnosed in 35 (10%). A vegetation was present in 261 (70%) of which 131 (50%) were highly mobile.
Vegetation length was 7 (4–11) mm and area was 25 (9–63) mm^2. Predictors (multivariable model including all parameters mentioned above) of increasing vegetation length were mitral valve IE (β = 2.3 mm, p = 0.01 compared to aortic), native valve IE (β = 2.9 mm, p = 0.004) and mobile vegetation (β = 1.7 mm, p = 0.04), combined R^2 = 0.10. Similar associations were seen for vegetation area (R^2 = 0.08).
Embolic events at time of admission were present in 111 (30%). Multivariable model yielded an AUC = 0.65 for vegetation length, no different from the fit by vegetation area, AUC = 0.64, difference in AUC: p = not significant (NS).
Surgical management of IE was performed in 204 patients (55%) and multivariable modelling including vegetation length showed an AUC = 0.79, while vegetation area performed better, AUC = 0.81, p = 0.02.

In-hospital mortality was 58 (16%) and multivariable modelling showed a AUC = 0.82 using vegetation length and AUC = 0.83 using vegetation area, p = 0.70.
Conclusions: Size of vegetation in IE may be more appropriately reported by area than by length only. The improved predictive power with regards to need for surgical management and in-hospital mortality is small, however, and likely to be of minor clinical importance.

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CLINICAL AND MICROBIOLOGICAL FEATURES OF MULTIVALVULAR INFECTIVE ENDOCARDITIS

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Background and aim of the study: Infective endocarditis (IE) sometimes affects more than one valve and is then considered to be a threatening disease. Our study aimed to assess the clinical and bacteriological features of multivalvular IE.
Methods: Over a 11-year period, 377 consecutive pts were admitted for treatment of IE to our institution which is both a primary and a tertiary referral center. Among them, 300 pts presented with definite IE according to the Duke University criteria and had a precisely identified site of infection. The 42 pts (14%) with multivalvular location (group 1, 31M/11F, 58±16 yrs) were compared to the 258 with monovalvular lesions (group 2, 178M/80F 58±14 yrs, ns for sex and age).
Results: Multivalvular location included both left heart valves in 31 pts, one left and tricuspid valve in 7 and 3 valves in 4 pts. Group 1 pts had less frequently a preexisting heart disease (native valve disease 36% vs 46%, prosthetic valve disease 9% vs 21%, p < 0.02). They had more often at least one extracardiac manifestation (81% vs 61%, p < 0.02) with a trend toward a higher rate of embolic events (43% vs 34%, ns). General distribution of causative micro-organisms differed significantly between both groups with a high rate of streptococcal and a low rate of staphylococcal IE in group 1 pts (staph: 14% vs 34%, strepto: 69% vs 47%, other microorganisms: 12% vs 7%, negative blood culture: 5% vs 12%, p = 0.01). Among streptococci, group D were more frequent in group 1 pts (70% vs 47%) than viridans (22% vs 38%) or other streptococci (7% vs 15%) (p = 0.08). Digestive portal of entry was found more often in group 1 patients (31% vs 16%, p = 0.03). Echocardiography demonstrated vegetation in 95% of group 1 pts vs 84% in gr 2 (p = 0.05), an abscess in 21% vs 14% (ns) and a significant regurgitation in 83% vs 56% (p = 0.002). Group 1 patients were more often operated on during the initial hospital stay (72 vs 51%, p = 0.01) with a shorter delay from diagnosis (15±13 vs 23±22 days, p = 0.07). They had a non significant higher mortality (26% vs 20%). Length of hospital stay was similar in the two groups (59±31 vs 62±32 days).
Conclusion: Multivalvular IE occur frequently in pts without preexisting heart disease infected by digestive streptococci. They result in more severe hemodynamic damage and require more often surgical therapy.

Complications

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RHEUMATOLOGIC ASPECTS OF INFECTIOUS ENDOCARDITIS

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Background: Unsatisfactory results of infectious endocarditis (IE) treatment are often determined by late diagnosis. Clinical polymorphism of the disease and development of immunopathologic features require differentiation with different diseases including wide spectrum of rheumatic ones.
Methods: Complex examination and treatment of 50 patients with IE hospitalized in the Institute of Rheumatology was performed. There were 26 male and 24 female aged 16 to 68 years (mean age 41.4±14.8 years). Primary IE was diagnosed in 30%, secondary IE – in 70% of patients. Hemoculture was positive in 48% of cases.
Results. 44 from 50 of patients had different laboratory immune disturbances. Rheumatoid factor (72%), circulating immune complexes (59.2%), hypergammaglobulinemia (58%) and anti-DNA antibodies (57%) were the most frequent of them. Cryoglobulinemia (44%) and antinuclear factor (35%) were less frequent. 88% of patients with IE had clinical immunopathologic signs including musculoskeletal pathology (60%), urinary changes (30%), nephritis (28%), vasculitis (18%), myocarditis (12%), pleuritis (8%). Musculoskeletal pathology included arthralgia (38%), arthritis (20%), tendonitis and enthesitis (18%), myalgia (14%), back pain (12%). Nephritis was significantly more prevalent in patients older than 50 years of age ($p = 0.03$). It was associated with cryoglobulinemia ($p = 0.04$), antinuclear factor ($p = 0.04$), high level of rheumatoid factor ($p = 0.03$) and staphylococcal etiology of IE ($p = 0.04$). Circulating immune complexes elevation was significantly more frequent in patients with vasculitis ($p = 0.007$). Musculoskeletal pathology, myocarditis, pericarditis and pleuritis were not associated with laboratory signs of immunopathology.
Conclusion: In case of IE suspicion additional examination should be performed aimed to early disclosure of immunopathologic features.

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VERTEBRAL OSTEOMYELITIS AND INFECTIVE ENDOCARDITIS (IE): INCIDENCE, RISK FACTORS AND OUTCOME IN SEVEN YEARS PROSPECTIVE STUDY

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The relationship between vertebral osteomyelitis and IE is uncertain, nevertheless it has been known that endocarditis may be source of pyogenic osteomyelitis more frequently than it has believed. We investigated the incidence, risk factors, clinical and therapeutic finding in patients with IE and concomitant spondylodiscitis.
In a seven years prospective study we analyzed 81 patients with clinical, radiological and microbiological evidence of pyogenic vertebral osteomyelitis: spondylodiscitis developed after spinal surgery in 27 patients (33.3%) (POS), in 16 patients (19.8%) it occurred in hospital not post surgical osteomyelitis (nPOS); 38 patients (46.9%) had a community acquired spondylodiscitis (COM).Demographic data, underlying conditions, source of infection, mean diagnostic delay between the onset of symptoms and diagnosis of IE and spondylodiscitis, clinical features were studied in patients with spondylodiscitis with and without IE. Of these patients 7 subjects (9%) had definite IE according to Duke criteria. Six patients with concomitant IE developed COM, 1 patients had hospital acquired not surgical IE and spondylodiscitis, due to vascular device. Concerning IE there was no significant difference in gender and age among the 3 groups. In all cases IE was diagnosed before spinal infection by transesophageal echocardiography (6 pts) and transthoracic echocardiography (1 pt), because all the 7 patients had back pain and the overall duration of symptoms was 35 days similar in the two groups. All patients had al least one comorbidity or underlying medical illness; two patients had an history of valve disease both subjects in COM spondylodiscitis group. The cardiac site involved was the following: aortic valve (5 pts), mitral valve (1 pt), tricuspid valve (1 pt). Four cases, all in the COM group, were complicated by embolic events. Blood cultures were positives in all the 7 patients with IE: *Streptococcus* spp. in 3 pts (*S. mitis*, *S. mutans*, *S. suis*), MSSA in 3 pts, *Candida glabrata* in 1pt. Antibiotic treatment and duration were performed according to causative microorganism: mean of iv therapy was 6.6 weeks followed by oral treatment. Follow up ranged from 12 to 48 months and 1 patient died (14.3%), antibiotic therapy alone was successful in 4 patients (57.1), 2 pts underwent cardiac surgery (28.6%). IE was found to be highly associated with pyogenic vertebral osteomyelitis and vice versa, when specifically sought; thus pyogenic osteomyelitis should always be considered in patients with IE and back pain.

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KIDNEY DISEASE IN INFECTIVE ENDOCARDITIS

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Background: Renal damage (septic emboli, renal infarction, glomerulonephritis-GN) occurs in infective endocarditis (IE) very often and influences its course and prognosis.
Purpose of the study: Study of kidney affection in IE.
Methods: 140 patients with confirmed IE (Duke criteria) between 2004 and 2008 were studied. Clinical, laboratorial and echocardiographic methods were used. Forty patients had a renal biopsy and fourteen a necropsy.
Results: Renal damage was revealed in 108 IE pts from 140 (77%). The chronic renal failure was occurred in 33% pts, nephrotic syndrome – in 2 pt. 91% pts had the uric syndrome (US). Hematuria was in 87% pts with IE. It was more often (100%) and severe in patients with the secondary IE. Other signs of US occurs more rarely. *Staphyloccus* spp. was revealed in blood in 57% pts, *Streptococcus viridans* – in 31%, *E. coli* – in 12%. Circulating immune complexes and deposits of IgM, IgG and complement components in glomerular structures were detected in 80% of pts with subacute IE and persistent bacteriemia. Common renal lesions were focal infarcts and acute GN. Over half of the renal infarcts were due to septic emboli, mostly in pts infected with *Staph. aureus*. Mesangioproliferative (75%), mesangiocapillary (10%), membranous (15%) types are revealed at biopsy. Mesangioproliferative GN was revealed in all 14 pts at necropsy, at 8 in a combination with focal infarcts of kidneys. Rapidly progressive GN was in 3 pts. Acute interstitial nephritis found in 10% seems to be attributable to antibiotics. Chemotherapy of IE with kidney damage assumes exception of nephrotoxic antibiotics and reduction of doses or frequency rates. The signs of kidney damage disappeared in 90% of our pts at adequate antibacterial therapy.
Conclusions: In IE kidney affection, the uric syndrome with moderately expressed hematuria, leukocyturia and proteinuria prevails. Renal failure concerns to the most frequent complications. The commonest type of GN is vasculitic, with or without deposition of immunoproteins in glomeruli. Kidneys affection has adverse prognostic value. A renal biopsy is helpful in the investigation of renal impairment and for differentiation of rapidly progressive GN and acute tubulointerstitial GN.

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CLINICAL SIGNIFICANCE AND PROGNOSTIC VALUE OF N-TERMINAL PRO-B-TYPE NATRIURETIC PEPTIDE (NT-pro-BNP) IN INFECTIVE ENDOCARDITIS: A PRELIMINARY STUDY

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Introduction: The B-type natriuretic peptide (BNP) is rapidly and transiently induced within ventricular cardiomyocytes and may be detected in the serum of patients early after acute myocardial mechanical stress. Thus, it is a useful diagnostic and prognostic marker in patients with heart failure (HF). BNP increases along with rising ventricular wall stress and inversely correlates with ejection fraction. The N-terminal fraction of the BNP prohormone (NT-pro-BNP) has a longer plasma half-life, reaches higher plasma concentrations and correlates more closely with clinical and echocardiographic parameters, making it the preferred subtype to measure. HF is a major complication of infective endocarditis (IE) and it is not always predicted by the degree of valve dysfunction alone. In this study, we aimed at evaluating the clinical correlates and the prognostic significance of NT-pro-BNP levels in a cohort of consecutive IE patients seen at our centre.

Methods: We studied 39 patients with definite IE admitted to our centre in the last year. NT-pro-BNP levels were measured in a serum sample obtained on admission by means of a commercial ELISA. We analysed the possible relation existing between NT-pro-BNP levels and the following variables: heart side involved, infected valve, type of valve involved (native vs prosthetic), rate of surgical therapy and outcome.

Results: NT-pro-BNP levels were higher in aortic versus mitral valve IE cases and significantly higher in left-sided compared with right sided IE cases (1176 vs 311 pg/ml). Prosthetic valve IE was associated with a higher level of NT-pro-BNP (1747.5 vs 1058 pg/ml). Interestingly, patients who were subsequently operated on also showed higher levels of serum NT-pro-BNP (2275.44 vs 1693.64 pg/ml in medically treated patients). The outcome of IE also appeared to be related to NT-pro-BNP levels as patients who died showed higher levels of this biomarker (4333 vs 742.5 pg/ml in those discharged home).

Discussion: Our preliminary experience suggests that NT-pro-BNP levels might have a prognostic value in IE. In particular, NT-pro-BNP levels were associated with both surgical rates and mortality. Moreover, aortic valve IE, that seems to be more often complicated by HF, was also characterized by greater levels of this biomarker. Further studies are necessary to define the potential usefulness of NT-pro-BNP determination in the management of IE patients.

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HEART FAILURE IN INFECTIVE ENDOCARDITIS: A REPORT FROM THE MULTICENTER, PROSPECTIVE, OBSERVATIONAL STUDY ON ENDOCARDITIS IN ITALY (SEI)

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Background: Heart failure (HF) is a major complication of infective endocarditis (IE). Its severity is ascribed to the degree of valve injury, but other factors could play a role. However, little data have been generated so far on the clinical and microbiological correlates of HF in IE. In this study, we analysed the prospective SEI database to evaluate in detail risk factors and correlates of HF in IE.

Patients and methods: We studied all cases of definite IE (n = 852) admitted to the 19 enrolling institutions over the last 5 years. Patients were grouped according to NYHA class (class I and II, n = 123; class III, n = 163; class IV, n = 121). Patients without HF (n = 445) served as controls. Statistical comparisons were performed by chi-square test or Wilcoxon rank sum test for categorical or continuous variables, respectively.

Results: The prevalence of diabetes increased with growing NYHA class while intravenous drug use was associated with reduced rates of HF. No major differences were found regarding the etiology of IE across the four patient groups. The use of aspirin was inversely related to the NYHA class (no HF 9.9%; class I-II, 7.3%; class III, 5.5%; class IV, 5%). HF patients showed higher rates of complications, including arrhythmias and myocardial abscesses but not stroke or peripheral embolism. The rates of fever, CRP elevation and blood culture growth were the same among groups. The proportion of patients with aortic valve involvement (both vegetation and valve regurgitation) increased with growing NYHA class (no HF 26%; class I-II, 43%; class III, 55%; class IV, 48%), as well as the number and size of vegetations. Coherently, the proportion of patients undergoing cardiac surgery (29% no HF; 54%, class I-II; 83% class III; 62% for class IV) and the death rates (9.7% no HF; 11.4%, class I-II; 21.4% class III; 52.9% for class IV) grew progressively with increasing NYHA class.

Conclusions: Our data, originating from a large cohort of IE patients, confirm that the degree of cardiac dysfunction in IE impacts the therapeutic approach and severely affects the prognosis. Aortic valve involvement, the presence of diabetes and the occurrence of arrhythmias and myocardial abscesses are associated with a higher risk of HF, while prior aspirin use might possibly have a protective effect. An otherwise comprehensive analysis of clinical, microbiological and echocardiographic findings did not allow us to identify further risk factors for HF in IE.

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INFECTIOUS ENDOCARDITIS AT AUTOPSY: "LOOKING TROUGH THE EYES OF THE PATHOLOGIST"

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Background: In a time in which autopsies are rarely performed, the postmorten study of IE may help to understand the pathophysiology and manifestations of this versatile disease.

Methods: Review of records and clinical charts of cases of IE with post-mortem examination in 2 different periods: 1 (1970–1986) and 2 (1987–2008). We tried to assess clinical and pathologic correlations and to know how frequently diagnosis was missed until autopsy.

Results: We reviewed 69 autopsies (40 and 29 in periods 1 and 2 respectively). The age of patients increased from 46.6 y (29–80) to 57.6 y (20–88) from 1 to 2. *S. aureus* was the most common etiologic agent in both periods. Co-morbidities were present in 27% and 100 of cases in periods 1 and 2. We found an increased number of cases with chronic renal failure on hemodyalisis and cases with cirrhosis of the liver in period 2. PVE was observed in 10 (25%) and 6 (20.6%) cases respectively. Cardiac pathology and the lesions observed (presence of vegetations, damage of cusps and perivalvular tissue, rupture of chords and papillary muscles, McCallum patches, fistulae, pericarditis and focal myocarditis) did not change over the years. For PVE, sewing ring vegetations, abscesses and dehiscense were the most common lesions. Obstruction of the mitral prosthesis was observed in 3 out of 6 cases of PVE of the mitral valve. The systemic pathology consisted of infarcts in the brain (59%), spleen (39%), kidney (30%), and myocardium (22%) and abscesses in the kidneys (19%) and lungs (14%). Except for brain and myocardial infarcts, most infarcts went unnoticed. Extensive hemorrhagic brain infarcts were found in individuals with PVE on coumadin therapy. Diagnosis was missed until autopsy in 35% and 34% in periods 1 and 2 respectively. Absence of murmurs and fever and the presence of another disease were the most common causes of diagnostic failure.

Conclusion: Co-morbidities, particularly chronic renal failure and cirrhosis of the liver, are nowadays commonly found at autopsy in

cases of IE. Despite modern diagnostic techniques, diagnosis of IE is frequently missed until autopsy.

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GENDER DIFFERENCES IN CEREBROVASCULAR COMPLICATIONS IN INFECTIVE ENDOCARDITIS

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Background: Most published studies show that infective endocarditis (IE) occurs more frequently in men than in women. Neurological manifestations are not discussed as sex disintegrated data in most studies.
Aim of study: To analyze the incidence of and possible gender differences in cerebrovascular complications (CVC) in IE.
Patients and methods: Prospective cohort study. IE patients treated in Copenhagen, Denmark (2002 to 2007) and Gothenburg, Sweden (1996 to 2007). Analysis of CVC frequency and mortality.
Results: Totally 684 left-sided IE were included, 223 (33%) women and 461 (67%) men. Women were older than men (64.6 vs 62.3 years; p = 0.037). Comorbid conditions, valve involved, presence, and length of vegetation did not differ between the sexes. *S. aureus* etiology was more common in women (31.8 vs 21.0, p = 0.032). Cardiac surgery was performed in 39.5% (women) vs 44.5% (men) (n.s.). CVCs were seen in 169 (25%) of the episodes, with a CVC frequency of 30% in women vs 23% in men (p = 0.039). *S. aureus* etiology conferred a higher risk for CVC. A CVC was seen in 52% of *S. aureus* IE in both sexes. When stratified for microbial etiology no difference in CVC frequency was seen between the sexes. There were no sex differences in in-hospital mortality. Twelve month-mortality was higher in women (31.3 vs 24.1%, p = 0.031).
Conclusions: Women were older than men and had more *S. aureus* IE. Cerebrovascular complications were more common in women, but when stratified for etiology no gender differences were seen. Twelve-month mortality was higher in women.

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PULMONARY INVOLVEMENT IN INFECTIVE ENDOCARDITIS IN CHILDREN AND ADOLESCENTS IN SIBERIA

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Background: Pulmonary affection and predictors of lung embolization (Em) has not yet been clear today in patients with Infective Endocarditis (IE) in child and adolescent.
Methods: 178 patients (pts) (age from 6 month – 18 years) with strictly definite IE according modified Duke criteria: 108 pts with native valve disease; of them 14 pts were intravenous drug users (IDU), 68 pts were operated due congenital heart disease. Patients were subjected to X-ray, echocardiography and pathomorphological investigations.
Results: The episodes of lung Em was detected in 100% in IDU population, in 45% of pts with native valve disease and in pts who were operated in "midterm" IE (50%) and in "late" IE (78%). The predictors of Em depend on localization of vegetation (tricuspid valve) and mobility of peduncles. Fast elevated D-dimers in plasma, time from starting of antimicrobial therapy (more, than two weeks) were additional risk factors of Em. Such affections as abscess, bilateral pneumonia, pleuritis in different combination were recorded with 35% frequency. The necrotic vasculitis and serous pleuritis were more rarely observed: 5 and 10% of cases, respectively.
Conclusion: The pulmonary affection in children and adolescents with IE may have different genesis: thromboembolic/thromboemorragic, infectious (due to uncontrolled dissemination of infection), and (possibly) immune complex. *S. aureus* as a causative pathogen of IE and bilateral pneumonia was a predictor of fatal outcome. Lung Em occurred in operated patients more frequently in "late" subacute IE and was always observed in IDU population. Immune-complex genesis of lung damage (vasculitis and pleuritis) is possible and more detailed investigations are needed.

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INCIDENCE AND SURVIVAL OF PATIENTS WITH CEREBROVASCULAR EVENTS SECONDARY TO INFECTIVE ENDOCARDITIS IN UNIVERSITY MALAYA

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Background: Cerebrovascular events (CVE) remain a major cause of morbidity and mortality in patients with infective endocarditis. The intention of this study was to document the demographics, clinical presentation and outcome of endocarditis patients who suffered cerebrovascular events in University Malaya. In addition, the one-year survival rate from the index admission and differences in patients with and without CVE were examined.
Materials and Methods: This was a retrospective study of 86 cases of IE in University Malaya Medical Centre, (UMMC) from January 2000 to December 2007. Data on the patients' demographic characteristics, predisposing factors, clinical findings, incidence of CVE, result of investigations, method of treatment and clinical outcome were extracted from the case notes. Data on 1-year survival was obtained from either phone interview with the patient or from the patient's medical case notes.
Results: From January 2000 to December 2007 there were a total of 86 confirmed cases of IE. At the index IE episode, the majority of patients had native valves except for 7% who had surgically repaired valves and 8% with valve replacements. The most common complications recorded were systemic embolization (24%) followed by cerebrovascular events (21%).
A total of 20 patients (23%) suffered a CVE in this study. All patients who suffered CVE had positive blood cultures. Haemorrhagic stroke contributed to 70% of CVE (14 patients) whilst 30% of cases (6 patients) had embolic stroke.
Out of 49 patients who had vegetations on their mitral valve, 12 patients (24%) suffered a CVE and, from 14 patients with vegetations on the aortic valve, 6 patients (43%) suffered a CVE.
From the index admission 71 (83%) patients were discharged alive whilst 15 (17%) had died. 12 patients who had died at the index admission suffered a CVE which is 80% of the total number of deaths. Out of the total number of patients who suffered CVE, 60% died at the index admission.
Conclusions: These results show that cerebrovascular event is one of the most important risk factors for a fatal outcome during IE. In-hospital mortality was much higher in patients with a CVE than those without a CVE. In conclusion, CVE is a common and severe complication occurring in every fifth patient with IE. The occurrence of CVE significantly contributes to the patients' poor outcome.

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CEREBRAL MICROBLEEDS: A NEW DIAGNOSTIC CLUE IN INFECTIVE ENDOCARDITIS

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Background: Early diagnosis of infective endocarditis (IE) is sometimes obvious (echocardiographic evidence of vegetation and sustained bacteremia), but frequently difficult and takes into account extracardiac signs, such as neurological ones. Cerebral microbleeds (CMBs) have been described using magnetic resonance imaging (MRI), in particular in patients with cardiovascular risk factors or prior stroke. CMBs have been reported in isolated cases of IE, however, the

frequency and association of CMBs with IE has not been studied so far.

Materials and Methods: In order to study the prevalence and association of CMBs with IE, we performed a case-control imaging study in a referral institutional center. Brain MRIs using T2 FLAIR-weighed sequences were analysed in 60 patients with IE and 120 age and sex-matched controls without IE. The presence, location and size of CMBs assessed by two independent neuroradiologists blinded to patient's characteristics.

Results: The level of inter-observer agreement about presence of CMBs was high with a Kappa coefficient (95% CI) ranging from 0.70 (0.42–0.98) for subcortical regions to 0.91 (0.82–0.99) for cortical areas. CMBs were more prevalent among IE patients (57%) than in controls (15%, n=) (matched odds ratio (OR), 10.06; 95% Confidence Interval (CI), 3.88–26.07). Moreover, the OR of IE increased with the load of CMBs, suggesting a causal relationship; the OR (95% CI) was 6.12 (95% CI, 2.09–17.94) for 1 to 3 CMBs and 20.12 (95% CI, 5.20–77.80) for more than 3 CMBs.

Conclusion: CMBs are highly frequent in patients with IE. The strong association found between IE and CMBs in this case-control study suggests that CMBs could be useful additional criteria for the diagnosis of IE.

Antimicrobial Treatment/New Drugs

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TRENDS IN GLYCOPEPTIDE AND DAPTOMYCIN SUSCEPTIBILITIES IN *STAPHYLOCOCCUS EPIDERMIDIS* ISOLATED FROM INFECTIVE ENDOCARDITIS (IE) OVER TIME (1992–2008)

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Background: The aim of the study was to know the evolution and antibiotic susceptibility pattern of *S. epidermidis* isolated from IE in Barcelona (Spain) between 1992 and 2008.
Methods: We studied 73 *S. epidermidis* strains isolated from 69 consecutive patients with IE (polymicrobial IE in 4 cases). These strains were identified by API ID 32 STAPH and the susceptibility of oxacillin, daptomycin, vancomycin and teicoplanin was studied by the E-test.
Results: Coagulase-negative staphylococci IE represented 16% of all cases of IE (111/713) diagnosed in our hospital. *S. epidermidis* strains represented 71% of all coagulase-negative staphylococci recovered from patients with IE (73/103). *S. epidermidis* native, prosthetic and pacemaker/defibrillator IE was diagnosed in 30%, 30% and 40% of cases, respectively. *S. epidermidis* IE was community-acquired and health-care associated in 49% and 51% of patients, respectively. Oxacillin, daptomycin, vancomycin and teicoplanin MIC50/MIC90 (μg/mL) for *S. epidermidis* strains were: 0.5/256, 0.5/0.75, 2/2 and 2/6. 48% of the *S. epidermidis* strains showed a vancomycin MIC = 2 μg/mL, 6 strains showed a vancomycin MIC > 2 μg/mL and 2 of these had intermediate resistance to teicoplanin. The Mantel-Haenszel test for trend did not show an increase in vancomycin MIC above 2 μg/mL over time for *S. epidermidis* strains (P = 0.255). Two strains showed a daptomycin MIC = 1.5 μg/mL.
Conclusions: *S. epidermidis* IE is an important cause of community-acquired and health-care associated IE, and involves one-third of native-valve cases. *S. epidermidis* was the most frequent species isolated from coagulase-negative staphylococci, and was oxacillin-resistant in 51% of cases. A vancomycin MIC of 2 μg/mL was common and did not increase over time. 3% of strains were daptomycin-resistant.

085

DAPTOMYCIN FOR NATIVE VALVE ENDOCARDITIS: EXPERIENCE FROM A REGISTRY

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Background: Daptomycin is approved in the US and Europe for treatment of right-sided infective endocarditis (IE) due to *S. aureus* at a dose of 6 mg/kg. Post-marketing data evaluating daptomycin for the treatment of native valve IE is presented.
Methods: Patients with a diagnosis of IE without an intracardiac foreign body infection were identified in a retrospective, multicenter observational registry (CORE 2004–7). Outcome (cured, improved, failed, nonevaluable) was assessed at the end of daptomycin therapy using protocol defined criteria. Surgical interventions were not collected. Success was defined as cure or improved. Nonevaluable patients were excluded from the efficacy analysis but included in the safety analysis.
Results: Of 4777 patients in the registry 189 (4%) met the search criteria, 141 (75%) were evaluable for efficacy. Eighty-seven (62%) were male, 47 (33%) patients were ⩾ 66 years of age, 51 (36%) had an initial creatinine clearance of <30 mL/min at the start of daptomycin and 29 of these were receiving dialysis. The most common underlying diseases were hypertension (41%), diabetes (23%). Sixty nine (49%) received daptomycin while in an intensive/critical care unit. The most common pathogens were *S. aureus* (n = 79, 84% MRSA), enterococci (n = 32, 38% vancomycin resistant). Ninety-two patients (65%) had left-sided IE. Most patients (121/141, 86%) received antibiotic therapy before beginning daptomycin. The median (min, max) initial daptomycin dose was 6 (3, 10) mg/kg. The median (min, max) daptomycin duration for those reported as a success was 28 (2, 96) days. Ninety-three (66%) patients received at least one dose of concomitant antibiotics with daptomycin, most commonly rifampin (33%), aminoglycosides (31%) and vancomycin (27%). The success rate in the evaluable patients was 84% (119/141); 84% (77/92) in left-sided IE; 82% for *S. aureus* and 78% for enterococci. Safety data was available for 142 pts from 2005–7; 2004 did not collect safety data. In 13 of 142 pts (9%), 22 adverse events were possibly related to daptomycin; in 3 (2%) of these patients the adverse events were serious. Sixteen (11%) deaths (10 failed daptomycin) were reported, none possibly related to daptomycin.
Conclusions: This non-randomized sample of mostly left-sided native valve IE patients included many with co-morbid conditions and renal dysfunction. Daptomycin appears effective in this group of patients with native valve IE.

086

DAPTOMYCIN FOR CARDIAC INFECTIONS INVOLVING PROSTHETIC MATERIAL: EXPERIENCE FROM A REGISTRY

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Background: Daptomycin is approved in the US and Europe for treatment of right-sided endocarditis due to *S. aureus* (native valve only) at a dose of 6 mg/kg. Post-marketing information evaluating daptomycin for the treatment of cardiac infections with prosthetic material is presented.
Methods: Patients with a diagnosis of endocarditis and/or intracardiac foreign body infection were identified in a retrospective, multicenter observational registry (CORE 2004–7). Outcome (cured, improved, failed, nonevaluable) was assessed at the end of daptomycin therapy using protocol defined criteria. Surgical interventions were not collected. Success was defined as cure or improved. Nonevaluable patients were only included in the safety analysis.
Results: Of 4777 patients in the registry 52 (1%) met the search criteria; 32 (62%) were evaluable for efficacy. Twenty-four (75%) were male, 12 (38%) patients were ⩾ 66 years of age, 8 (25%) had an initial creatinine clearance of <30 mL/min at the start of daptomycin and 4 of these were receiving dialysis. Underlying diseases included hypertension (47%), congestive heart failure (28%), arrhythmias (28%), and diabetes (28%). Sixteen (50%) received daptomycin while in an intensive/critical care unit. The most common pathogens were *S. aureus* (n = 12, 75% MRSA), coagulase-negative staphylococci (n = 6), and enterococci (n = 5, 40% vancomycin-resistant). Most patients (29/32, 91%) received antibiotic therapy before beginning daptomycin. The median (min, max) initial daptomycin dose was 6 (4, 9.5) mg/kg. The median (min, max) daptomycin duration for those reported as a success was 24 (2, 62) days. Twenty (63%) patients received at least one dose of concomitant antibiotics with daptomycin, most commonly aminoglycosides (35%), rifampin (20%), and vancomycin (20%). The success rate in the evaluable patients was 88% (28/32). Success by primary pathogen was; 92% for *S. aureus*, 100% coagulase-negative staphylococci, and 100% for enterococci. Safety data was available for 40 pts from 2005–7; 2004 did not collect safety data. There were no adverse events possibly related to daptomycin in the safety population (n = 40). Five (13%) deaths (4 failed daptomycin) were reported, none possibly related to daptomycin.

Conclusions: Daptomycin appeared effective in this group of patients with prosthetic cardiac material. Further clinical studies in this population are warranted.

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VANCOMYCIN CREEP PHENOMENON IN METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* INFECTIVE ENDOCARDITIS

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Introduction: *S. aureus* has become the most common cause of infectious endocarditis in many settings (SAIE). SAIE is related to a very high rate of morbidity and mortality, mainly when the isolate is methicillin resistant (MRSA). Vancomycin has been the mainstay of MRSA IE therapy, but the failure rate is high. The challenge is currently enhanced by the debate around the phenomenon of vancomycin creep, which has never been analyzed specifically in patients with endocarditis. We provide the first series of MRSAIE that compares outcome with the Vancomycin MICs detected both with microdilution and E-test.

Material and Methods: Prospective series of IE from 1994–2008 in a reference tertiary hospital. Modified Duke's diagnostic criteria were used. MRSA-IE episodes were selected from the database and the available strains were recovered. Susceptibility testing was performed against vancomycin, linezolid and daptomycin with the standard microdilution method and with the E-test. Corresponding control strains were run with each batch. Clinical characteristics and outcome were analyzed. Death was considered related to the episode of endocarditis if the patient died during antimicrobial therapy with a clinical course suggesting persistent infection, and if death could not be clearly attributed to other causes.

Results: Out of the 469 cases of IE diagnosed in the last 15 years, 26 (5.5%) MRSA-IE were diagnosed and treated in our institution. Mean age was 62.5 years old and 38.5% were women. Acquisition was nosocomial in 19, nosohusial in 1, and in the community in 6 (3 IVDU). Eleven of the cases affected a prosthetic valve and 84.6% were left-sided. All patients received vancomycin, as part of their therapeutic scheme, and 9 (34.6%) were operated on. Overall mortality was 50%. Twenty strains were available for the susceptibility tests. The distribution of MICs with both methods and the proportion of patients dying is as follows: microdilution method: MIC 0.5 μg/dl: 8 (38% died), 1 μg/dl: 11 (54% died), 2 μg/dl: 1 (100% died); With the E-test: MIC 1 μg/dl: 4 (75% died), 1.5 μg/dl: 8 (50% died), 2 μg/dl:2 (50% died), 2.5 μg/dl:4 (50% died) and 3 μg/dl:2 (0% died). All strains were susceptible to linezolid and to daptomycin.

Conclusion: There was a clear discrepancy between vancomycin MIC's depending on the detection method and we could not find a clear relationship with the outcome, mainly when the E test method was used.

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EXPERIENCE WITH THE COMPASSIONATE USE OF DAPTOMYCIN AS SEQUENTIAL THERAPY IN LEFT-SIDED INFECTIOUS ENDOCARDITIS (L-IE)

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Background: Management of left-sided IE in patients with renal failure or prosthetic valve involvement, particularly when surgery is rejected, is very difficult. Besides, some of these patients, request to receive home therapy. Daptomycin has demonstrated its efficacy against staphylococcal bloodstream infections and right-sided endocarditis. However, there is not much experience in the therapy of left sided and prosthetic IE, especially in those difficult conditions.

Objective: To describe our experience with 7 patients with L-IE treated with daptomycin as sequential therapy.

Materials and methods: Daptomycin was selected as a last resort compassionate drug due to either toxicity or impossibility to receive standard drugs, or because of its advantageous dosing properties in patients requesting OPAT. The decision was adopted within a multidisciplinary group of specialists and the patients gave their consent.

Results: Of the 90 patients with definite IE treated in 2007 and 2008, 7 left-sided IE (6 mitral, 1 aortic) were treated with daptomycin. IE episode affected prosthetic valves in 5 of the cases and surgery was only performed on one of the patients. All, but one patient (IE due to *E. faecium*), received 1–27 days (mean 16±8.8 d) of other drugs before daptomycin. The reasons to start daptomycin were: renal failure (4, 57%) or hospital discharge for outpatient parenteral therapy (3, 43%). The dose of daptomycin was 6 mg/kg/d in 3 (42.9%) cases, 6 mg/kg/48 hr in 3 (42.9%) and 12 mg/kg/d in one (14.3%). Median length of daptomycin treatment was 38±8.8 days. Mean age was 74±14 years, and the mean Charlson's score was 4.3, SD 1.9. Most common underlying disease was neoplasia (71.4%). One episode was nosocomial and 6 (85.7%) were community-acquired. The etiology was: *Enterococcus* spp. 3 cases (42.9%) (*E. faecalis* 1, *E. faecium* 1, *E. gallinarum* 1), coagulase negative staphylococci 1 case (14.3%), *Streptococcus bovis* 1 case (12.5%), MS *Staphylococcus aureus* 1 case (14.3%), and culture negative one case. Surveillance blood cultures were performed in all patients and remain negative. No emergence of daptomycin resistance, nor relapse have been detected so far. The outcome was favorable in all the cases and no adverse events including CPK elevation were observed.

Conclusions: Daptomycin in our experience showed to be a reasonable option for sequential therapy even under very difficult to treat L-IE.

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DAPTOMYCIN USE FOR ENDOCARDIAL INFECTION IN LEEDS, UK

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Background: Daptomycin was approved by the EuMA in 2007 at a dose of 6 mg/kg for bacteremia including right-sided endocarditis due to *S. aureus*. Data for daptomycin use in left-sided, pacemaker lead and prosthetic valve endocarditis is limited. A series of 8 patients treated with daptomycin is reported, with the aim of examining the reasons for daptomycin use and clinical outcomes.

Methods: Routine clinical data is prospectively collected. This analysis describes patients with endocarditis who received daptomycin during 2007 and 2008. Data pertaining to patient age; sex; underlying pathology; type of valve infection; causative organism and susceptibility; initial antimicrobial therapy and duration; dose, duration and indication for daptomycin therapy; need and date of surgery; number of days from start of episode to daptomycin therapy and number of days from start of episode to surgery; CK measurements; whether acute kidney injury (AKI) occurred and all outcome measures were assessed.

Results: See the table.

Conclusions: The predominant indications for daptomycin were failure of therapy with first line agents or reduced susceptibility of the causative organism. This non-randomized sample of endocarditis patients included patients with co-morbid conditions and renal failure. In this series of difficult-to-treat patients, daptomycin 6 mg/kg was associated with a cure in 4/8 patients. Further clinical studies are needed to extend experience with daptomycin for infective endocarditis.

Age/sex	Final diagnosis	Cause	Indication for daptomycin	Outcome
2007				
82/F	PLI with VO	*S. aureus*	Pen-allergic patient. Failure of therapy on vancomycin, gentamicin and rifampicin	S but relapsed, subsequently cured with teicoplanin
55/M	NVE	*S. epidermidis*	Flucloxacillin, gentamicin, rifampicin, vancomycin-"resistant" organism	S
65/M	PVE	*Corynebacterium kroppenstedtii*	Pen-allergic patient developed thrombocytopaenia on vancomycin	S
45/M	NVE	MRSA	Failure with vancomycin + gentamicin + rifampicin	S
61/M	NVE	*S. aureus*	Failure with flucloxacillin + gentamicin + rifampicin and failure with linezolid + gentamicin + rifampicin	D
2008				
32/M	PVE	*S. epidermidis*	Flucloxacillin-resistant, vancomycin-"resistant" organism	S
67/M	PLI	*S. epidermidis*	Failure with vancomycin + gentamicin + rifampicin	S, but relapsed. Daptomycin stopped due to rash
79/F	PVE	*S. epidermidis*	Failure with vancomycin + gentamicin	D

Key: PLI = Pacing lead infection; VO = vertebral osteomyelitis; NVE = Native valve endocarditis; S = Survived; D = Died.

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USE OF DAPTOMYCIN IN INFECTIVE ENDOCARDITIS: REPORT ON TRHEE CLINICAL CASES

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Background: Daptomycin demonstrates potent bactericidal activity against gram-positive bacteria, including MRSA. It is unclear if this option can offer a real advantage compared to cheaper glycopeptides.
Case report: We report three cases for whom daptomycin was preferred to vancomycin as a first-line treatment for IE: the clinical rationale for this choice is discussed.
A 37-year old IVDU was admitted with mild dyspnoea and fever. TTE showed a 1.5 cm^2 friable tricuspidal vegetation. Blood culture was negative due to previous antibiotics. Acute renal failure was noted and daptomycin/ceftazidime were initiated, resulting in progressive reduction of vegetation and clinical improvement. Surgery was avoided.
A 22-year old man with aortic bicuspid valve, submitted to otorinolaringoiatric surgery 40 days before without antibiotic prophylaxis, complained fever for 10 days despite two 7-days antibiotic cycles with ciprofloxacin and ceftriaxone. A MRSA (vancomycin MIC > 2) was isolated on blood culture. TTE revealed an endocardial aortic valve thickening and pericardial effusion. Fever disappeared after 5 days of therapy with daptomycin/ceftazidime/amikacin. TTE two weeks later showed reduction of thickening and pericardial effusion. The patient continued daptomycin in day-hospital for another two weeks with complete resolution.
A 37-year old IVDU was hospitalized for left-side paresis and fever. A cranial TC scan revealed a right cortical-subcortical lesion while TTE evidenced an aortic vegetation prolapsing in left ventricule with severe aortic failure. Blood cultures were negative due to previous antibiotics. Administration of daptomycin/ceftazidime/amikacin determined rapid improvement. He underwent a successful valve replacement after 20 days continuing daptomycin for 2 weeks.
Conclusion: Three cases of successful IE treatment based on daptomycin are described, without toxicity. The concomitance of acute renal failure influenced our choice in the first case as significantly less nephrotoxicity was reported for daptomycin compared to vancomycin. In the second case, a MIC > 2 for vancomycin lead us to prefer daptomycin as the breakpoint for vancomycin susceptibility for MRSA was recently reduced to 2 mg/L. Lastly, rapid bactericidal activity of daptomycin was the reason of the choice in the third case. As MRSA are prevalent and empirical therapy is frequently required, daptomycin represents a valid alternative in IEs.

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CLINICAL EXPERIENCE WITH DAPTOMYCIN MONOTHERAPY FOR PACE-MAKER (PM)/IMPLANTABLE CARDIAC DEFIBRILLATOR (ICD) INFECTIONS AND ENDOCARDITIS

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Background: Daptomycin (D) may be a valuable option for the treatment of infections related to intravascular devices.
Methods: We retrospectively evaluated 11 patients treated with D at Pisa tertiary care-university Hospital in the period from April 2007 to December 2008. Age, gender, type of infection, microorganism, daily dose of D, days of treatment, adverse events and outcome were reviewed. Outcome were defined as failure, improvement or healing.
Results: 11 patients were included in the study, 8 were treated with antibiotic therapy and transvenous removal of the cardiac device. Mean age ± SD was 68±28 years, all patients were male. 5 patients had endocarditis (2 of these with embolic pneumonia, 4 caused by *S. aureus* and 1 by *S. epidermidis*), 4 patients had local PM/ICD infections, 2 patients had systemic infection due to *S. aureus* without endocarditis. The causative microorganism were: 4 *S. epidermidis*, 3 MRSA, 3 MSSA, 1 *Propionibacterium* spp. Four out of the 10 staphylococci included in the study were methicillin-resistant. Mean D dose ± SD was 6.5±0.6 mg/kg/die. Mean treatment duration ± SD was 37±25 days. All endocarditis related to PM/ICD were cured, including 3 *S. aureus* and 1 *S. epidermidis* endocarditis treated with transvenous removal of the device (2 pts with negative cultures of the leads) and 1 *S. aureus* endocarditis treated with antibiotic therapy only. The 4 patients with local PM/ICD infections were also cured with antibiotic therapy and device removal. Both systemic infection due to *S. aureus* were treated with antibiotic therapy only, one of the two patients failed, having local infection relapse due to same microorganism. In 8 out of 11 patients with PM/ICD infections a new device was implanted 48 hours after the removal of the infected one, during D therapy, without relapse of infection. None of the treated patients experienced adverse events.
Conclusions: D monotherapy might be an effective therapy in the treatment of local infections and endocarditis related to PM/ICD.

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CLINICAL EXPERIENCE WITH LINEZOLID FOR ENDOCARDITIS: MONOTHERAPY, COMBINATION THERAPY AND CONTINUING INFUSION

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Background: Linezolid (L) may be a valuable option for the treatment of severe infections due to gram positive bacteria. L might be bactericidal against *Streptococcus* spp. and may have slow bactericidal activity against *S. aureus*. Therefore we reviewed the case of endocarditis admitted to Pisa Hospital in Italy, in the last 8 years, to determine the outcome of those patients treated with linezolid.
Methods: We retrospectively evaluated patients with endocarditis and treated with linezolid. We considered linezolid therapy as first, second or third line therapy. Clinical outcome was defined as

failure, improvement or success. Microbiological eradication was also considered. Age, type of infection, microorganisms, days of treatment, adverse events and outcome were reviewed.
Results: 14 patients were included in the study. Mean age ± SD was 61±39 years. 10 patients had left-side endocarditis, 7 native valves and 3 prosthetic valves. 4 patients had PM associated right side endocarditis. 2 endocarditis were polymicrobial. 16 microorganisms were isolated: 5 MRSA, 3 MSSA, 4 CNS, 3 *Enterococcus* spp., 1 *Streptococcus* spp. Linezolid was the first line therapy in 10 patients, in 3 cases as monotherapy, in 7 cases as combination therapy: 4 with a carbapenem, 2 with a penicillin, 1 with rifampin. In 3 cases L was second line therapy, in 1 case L was third line therapy. Mean duration time ± SD was: 20±9 days. 7 patients were considered healed, 5 patients improved and 2 patients failed: 1 with PM MRSA endocarditis failed clinically and microbiologically, the other a MSSA mitral valve endocarditis with cerebral embolic lesions in drug addict failed clinically with blood cultures negative. In only 1 case there was microbiological failure. In 3 cases PMs were removed transvenously. In 2 cases prosthetic valve was replaced surgically. In 1 case L was stopped due to anaemia. In 2 cases L therapy was used as continuing infusion; in both cases we were able to demonstrate bactericidal activity of the serum against the microorganism causing endocarditis.
Conclusions: L might be considered in endocarditis when other antibiotic options are not useful.

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OUTPATIENT PARENTERAL ANTIBIOTIC THERAPY FOR INFECTIVE ENDOCARDITIS. SINGLE-CENTRE EXPERIENCE

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Background: Patients with infective endocarditis (IE) often face a prolonged course of parenteral antibiotic therapy, which traditionally has been administered in the hospital setting. Although outpatient parenteral antibiotic therapy (OPAT) is increasingly being used for various infectious diseases, outpatient treatment of IE is still uncommon. Efforts to reduce the cost of medical service have led to consideration of OPAT for patients with IE.
Methods: A retrospective analysis of clinical and microbiologic data was performed for 18 patients with infective endocarditis treated in our 439-bed general hospital partially in the outpatient setting during the period 2001–2008. Strictly selection criteria were used in order to include low-risk patients in the OPAT program.
Results: Of the 18 patients, 13 were male and 5 female, with a median age of 68 years (range 35–83). Eleven of the OPAT-treated patients had native-valve infection; the remaining seven had late prosthetic-valve endocarditis. Sixteen patients had left-sided involvement and two had right-sided involvement; there were no known IV drug abusers. All of the patients had definite endocarditis based on Duke's criteria, and all but one had culture-positive infection. Causative organisms were *Streptococcus* spp. (9), *Enterococcus faecalis* (5), *Staphylococcus aureus* (2), and *Pseudomonas* spp. (1). All of the patients had been admitted to the hospital, but were sent home within a median time of 20 days (range 7–42) and were treated at an infusional centre to complete therapy on an outpatient's basis. Several antibiotics regiments were used in these patients; the most common antibiotics used were ceftriaxone, gentamicin and vancomycin. The majority of the intravenous lines (89%) were peripheral. The mean duration of OPAT was 20.3±8.9 days per patient and globally supposed 345 days of hospital admission savings. Clinical and microbiologic cure was achieved in 89% of the cases: one patient developed hearth failure and surgery was performed in two patients during antibiotic therapy.
Conclusions: The use of OPAT programs in the treatment of IE is likely to increase due to ongoing efforts to shorten hospital stays and reduce health-care costs. Selection criteria and careful medical monitoring of patients are critical in determining the success of any OPAT program and particularly in case of IE. This preliminary experience suggests that OPAT programs can be promoted in IE stable patients with advantage.

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OUTPATIENT PARENTERAL ANTIBIOTIC THERAPY FOR INFECTIVE ENDOCARDITIS

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Background: Outpatient parenteral antibiotic therapy (OPAT) for infective endocarditis (IE) allows for shorter hospital stays and lower cost of the process. The aim of our study was to describe our experience of the OPAT for IE during ten years in our hospital in order to a protocol.
Methods: Descriptive study of a cohort of 48 IE episodes treated in La Princesa Hospital during 1998 to 2008 that received OPAT for some portion of their treatment.
Patient selection criteria: (a) family support, (b) ability to understand the potential benefits and risks of OPAT and the dinamic nature of IE, (c) home near hospital, (d) uncomplicated IE. Contraindications for OPAT: (a) IE with clinical or echocardiographical complications, (b) virulent microorganisms IE (*S. aureus*)*, (c) prosthesis IE for the first two weeks*. * In the continuation phase of therapy (at the third week and afterwards) and those who underwent valve replacement surgery while they were hospitalized with IE, received OPAT when they were medically stable.
Results: 35 men (73%), 13 women (27%). Location; 14 mitral native valve (29%), 9 aortic native valve (18%), 1 aortic-mitral native valves (2%), 10 prosthesis mitral valve (12%), 7 prosthesis aortic valve (14%), 1 doubled prosthesis aortic-mitral valve (2%), 4 pacemarker (8%) and 2 tricuspid native valve (4%). Antibiotics: 32 ceftriaxone (53%), 8 vancomycin (13%), 9 teicoplanin (15%), 5 gentamicyn (8%) and 6 others antibiotics (10%). Antibiotic duration; 7 weeks one patient, 6 weeks three patients, 4 weeks six patientes, 3 weeks eight patients, 2 weeks fifteen patients, 1 week thirteen patients and half week two patients. In our serie of 48 patients, nine had complications while at hospital on OPAT and eight were admitted to hospital; 1 periferic embolism, 1 cerebral embolism, 2 fever, 2 congestive heart failure, 1 subdural hemorrhage and 2 adverse effects of antibiotics.
Conclusions: The outpatient parenteral antibiotic therapy let us to treat native and prosthesis IE caused by different micoorganisms, being the commonest the less virulent and to save 819 days of hospitalization. Life-threatening complications were infrequent.

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OUTCOMES OF TREATMENT OF INFECTIVE ENDOCARDITIS (IE) WITH HOME INTRAVENOUS ANTIBIOTIC THERAPY (HIVAT)

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Background: To evaluate outcomes of patients (pts) with EI treated with HIVAT during a year.
Methods: IE cases were identified during 2008. Information was extracted from hospital records with follow up of all cases. The outpatient were treated and followed up for a Hospital at Home Unit.
Results: Of 24 cases of IE, 10 (41.67%) received HIVAT. 80% male. Age mean 63 yrs. All patients were medically stable, 3 pts needed surgery. Valves involved: mitral native (4), aortic (3: 2 prosthetic, 1 native), tricuspid (2), pulmonary and pacemaker wire (1). One case had two valves involved (Aop + Min). Causative microorganisms: *S. epidermidis* (3), *S. bovis* (2), *G. morbillorum*, *S. gallolyticus*, *S. oralis*, *Enterococcus* sp. and culture negative (1, each). In all cases, treatment was initiated in hospital. Antimicrobial agents used: ceftriaxone (4, + gentamicin in 3 cases), vancomycin/gentamicin (3) and ampicillin/gentamicin. 4 cases treatment were changed to

daptomycin. IV access used: PC (5), PICC (4) and CC (1). Mean hospital LOS was 17 d and at home 19 d. 52% of treatment was realized at home. 7 cases ended treatment at home with good clinical response. 3 patients return at hospital (days 2, 20, 21), two iv access problems (thrombosis and related catheter infected), one (day 2) intracerebral hemorrhage. Follow up: 9 patients were cured. One patient died.
Conclusions: In our group, after a carefully inpatient selection and follow up, pts with IE can be treated reasonably safely at home. Other microorganisms than *S. viridans* had not worse outcomes.

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OUTPATIENT PARENTERAL ANTIBIOTIC THERAPY IN INFECTIVE ENDOCARDITIS. SPANISH EXPERIENCE AT AN HOSPITAL AT HOME UNIT

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Background: Outpatient parenteral antibiotic therapy (OPAT) is a flourishing assistential option due to its advantages for the patient and cost-saving in hospital expenditure. High mortality and acute onset of life-threatening complications hamper OPAT in infective endocarditis (IE). The availability of Hospital at Home Units (HHU) allow the infusion of different antibiotics and daily and specialized follow-up of the patient.
Objectives: To evaluate the characteristics of patients admitted to a HHU suffering from IE, assess the safety of home treatment of IE, and widen the American restrictive criteria (Andrews & von Reyn 2001) for OPAT.
Patients and Methods: Prospective registry of patients with IE admitted to our HHU. The following parameters were studied: age, gender, type and location of affected valve, isolated microorganisms, antibiotics used, cardiac surgery, hospital stay, adverse events, early mortality rate and days of home therapy.
Results: 33 episodes were analyzed. The mean age was 69.3 years (range 27–87 years), 18 (54.5%) patients were $\geqslant$ 70 years old; male 20 (60.6%); previous hospital stay 20.2 days (SD 10.5, range 5–46 d). Left side IE took place in 30 (90.9%), aortic in 13 (39.4%), mitral in 20 (60.6%), tricuspid in 2 (6.1%), polyvalvular in 3 (9.1%), and pacemaker IE in 2 (6.1%). Cases of prosthetic IE were 8 (24.2%), nosocomial IE 9 (27.3%); cardiac surgery in 8 patients (24.2%). Aetiology: *S. viridans* group, 10; *Enterococcus* spp., 6; *Staphylococcus* coagulase negative, 5; *S. bovis*, 3; *S. aureus*, 3; other *Streptococcus*, 3; culture negative, 4. Only 5 cases (15.2%) fulfilled Andrews & von Reyn criteria for OPAT. Reasons for OPAT exclusion were: prosthetic IE (8), aortic involvement (13), aggressive microorganism (5), severe complications (14) and insufficient inpatient treatment (2). The antibiotics used at home were: ceftriaxone (18), daptomycin (8), gentamycin (6), ampicillin (3), vancomycin (2) and others (4). In 7 cases two i.v. antibiotics were used. Seven patients required electronic portable infusion pump. In 4 patients central venous line was used. The mean stay in HHU was 18.1 days (SD 8.6, range 4–35 d). In only 3 patients return to conventional inpatient care was necessary.
Conclusions: A high complexity level (elderly, prosthetic IE, surgery) of patients with IE admitted to our HHU was detected, albeit with a favourable outcome. It necessary makes reconsider the American restrictive criteria in our environment if daily specialized control is ensured.

Surgery

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IS NATIVE VALVE ENDOCARDITIS (NVE) A PREDICTOR OF REOPERATION FOR PROSTHETIC VALVE ENDOCARDITIS (PVE)?

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Background: Cardiac surgery plays a major role in the effective therapy of patients with PVE. The purpose of the present study is to determine the role of the NVE as a predictor of reoperation for PVE relative to the time of diagnosis.
Methods and results: 85 patients with PVE were observed retrospectively, using Chi-square tests and modifications for statistical analyses.They were divided into two groups: First group (F1) – 37 patients (43.5%) with very early diagnosis (<10 days) and second group (F2) – 48 patients (56.6%) diagnosed >10 days after operation. Overall, the reoperations were 39 (45.9%). 9 patients (24.3%) were reoperated in F1 and 30 patients (62.5%) in group F2. All patients with previous NVE were 27 (31.8%). In F1 they were 13 (35.1%) and 14 (29.2%) in F2. Reoperations in group F1 were performed to 4 patients (30.8%) and to 5 patients without NVE (20.8%). Reoperations in F2 were performed to 12 patients with NVE (85.7%) and to 18 (52.9%) patients without NVE. For group F1, no significant results were observed between reoperated patients and non-reoperated patients with NVE 44.4% versus 32.1% ($p = 0.691$). In group F2, the percentage of reoperation of patients with NVE was significantly greater than the percentage of patients treated without reoperation (40% vs 11.1%; $p = 0.032$). In both groups, the patients without previous NVE did not show significant results and were not dependent on reoperation.
Conclusions: NVE is a predictor of reoperation for PVE in patients diagnosed more than 10 days after operation (F2).

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THE IMPACT OF VALVE SURGERY ON SHORT- AND LONG-TERM MORTALITY IN LEFT-SIDED INFECTIVE ENDOCARDITIS

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Background: The impact of valve surgery (VS) on survival of patients with infective endocarditis (IE) was recently assessed in 5 studies that gave conflicting results. Objectives were to evaluate the effect of VS on 5-year mortality in patients with left-sided IE, and to explain these conflicting results.
Methods: 449 patients with a definite left-sided IE were selected from a prospective, population-based study conducted in France. Association between VS and 5-year mortality was examined through a Cox model adjusted for prognostic factors and predictors of surgery. VS was coded as two time-dependent covariates, which reflect the short- and long-terms effects of surgery on mortality. To determine the impact of methodological approaches, we also analyzed the relationship between VS and mortality in our database, according to each method used in the five previous studies.
Results: VS was performed in 240 patients (53%). The 5-year survival was 41%. VS was associated with a significant increase in short-term mortality (within the 14 postoperative days; adjusted HR, 3.69; 95% CI, 2.17–6.25; $P < 0.0001$) and a significant decrease in long-term mortality (0.55; 95% CI, 0.35–0.87; $P = 0.01$). At least 188 days of follow-up were needed for the long-term beneficial effect of EVS to compensate for the high post-surgery mortality rate (equity point). Through recreating similar statistical and methodological conditions we obtained results consistent with those of the five previously reports.
Conclusion: VS is significantly associated with reduced long-term mortality in patients with left-sided IE. Conflicting results between previous reports could be due to differences in the methods used.

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INFLUENCE OF TIME OF CARDIAC SURGERY (CS) ON THE OUTCOME OF PATIENTS WITH INFECTIVE ENDOCARDITIS (IE) AND STROKE

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Background: The optimal time-to-CS after stroke in patients with IE is still controversial. The goal of this study was to quantify how such operative decisions influence patients' outcome.
Methods: Data from the ICE-PCS Study Group were used. Inclusion criteria were: definite IE complicated by stroke, CS performed after stroke, known dates of both stroke and CS. Outcome parameters were in-hospital mortality and one-year follow-up mortality. Patients were divided into five groups regarding days between stroke and CS – group 1: 1–3 d (30 patients); group 2: 4–7 d (37 patients); group 3: 8–14 d (50 patients), group 4: 15–21 d (43 patients); and group 5: >21 d (85 patients).
Results: Two-hundred-forty-five patients satisfied inclusion criteria. There were no differences regarding demographic and base-line clinical characteristics. Stroke was characterized as embolic in 204 (83.3%), hemorrhagic in 20 (8.2%), and not specified in 21 (8.6%) patients. Hospital mortality was significantly higher if CS was performed within 14 d of stroke event (26.7%, 21.6%, 22.0% vs. 4.7%, 12.9%, $p = 0.033$). There were no differences in the mortality at the one-year follow-up period among hospital survivors. The incidence of intracardiac abscess was more common in earlier CS groups: (33.3%, 27.0%, 48.0% vs. 20.9%, 24.7%; $p = 0.016$). The incidence of other manifestations of complicated IE did not differ between groups. There were no differences in mortality in the follow-up period.
Conclusions: The risk of in-hospital mortality is clearly higher if CS is performed within 14 days from stroke onset in IE. However, such hazards may be unavoidable if urgent CS is mandated by uncontrolled infections (e.g. intracardiac abscess).

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CRITERIA FOR CLINICAL STADIATION OF NATIVE VALVE INFECTIVE ENDOCARDITIS FROM A 30-YEAR SURGICAL EXPERIENCE

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Background: Development of a in-hospital mortality risk score in surgery for native valve infective endocarditis.
Methods: From the analysis of our 30-year surgical series (405 patients, age 48±16 years, 72% males), three stages of disease severity were extrapolated. Univariate analysis identified the factors associated with higher mortality, which were included in a discriminant analysis

model. Classification function coefficients were stratified in quartiles of risk and based on quartiles of coefficients sums, three groups of patients were identified (first + second quartile = 1st group; third quartile = 2nd group; fourth quartile = 3rd group). According to its prevalence in each group, to each factor was then assigned an arbitrary score. Age, pre-operative renal insufficiency, NYHA class III and IV, preoperative mechanical ventilation for pulmonary oedema, emergency surgery, Gram negative endocarditis; and perivalvular involvement (abscess/fistula) were main model variables. Range score from 0 to 2 points defined inclusion in stage 1 (low-risk); 3 to 8 points in stage 2 (average risk); 9 or higher in stage 3 (high-risk).
Results: Hospital mortality (overall 9.1%) was: 1.2% in Stage 1 (168 patients), 7.0% in Stage 2 (129 patients), 24.1% in Stage 3 (108 patients) ($p < 0.001$). Follow-up was 96% complete. Overall actuarial survival was 82%±0.023 at 5 years, 73%±0.03 at 10 years, 59%±0.04 at 15 years. Ten-year survival was 81%, 70%, 59% in stage 1, 2 and 3 respectively (log-rank test: $p = 0.002$).
Conclusions: The newly developed stratification method, computed on clinical preoperative criteria, clearly discriminated patient groups with significantly different in-hospital and long-term prognosis.

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THE PATHOLOGY OF PROSTHETIC VALVE ENDOCARDITIS (PVE): "LOOKING THROUGH THE EYES OF THE SURGEON"

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Background: PVE represents 20% of all cases of infectious endocarditis seen in tertiary care facilities. Many patients develop cardiac complications that must be treated with valve replacement. To improve the understanding on pathogenesis, we assessed the surgical pathology of PVE.
Methods: Retrospective review of consecutive cases of active PVE studied at an university-affiliated hospital in Madrid during period of 20 years (1987–2008). Medical records and surgical charts of patients with PVE in whom valve replacement was undertaken during the active phase of the infection (positive blood cultures within 2 weeks preoperatively or valve culture positive at the time of surgical procedure) were reviewed.
Results: 71 episodes of PVE were found (15 early-onset PVE and 56 late-onset PVE). Fifty-two patients (11 early-onset PVE and 41 late-onset PVE) were operated on during the active phase of the infection. *S. aureus*, coagulase-negative staphylococci, enterococci and viridans streptococci were the causative agents in 71% of cases. Cardiac failure was the main indication for the surgical treatment. Fifty-six valves (49 mechanical prostheses and 7 bioprostheses) were studied. Ring abscesses (47%) and paravalvular leaks (38.7%) were the most common findings. Infection with staphylococci was frequently associated with ring abscess an dehiscense. Vegetations in the absence of other abnormalities were observed in only 26.5% of valves. Obstruction was observed in 9 mitral valves (30%). For bioprostheses, the location of the infective process seemed to depend on the type of PVE: for early-onset PVE, vegetations and abscesses were on the sewing ring, while in late-onset PVE, the endocarditic lesions were located on porcine cusps producing small vegetations, tears and rupture of the cusps.
Conclusion: Ring abscesses and prosthetic dehiscense were the findings most frequently observed. Obstruction was found in one-third of patients endocarditis of the mitral prosthesis. The pathology of PVE on porcine bioprostheses seemed to depend on the pathogenesis of infection, with ring involvement in cases of early-onset endocarditis and cusp involvement in cases of late-onset endocarditis of hematogenous origin.

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SURGICAL TREATMENT OF INFECTIVE ENDOCARDITIS: INITIAL EXPERIENCE OF A NEW UNIVERSITY CARDIAC SURGICAL UNIT

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Objectives: Indications and optimal timing for surgical treatment of infective endocarditis (IE) are not yet established. For this purpose, an IE surgical database was initiated in a recently founded cardiac surgical university program. We present our initial experience of 14 consecutive patients.
Patients-methods: Demographics, indication for surgery, prior cardiac surgery, nosocomial IE (NIE), preoperative status (e.g. congestive heart failure (CHF) class, severity of valve insufficiency, sepsis, shock), comorbidities (e.g. coronary artery disease (CAD), stroke, renal failure (RF CrCl <50 ml/min), anticoagulant and other drug administration, were prospectively evaluated. Intraoperative variables and postoperative outcome were also recorded.
Results: Men (78.5%) and the elderly median (+IQR) age (65 [50.7–68.7] years) predominated. Comorbidities included diabetes mellitus (n = 5), cardiovascular disease (n = 9), COPD (n = 3), IVDA (n = 1), psoriasis (n = 2). IE pathogens were distibuted as follows: MSSA (n = 5), MRSA (n = 1), MRSE (n = 2), Viridans streptococci (n = 1), *Aspergillus* spp. (n = 1), *E. faecium* (n = 1), *E. faecalis* (n = 1) and culture negative IE (n = 2). Aortic valve (n = 8), mitral valve (n = 5), double valve (n = 1) and pacemaker associated IE-tricuspid valve (n = 1) were affected. All but 2 patients were operated on urgently. Valve replacement with mechanical prosthesis (n = 7), bioprosthesis (n = 3) or aortic homograft (n = 2), vegetectomy/valve repair (n = 1) and pacemaker removal (n = 1) were performed, along with coronary artery bypass grafting (n = 3). Death (n = 5) occurred within 48 h post-operatively (n = 3), because of low cardiac output syndrome and after 15 (n = 1) and 56 days (n = 1), as a result of further infection. CHF NYHA III-IV (n = 4), valve insufficiency grade 4 (n = 3), severe RF (n = 3), shock requiring inotropes (n = 2) were found in patients who died, but small sample size does not allow statistical correlations. Median (range) values of perfusion and cross clamp time were 168 (30–462) and 141 (57–190) min respectively in patients who died.
Conclusions: Severe preoperative hemodynamic compromise associated with end-organ failure and major local tissue destruction requiring longer times for repair as well as postoperative nosocomial infections appear to be related with increased hospital mortality after surgical treatment of IE. Out initial experience, although statistically unsubstantiated, suggests early surgery to avoid critical preoperative status.

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LOW RATE OF EARLY VALVE SURGERY (EVS) IN *STAPHYLOCOCCUS AUREUS* (SA) NATIVE VALVE (NV) INFECTIVE ENDOCARDITIS (IE): CAN WE SOLVE THE CONUNDRUM?

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Background: Mortality of SA IE is high. Although EVS, surgery performed during the course of antibiotic treatment, is thought to improve the prognosis of IE, rates of EVS in SA NVIE are lower than in other subgroups. This study sought to identify potential explanations for these low rates of EVS in SA NVIE.
Methods: Of the 3,284 cases of IE that had been enrolled in the International Collaboration on Endocarditis-Prospective Cohort Study at the end of 2007, we extracted 1,502 cases of Duke definite left-sided NVIE that occurred in non-IVDUs. These included 392 cases of SA

IE and 1,110 cases of IE due to other pathogens (non-SA NVIE). Two-group comparisons and adjusted survival analysis were performed.
Results: Compared to non-SA NVIE, SA NVIE occurred more frequently in older subjects ($p = 0.01$). It was less often community-acquired ($p < 10^{-4}$), more frequently diagnosed within the first month of symptoms onset ($p < 10^{-4}$) and associated with comorbidities ($p < 10^{-4}$). SA NVIE was more often complicated with stroke ($p = 0.0009$) and emboli ($p = 0.008$). By contrast the frequencies of cardiac failure and intracardiac abscess were the same in the two groups. EVS and 60-day in-hospital mortality rate were lower (34.2% vs. 50.1%, $p < 10^{-4}$) and higher (26.5% vs. 11.9%, $p < 10^{-4}$), respectively. In multivariate analysis, when compared to non-SA NVIE: (1) the probability of EVS was significantly lower in SA NVIE (HR 0.66, 95 CI 0.54–0.80, $p < 0.0001$); (2) the probability of in-hospital death was significantly higher (HR 1.68, 95 CI 1.28–2.22, $p < 0.0001$), which was true both in operated and non-operated patients.
Conclusion: This study confirms that SA NVIE is associated with higher rates of comorbidities and mortality. It is also associated with a lower rate of EVS, which is neither explained by a higher frequency of comorbidities/complications that would contraindicate surgery nor by a lower frequency of conditions that would require surgery.

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SURGERY OF INFECTIVE ENDOCARDITIS IN PATIENTS WITH LIVER CIRRHOSIS: A DIFFICULT DECISION-MAKING PROCESS

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Objectives: To evaluate the outcome after surgery for infective endocarditis (IE) in patients with liver cirrhosis.
Methods: Consecutive patients with IE and cirrhosis from the prospective database of the Hospital Clinic IE Study Group between 1998 and 2008 were included. Modified Duke criteria used to diagnose IE and severity of cirrhosis established according to Child-Turcotte-Pugh classification. A descriptive analysis of patients undergoing surgery was performed.
Results: Out of 495 patients diagnosed of IE, 44 (8.9%) were found to have cirrhosis and 19 of them (43.2%) underwent 20 operations. There were 18 male and 1 female, median age 50.5 years (range 36–79). HCV infection was present in 13 (68.4%), 2 were HIV+ and alcoholic cirrhosis in 8 (42.1%). Child classification: A-6, B-9, C-4. Main pathogens were *S. aureus* (4) and coagulase-negative staphylococci (3). Two cases were culture-negative IE. On TTE/TEE, native aortic valve involved in 7, native mitral in 2, native tricuspid in 2, native aortic+mitral in 1, aortic prosthesis in 5, mitral prosthesis in 2 and VVI pacemaker in 1. Seven patients had perivalvular abscess and 5 aorto/cavitary fistula. Operations under extracorporeal circulation were elective (10), urgent (5) and emergent (5). Valve replacement included aortic (8), mitral (3), tricuspid (2), aortic root (3) aortic+mitral (3) and removal of multiple pacemaker leads (1). Replacement devices were mechanical bileaflet prostheses (3), bovine pericardial xenografts (10), cryopreserved aortic homografts (7) and cryopreserved mitral homografts (2). Associated procedures were CABG, replacement of the ascending aorta, PTFE cavoatrial bypass and splenectomy. Median preoperative additive EuroSCORE was 11 (5–19) with a median expected mortality of 27.6% (range 4–94%) according to logistic EuroSCORE. Two patients died in the operating room. Overall in-hospital mortality was 60%. Mortality according to Child classification was A – 50%, B – 56%, C – 75%. Two patients had no postoperative complications. Sepsis and multiorgan failure were the predominant causes of death.
Conclusions: The subset of patients with IE and liver cirrhosis is of highest surgical risk with a very high observed morbidity and mortality. EuroSCORE does not perform as an appropriate preoperative stratification score in these patients. Surgery has to be carefully indicated and probably should not be offered to those with advanced liver disease (Child C).

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PROSTHETIC VALVE INFECTIVE ENDOCARDITIS: HOW DOES TREATMENT STRATEGY INFLUENCE MORTALITY?

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Background: Decision making regarding surgical intervention in prosthetic valve endocarditis (PVE) is often complex, and surgery is withheld in a number of patients, either because medical treatment is considered best treatment or because the risk of operation is considered too high.
The aim of this study was to investigate outcome of surgical therapy for PVE compared to patients receiving conservative treatment with or without a definite indication for surgery.
Methods: In a prospective cohort study data from 101 consecutive PVE patients were collected at two tertiary University Hospitals in Copenhagen, Denmark. Patients were divided into 3 groups. (I) Receiving medical treatment alone without indication for surgery ($n = 41$); (II) patients receiving surgical and medical treatment ($n = 35$); (III) patients receiving medical treatment with a definite indication for surgery, but with a too high risk ($n = 25$).
Results: Patients receiving cardiac surgery were significantly younger compared to patients receiving medical treatment alone, (I) 68 years (15), (II) 60 years (13), (III) 74 years (9). No significant differences were found in comorbidity between patients in group I and II. Patients receiving medical treatment with indication for surgery were more likely to have kidney dysfunction compared to patients receiving surgical intervention [7 (28%) vs. 2 (6%); $P = 0.02$]. Patients in group II and III were significantly more likely to have intracardiac abscesses and pseudoaneurysms as well as heart failure compared to group I. *Enterococcus* (32%) was the most common microorganism causing PVE in group I. *Staphylococcus aureus* (20%) and Coagulase-negative *Staphylococcus* (29%) were the causative microorganisms in most cases in patients treated with cardiac surgery. In patients receiving medical treatment with indication for surgery the causative microorganisms most often identified were *Staphylococcus aureus* (20%) and *Enterococcus* (28%).
In-hospital mortality in group I (2%) was significantly lower compared to the two other groups II (26%) and III (24%). After 6 month 52% of the patients in group III were dead compared to 10% and 29% in groups I and II, respectively (log rank $P < 0.002$).
Conclusions: Our study suggests that a conservative treatment strategy is well indicated in a selected group of PVE patients. An expectant treatment strategy in patients with indication for surgery can be well indicated early on, but is associated with a high mortality if surgery is not performed.

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MID-TERM OUTCOMES OF MITRAL VALVE REPAIR IN ENDOCARDITIS

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Background: Despite advantages in therapeutic strategies, valve endocarditis remains associated with important morbility and high mortality rates. The objective of this study is to review the mid-term outcomes of mitral valve repair in endocarditis of our series for the last 4 years.
Methods: A total of 101 patients underwent cardiac surgery for valve endocarditis in two Hospitals over a 4-year period. Native mitral valve repair techniques were performed in 14 patients with radical resection of infectious tissue and reconstruction techniques with pericardial patch and annuloplasty. Mean follow up period of

25±14.8 months (range 48–2 months) and was complete. Mean age of 68.9 years, and 57% were male. *Staphylococcus* was the most commonly isolated source of infection (35%) follow by *Streptococcus* (21%) and *Enterococcus* (14%). Two patients had sterile blood and cardiac valve cultures.

Results: there were none in-hospital deaths and one late non-cardiac related death. Overall survival at 4 years was 92.8%. One patient had recurrent endocarditis at 6 months and one presented mitral insufficiency after 20 months, both were treated with valve replacement. Freedom from recurrent endocarditis or mitral insufficiency was 85.7%.

Conclusions: In our experience, surgical repair for isolated active mitral valve endocarditis is associated with excellent in-hospital mortality and mid-term outcomes.

Prophylaxis

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COLLAGEN-GENTAMICIN IMPLANT FOR PREVENTION OF STERNAL WOUND INFECTION; LONG TERM EFFECTIVENESS

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Background: Sternal wound infection (SWI) including mediastinitis after cardiac surgery is a serious cardiovascular infection with high reported mortality. Intraoperative prophylaxis with intravenous beta-lactam antibiotics is recommended and routinely applied. However, an increasing proportion of these infections are caused by staphylococci resistant to beta-lactam antibiotics. In a previous randomized controlled trial (LOGIP-trial) the addition of locally applied collagen-gentamicin reduced the incidence of postoperative sternal wound infections compared with intravenous prophylaxis only. Subsequently the technique with local gentamicin was introduced in clinical routine at our centres. The aim of the present study, the LOGIX-trial (ClinicalTrials.gov NCT00484055) was to re-evaluate the technique regarding a sustained effect on wound infections and potential shifts in microbiological findings over time.
Methods: In this prospective two-centre study all patients undergoing cardiac surgery via median sternotomy received prophylaxis with application of two collagen-gentamicin sponges between the sternal halves in addition to the routine intravenous antibiotics. The incidences of deep and superficial SWI within 60 days postoperatively were recorded and compared with the previous control group without local collagen-gentamicin.
Results: From Jan 2007 to May 2008 1359 patients were included. The total incidence of SWI was 3.7%. The incidences of all SWI and of deep SWI were significantly reduced compared with the control group, also after correction for other risk factors (OR = 0.34 for deep SWI, $P < 0.001$). The majority of SWI were caused by coagulase-negative staphylococci (CoNS), of which 80% were resistant to methicillin. Also 80% of the CoNS were resistant to aminoglycosides (gentamicin or tobramycin), but there was no increase in the absolute incidence of aminoglycoside resistant agents compared with the previous study. The incidence of SWI caused by *S. aureus* was 0.4% (0.07% deep SWI).
Conclusion: The results indicate a maintained effect of the prophylaxis over time without absolute increase in aminoglycoside resistance and without shifts in causative microbiological agents. The low incidence of SWI caused by *S. aureus* was particularly noteworthy. The extremely high local antibiotic concentrations achieved with local application of gentamicin may be effective against agents normally considered resistant.

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MEDICAL INTERVENTIONS, PROPHYLAXIS AND THE RISK OF INFECTIVE ENDOCARDITIS. DATA FROM THE ITALIAN REGISTRY OF INFECTIVE ENDOCARDITIS (RIEI)

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The prophylaxis of infective endocarditis (IE) is more based on custom rather than evidence. The restriction on the use of antibiotic prophylaxis proposed by the more recent guidelines is the expression of a more critical view of the scientific community on the real utility and efficacy of antibiotics in the prevention of IE. Due to the lack of prospective randomized studies, observational data are valuable for the study of the efficacy of IE prophylaxis.
Aim: To provide data from the Italian registry of IE (RIEI) on the incidence of medical interventions on the risk of IE and data on the failure of prophylaxis, when applied.
Methods: RIEI prospectively collects data on new cases of IE in Italy, by an Internet accessible database. Sixteen centres are participating, and variables are related to epidemiological, clinical, instrumental, prognostic, and therapeutic aspects of IE (1). Cases are consecutively enrolled. The quality and reliability of data are controlled by a central operator. Descriptive statistical data are reported on medical interventions before IE.
Results: Data are available on 267 patients with a definite IE (mean age 60 ± 15 years, 152 males).
Before IE, dental procedures were observed in 18 (6.7%) with prophylaxis done in 8 (44%). Non dental procedures were 39 (15%) with prophylaxis in 18 (46%): 9 cardiac surgery*, 5 cardiac catheterism*, 7 PM/ICD implantation*, 3 central venous line*, 5 gastrointestinal, 4 genito-urinary, 2 general or ortopedic surgery, 2 arthro-lumbar puncture; prophylaxis was done respectively in 7 (78%), 0, 5 (71%), 2 (67%), 1 (20%), 2 (50%), 1 (50%), 0. Intravascular access were observed in 43 cases (16%): endocavitary devices 17, other 26.
Comments and Conclusions: In the absence of randomized studies, these data suggest that dental and non-dental interventions may be responsible of a limited number of cases of IE, while more than 3 of 4 cases are not related to medical interventions. Antibiotic prophylaxis is often not efficacious before interventions either dental or not, especially before endovascular intervention (*), the commonest in Italy. Overall, data from the RIEI justify the restriction of the indication to prophylaxis of IE as recommended by recent guidelines.

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INFECTIVE ENDOCARDITIS IN LEFT-SIDED VALVES AFTER DENTAL PROCEDURES

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Aim: To analyze influence of previous dental procedures (DP) in episodes of left-sided infective endocarditis (IE).
Methods: We analyzed 725 consecutive episodes of IE, 601 of which were located in left-sided valves. They were prospectively recruited at four tertiary referral centers between 1996 and 2008. We established 2 groups: Group I ($n = 52$), episodes of left-sided IE after DP, and Group II ($n = 549$), episodes of left-sided IE without history of a previous DP.
Results: Males were more frequent in Group I (80.8% vs 61.6%; $p = 0.006$) without differences in distribution of age. In Group I

community acquired infections and antibiotic prophylaxis were more common (17.6% vs 12.3%; p = 0.001). Although the prevalence of previous cardiac disease was similar in both groups, mixoid valves were more frequent in Group I (12.5% vs 3.2%; p = 0.002). No differences were observed in previous comorbidity, except a lower rate of immunodepression in Group I. At admission, fever, lumbalgia, mialgia and artralgia were more common in Group I. S viridans (34.7% vs 13.1%; p = 0.000) and negative cultures (24.5% vs 13.3%; p = 0.032) were more frequent in Group I, whereas *S. aureus* (6.1% vs 19.9%; p = 0.018) was isolated more rarely. During hospitalization, septic shock (0% vs 17.5%; p = 0.001), persistent infection (9.1% vs 29.6%; p = 0.012), heart failure (34.4% vs 55.4%; p = 0.023), and IE related death (50% vs 88.5%, p = 0.028) were less frequent in Group I. The need of cardiac surgery was similar in both groups.

Conclusion: Infective endocarditis after a dental procedure was common in this series. No differences in previous cardiac disease were observed between patients with and without a previous dental procedure. Complications during hospitalization were less frequent. This results suggest that antibiotic prophylaxis before a dental procedure should be reevaluated.

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CUMULATIVE DENTAL BACTERAEMIA: A NEW APPROACH

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Background: The mouth is an important reservoir of bacteria causing Infective Endocarditis (IE). Approximately 50% of cases of IE are caused by oral *Streptococcus* species. Conventional broth cultures provide the percentage prevalence and species identity. Lysis Filtration provides the prevalence and identity and in addition the number of colony forming units of bacteria/ml of blood.

Methods: Data were entered into a spreadsheet. These were (1) % Prevalence [%Prev], (2) Intensity, cfu/Litre blood [cfu/L], (3) Cardiac Output [CO], (4) Duration of procedure [DProc], (5) Duration of post procedure bacteraemia [DBac], (6) Frequency of procedure [FrProc]. This estimates the number of bacteria passing through the heart.

Results: Thirty five calculations were carried out showing the high number of bacteria from everyday procedures (table).

	Procedure	
	Single extraction	Tooth brushing
(1) % Prevalence	38.7	19
(2) cfu/Litre	1.3	390
(3) CO L/min	4	4
(4) Duration procedure	2	1
(5) Duration bacteraemia	11.25	11.25
(6) Freq Proc per annum	0.04	730
Cumulative frequency event(s)	181	243,418,500 (243×10^6)
Cumulative index	1	1,344,853 (1.34×10^6)

Conclusions: Everyday procedures such as tooth brushing result in 1.34×10^6 bacteria passing through the heart during one year. This is over a million times greater than the number from a single extraction. This is just one example illustrating the surprisingly large number of bacteria that enter the blood stream following 'everyday procedures'.

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ENDOCARDITIS PROPHYLAXIS & FATAL ANAPHYLACTIC REACTIONS ASSOCIATED WITH AMOXICILLIN REPORTED VIA THE YELLOW CARD SCHEME IN THE UK

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Background: Since recent UK guidance no longer recommends antibiotic prophylaxis of endocarditis, there is renewed interest in the number of deaths from anaphylaxis after amoxicillin use, the main agent recommended previously for preventing endocarditis after dental procedures.

Method: A search of the Medicines and Healthcare Products Regulatory Agency's database on suspected amoxicillin associated anaphylactic reactions voluntarily reported via the Yellow Card Scheme in the UK between 01/07/1963 and 10/10/2008 was performed.

Results: Anaphylactic reactions were reported in 273 cases, 12 of which were fatal: 69% of the reports followed oral amoxicillin. Of the fatal anaphylactic reactions, 3 following oral amoxicillin and 7 following intravenous route of administration; in 2 cases the route was unknown. None of the cases had amoxicillin for endocarditis prophylaxis. Amoxicillin is used extensively: approximately 100 million courses of oral amoxicillin were given in the UK during a 5 year period up to 2007. Yellow Card data cannot be used to calculate the incidence of a particular adverse drug reaction as denominator data are not available, and causality is not certain. Anaphylaxis is a known adverse reaction to amoxicillin, and there is under-reporting of known adverse reactions even if severe, in addition to under-reporting in relation to long-established products such as amoxicillin.

Conclusion: This data provides circumstantial evidence that fatal anaphylaxis after oral amoxicillin may be extremely rare and also less frequent than earlier estimates for parenteral penicillin. Good studies to determine the incidence of fatal anaphylaxis following oral amoxicillin are required.

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INFECTIVE ENDOCARDITIS FOLLOWING UROGENITAL AND GASTROINTESTINAL PROCEDURES. A SEVEN YEAR SURVEY

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Background: In the 2007 guidelines, gastrointestinal (GI) and urogenital (UG) procedures were excluded from the list of procedures for which prophylaxis is recommended.

Methods: Our two previous series of patients with infective endocarditis (IE) including 212 episodes during 7 years were retrospectively reviewed for cases of IE that developed following an invasive procedure.

Results: Twenty cases (9% of 212) had an invasive GI or UG procedure within 3 months preceding admission for IE. The procedures included: Foley catheter insertion and/or manipulation, urologic surgery, biopsy of prostate, intestinal surgery, colonoscopy with or without resection of colonic polyp, and labor. Twenty two pathogens were recovered from these 20 cases, 16 (80%) of which involved enteric organisms with *Enterococcus faecalis* being the most common (14 cases). Thirteen of the 20 procedures were performed during a recent previous hospitalization. Underlying cardiac conditions included prosthetic valves in 9 (45%) cases, and other valvular heart disease in 6 (30%). In-hospital mortality was 25% (5 of 20).

Conclusions. GI and UG procedures pose a non negligible risk for acquisition of IE, with *Enterococcus faecalis* constituting the most common pathogen (70%). In spite of the uncertainty of the usefulness of IE prophylaxis in general, it is recommended here, that people at high risk to develop IE, who are entitled to receive standard surgical prophylaxis for GI or UG procedures (often given cephalosporins or fluoroquinolones), receive prophylaxis that includes an anti-enterococcal agent. It is suggested that such an amendment be added to the guidelines for IE prophylaxis.

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INFECTIVE ENDOCARDITIS CAUSED BY *GEMELLA SANGUINIS*

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Background: 23 year old male patient with Behçet's disease and repaired VSD and aortic valve diagnosed to have infective endocarditis due to unusal organism.
Case summary: 23 year old with Behçet's disease and repaired VSD and aortic valve presented with fever and abdominal pain. CT abdomen showed wedge infarction of the kidney. TEE confirmd presence of large vegetation in the aortic valve. Blood culture grew *Gemella sanguinis* after sent to refrence lab. Patient was treated with ceftriaxone and responded clinically and microbiologically. 4 weeks later he developed new ischaemic insult to his right Ring finger and new infarcion in the kidney. It was attributed to hypercoagulable state caused by active Behçet's disease and patient started on anticoagulation. Few days later patient developed intracerebral bleeding which led to his demise.
Conclusion: This is only the 3rd case of infective endocarditis caused by *Gemella sanguinis*. It caused a big vegetation and probably was complicated with cerebral mycotic aneurysm. Mouth ulcers caused by Behçet's disease is the most likely port of entry for the bacteremia and endocarditis caused by *Gemella sanguinis* in our patient.

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SIMULTANEOUS THROMBOSIS AND ENDOCARDITIS OF A MITRAL VALVE PROSTHESIS

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Background: Both infectious endocarditis and prosthetic valve thrombosis are rare diseases, and simultaneous occurence is even rarer. We present here a case of simultaneous culture negative endocarditis and thrombosis of a mitral valve prosthesis.
Case report: A 56-year-old man was admitted to the intensive care unit in shock. Twelve months previously he had undergone mitral valve replacement for degenerative mitral regurgitation, and pacemaker implantation for atrioventricular conduction disturbances. Two months before presentation, non-diabetic neuropathy had led to osteomyelitis of several toes for which amputations were necessary. Penicillin susceptible Corynebacteria were cultured. Administration of antivitamin K was interrupted for a number of days around the surgical procedure.
At admission the patient was soporific but agitated, afebrile and in shock. Prosthetic valve sounds were inaudible. Transesophageal echocardiography (TEE) demonstrated almost complete immobilization of both prosthetic valve leaflets resulting in severe mitral stenosis with a mean pressure drop of 18 mmHg and moderate valvular regurgitation. Thrombotic material was seen on the prosthesis. The pacemaker wires were free of vegetations.
Initial treatment consistend of alteplase which resulted in rapid clinical improvement. Prosthetic valve sounds rapidly returned to normal. Repeat TEE showed normal prosthetic valve motion and no obstruction to flow or regurgitation anymore, but vegetations were seen on the atrial side of the prosthesis. All blood cultures remained sterile. High dose penicilline and gentamicin were given for 6 and the first 2 weeks, respectively, and the patient recovered completely. TEE demonstrated disappearance of the vegetations. At 6-month follow-up the patient was doing well.
Conclusion: Interuption of anticoaculation and toe osteomyelitis resulted 2 months later in simulaneous prosthetic valve endocarditis and thrombosis. Preventive measures should have been taken more seriously.

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ENDOCARDITIS TREATMENT AND ANTIBIOTIC HYPERSENSITIVITY

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We describe a case of a staphylococcal endocarditis in a young man with therapeutical challenges due to polyallergy.
C.C.T., a 36 year old white male, was admitted in our unit complaining cough, fever, dispnoea. He was previously treated for interstitial pneumoniae with azithromicin and corticosteroids. He performed several trips in South America. His medical history was inespressive, physical examination negative, except for a mild increase of the first tone in the aortic focus.
In a TC-scan we observed an hypodense area (2.6 cm in diameter) in the posteroinferior splenic pol, compatible with a splenic infarct.
Because of the early development of Gram + cocci from a blood culture, we began an empiric therapy with vancomicin and rifampin. These drugs were soon stopped because of the development of cutaneous allergy. In the meantime multiple blood cultures drawn in the first days of hospitalisation became positive for *S. aureus* oxacillin-sensitive.
A transtoracic and transesophageal ecocardiography showed a dilated cardiopathy and multiple vegetation on the aortic valve. Before starting a new therapy, we consulted an allergologist, that prescrived a desensitization trial with amoxicillin/clavulanate, followed by a full dose treatment with amoxicillin/clavulanate plus ampicillin and gentamycin. During the tenth day of therapy the patient developed a new rash, so we decide to stop this therapy and start linezolid. Morover we observed another embolic complication in an hand vessel (echocolordoppler diagnosis). Besides that, another total body scan was performed and it showed a new infarctual area in the spleen.
For these reason the patient was transferred to the cardiosurgery unit, where the native aortic valve was substituited with a bioprostesis (mod. Carpenter Edwards 27 mm). The post-surgical course was uneventful and the patient was discharged after an antibiotic course with linezolid and imipenem.
The follow-up did not show any complication and the patient now is in good health althought he has to continue a cardiologic therapy.
In these report we underline the young age and the lack of risk factors of the patient, the early occurrence of embolic complications and the necessity of several drug-switches due to allergy.

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EARLY POST OPERATIVE ENDOCARDITIS (IE) CAUSED BY TOXIGENIC *CORYNEBACTERIUM DIPHTHERIAE* (Cd) IN A CHILD WITH TOTAL ATRIAL SEPTAL DEFECT (ASD)

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Background: Endocarditis caused by *C. diphtheriae* (Cd) is an uncommon condition. It is important in the pre-operative management to optimize prophylactic measures to avoid post operative infections. In paediatric patients, immunization is particularly important. In a recent review about *Corynebacterium* endocarditis caused by toxigenic strains, IE was associated with pediatric infections ($p < 0.001$) and decreased survival ($p = 0.001$).We describe a case of Cd IE which occurred post operatively.
Case report: A 7-year-old girl was admitted to have a recently diagnosed total ASD corrected. She was discharged 11 days post-operatively. A routine transthoracic echocardiogram (TTE) 3 months later showed persistent pulmonary hypertension (PAP = 130 mmHg). Four and a half months later she was re-admitted due to breathlessness, chest pain and fever of acute (2 days) onset. Blood cultures (5 of 6 bottles) showed a Gram-positive, aerobic, coryneform-

like bacillus identified by a reference laboratory as *Corynebacterium diphtheriae*. A TTE showed a vegetation on the septal leaflet of the tricuspid valve. Her mother informed then that she had incomplete immunization. She had been given vancomycin and amikacin for 3 weeks, and this treatment was changed to aqueous penicillin plus gentamicin. She improved on the following week of switch therapy. Results of toxin production were available 3 weeks later, and she was given 80,000 IU diphtheria antitoxin and carnitine. However, she developed metabolic acidosis, shock and renal failure. She died from cardiac and renal failure 1 month after admission.
Conclusion: Pre operative knowledge of immunization status is essential in the management of pediatric patients before cardiac surgery.

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DIFFICULT DIAGNOSIS OF INFECTIVE ENDOCARDITIS (IE) WITH A MASK OF AN HEMATOLOGY DISEASE: REPORT OF A CASE

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Background: Diagnosis of infective endocarditis (IE) remains rather difficult because of the non-specific clinical signs such as weakness, fatiguability, fever, multiorganic dysfunction. We report a case of IE, at first admission presented with symptoms and signs of osteomyelofibrosis.
Case report: A 34-year-old man admitted with six-month history of subfebrile condition, losing weight, dyspnea, clinical signs of hemostasis system dysfunction such as nasal bleeding, conjunctival hemorrhage. Computer tomography of abdominal organs revealed hepatosplenomegaly, focal formations of liver and spleen. The patient was examined by oncologist and an oncological process was excluded. The patient had critical anemia (hemoglobin 52 g/l, erythrocyte count 2.3×10^{12}/l), severe leukopenia (leukocytes 1.8×10^{9}/l), thrombocytopenia (thrombocytes 80×10^{9}/l), thrombocyte hypoaggregation and hypocoagulation. Trepanobiopsy showed severe cell impoverishment of red bone marrow with multiple hemorrhages. Transesophageal echocardiography discovered 8.3 mm-, and 8.2 mm-vegetations of the aortal valve and 19.8 mm-vegetation of the mitral valve. All blood cultures showed *Streptococcus haemolyticus* (*S. pyogenes*). The patient was treated for IE with intravenous cefepime, 4000 mg a day. After 6 weeks of treatment all hematological values went to subnormal level (results of common blood analysis: hemoglobin 89 g/l, erythrocytes 3.4×10^{12}/l, leukocytes 7.8×10^{9}/l, thrombocytes 150×10^{9}/l) with decreasing of IE activity, that shows the second character of red bone marrow damage. After that an elective open heart-surgery was performed. It confirmed infective endocarditis with a 20 mm-vegetation of the mitral valve with damage of its anterior leaflet and 10 mm- and 12 mm-vegetation of the aortic valve. A replacement of the mitral and the aortic valve had to be performed. The intravenous treatment with imipenem was continued for 30 days. All hemostasial values went to normal level in 15 days and other hematological parameters – in 30 days.
Conclusion: the case showed a difficult diagnosis and successful treatment of IE with a mask of an hematologic disease.

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PROSTHETIC VALVE ENDOCARDITIS (PVE) CAUSED BY LANCEFIELD GROUP C *STREPTOCOCCUS*

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Lancefield Group C *Streptococcus* is a rarely reported cause of Infective Endocarditis (IE) on native or prosthetic valves. We report the case of a 61-yr-old male three years post aortic valve replacement (AVR) and aortic root replacement with a Group C *Streptococcus* prosthetic valve endocarditis (PVE) and aortic root abscess. The patient had undergone a routine dental procedure 4 months prior to presentation and not received antibiotic prophylaxis as recommended in the most recent NICE guidelines published 2008. At presentation the patient gave a four day history of sweats, rigors and arthralgia. Group C *Streptococcus* was isolated from both bottles of 1 set of blood cultures taken on the day of admission. The isolate was penicillin and ceftriaxone sensitive with a minimum inhibitory concentration (MIC) of 0.016 mg/L and 0.064 mg/L respectively. Transoesophageal Echocardiogram (TOE) on admission showed a vegetation on the prosthetic Aortic Valve (AV) and dilatation of the aortic root.
The patient was initially treated with high dose intravenous (IV) benzylpenicillin and gentamicin. However, his treatment course was complicated by a hypersensitivity reaction to penicillin after three weeks treatment. As a result, treatment was changed to IV ceftriaxone. Despite an eight week intravenous course of antibiotics and full resolution of symptoms, the patient's repeat TOE showed a persistently dilated and thickened aortic root. He therefore underwent a redo AVR and aortic root replacement. His post-operative course was uneventful and the patient remains well. Culture of prosthetic aortic valve at time of explantation was negative.
The patient has opted for antibiotic prophylaxis during future dental procedures. The importance of reporting unusual bacterial cases of IE is stressed in light of recent changes in antibiotic prophylaxis guidelines.

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INFECTIVE ENDOCARDITIS (IE) CAUSED BY *SALMONELLA ENTERITIDIS* IN A ELDERLY PATIENT WITH AN AORTIC BIOPROSTHESIS

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Background: IE caused by Enterobacteriacea is uncommon. A case involving an aortic bioprosthesis (AP) with a rapidly progressive course is described.
Case report: A 73-year-old male, with a 6-year-old AP, presented with an 8-day history of high fever and prostration. He denied dyspnoea, cough, vomiting, diarrhea or abdominal pain. He denied eating or drinking unusual or suspicious food or water. He denied animal contact or recent trips. On physical examination, he was febrile and anaemic. A pansystolic murmur was audible in the mitral and aortic areas; bp, 120/80 mHg, hr, 88 bpm. Crackles were heard on the right lung base. Blood cultures (BC) were drawn and intravenous (IV) cefuroxime (CXM) started. TEE showed a 0.5 cm vegetation on the AP. BC were positive with *S. enteritidis* and treatment was changed to IV ciprofloxacin (day 4). On day 5, he became dyspnoeic at rest; his fever relapsed (38.5ºC). On day 7, he developed a bradyarrhytmia and hypotension, and had a rapidly reversed cardiac arrest. He was entubated and ventilated, and a transcutaneous pacemaker was inserted. A bedside TEE showed a peri-prosthetic abscess. Few hours later he had another cardiac arrest and died before the surgical team was ready in theatre.
Conclusion: IE caused by *Salmonella* is a rare event; this was the first case documented in our hospital. A classical epidemiological history for *Salmonella* acquisition is lacking. Cases in the literature show predilection of *Salmonella* for the aortic position and high mortality, surgery being recommended early.

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TUBERCULOUS ACUTE AORTIC INSUFFICIENCY AND VALSALVA SINUS ANEURYSM IN A CHILD

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Background: Tuberculosis (TB) is highly endemic in Rio de Janeiro, with an incidence above 100/100,000 persons-year. Pericarditis is reported occasionally; myocarditis and especially endocarditis are rare. Infectious acquired Sinus of Valsalva (SV) aneurysms may be due to bacterial or tuberculous endocarditis and syphilis.

Case report: A 9-year-old girl presented with progressive dyspnoea and heart failure (HF) in 2 months. There was no history of fever, weight loss or malaise. Physical examination showed a new murmur of aortic regurgitation (AR). A transthoracic echocardiogram showed severe AR, left ventricular systolic dysfunction and ectasia of the SV. She was managed with vasopressors, diuretics and captopril. A chest tomograph scan showed pulmonary apical images highly suggestive of TB. Family history revealed that her father had been treated for pulmonary TB the previous year. Patient sputa were negative for acid fast bacilli. Rifampin, isoniazid and pyrazinamide were started and she was discharged 3 weeks after admission. She returned 2 weeks later, with acute HF. A transesophageal echocardiogram showed worsened AR and an aneurysm of the SV. She was operated for aortic valve replacement and SV aneurysm resection. In the immediate post operative period she developed refractory cardiogenic shock and died 48 hours later. Sputum culture grew Mycobacterium tuberculosis. Valve histopathology showed valvulitis with a lymphocityc infiltrate.
Conclusion: This case report illustrates that in a highly endemic area for TB, this etiology must be thought of in cases of VS aneurysms and acute aortic insufficiency, even if the patient has no systemic symptoms of infection.

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PROSTHETIC VALVE ENDOCARDITIS AND SPONDYLODISCITIS DUE TO MRSA WITH BORDERLINE MIC TO VANCOMYCIN – A CASE REPORT

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Background: Infections due to methicillin resistant *Staphylococcus aureus* have been reported increasingly throughout the world. Cases of severe sepsis caused by this pathogen still present therapeutic challenge. Monotherapy with vancomycin seems to be insufficient, due to high rate of treatment failures and growing number of infections caused by isolates with reduced vancomycin susceptibility.
Case report: We describe a case of 67 year old diabetic patient with implanted prosthetic aortic valve, mitral biologic valve and pacemaker who was admitted due to MRSA bacteremia and infective endocarditis on mitral biological valve. The isolate was resistant to methicillin and susceptible to non beta-lactam antibiotics. After 46 days of successful treatment with vancomycin and rifampin the patient was discharged with trimethoprim-sulfamethoxazole for another month. Only three days after completed antibiotic treatment the patient was readmitted due to MRSA bacteremia, complicated by endocarditis on prosthetic aortic valve, paravalvular abscess near mitral valve and spondylodiscitis of thoracic spine. Initial treatment with vancomycin was discontinued due to persistent bacteremia. MIC for vancomycin was 4 mcg/ml. Daptomycin was initiated and mitral and aortic valve replacement surgery was performed. Despite apparent initial success of this treatment a recurrence of bacteremia and endocarditis occurred. Re-operation was not possible due to various complications. Bacteremia persisted even after three months of various antibiotic combinations resulting in septic shock with fatal outcome.
Conclusion: Failure to treat our patient in whom combined antibiotic therapy and surgery was employed, proves again that current therapeutic options for treating complicated cases of MRSA bacteremia and endocarditis remain suboptimal.

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***ALCALIGENES XYLOSOXIDANS* MITRAL NATIVE VALVE ENDOCARDITIS SECONDARY TO CATHETER-RELATED BACTERAEMIA ONE YEAR BEFORE**

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A 50 year-old man presented with fever and blood cultures positive for *Alcaligenes xylosoxidans* 11 months after the implantation of a permanent jugular catheter for hemodialysis. Transthoracic echocardiography (TTE) did not demonstrate vegetations. Catheter was removed and meropenem was administered for 14 days. Later, he had several bouts of culture sterile postdialysis fever at months 3, 5 and 9 that seemed to respond to vancomycin. At month 11 he again presented high fever and blood cultures positive to *A. xylosoxidans*. The hemodialysis catheter was removed and meropenem was administered for 14 days; again TTE was negative. Five days after finishing antibiotics he presented with fever, sepsis and blood cultures positive to A xylosoxidans; transesophageal echocardiography demonstrated an 1.4×1.3 cm vegetation on the posterior leaflet of the mitral valve. Congestive heart failure did not happen. With the diagnosis of endocarditis by A, xylosidans, meropenem was given on the basis of the results of disk susceptibility testing. On the third day trimethoprim-sulfamethoxazole was added because of persistant bacteraemia. As recurrent bacteraemia was detected at days 7 and 12 a mitral valve replacement was performed on day 16. After 48 hour he died because of post-surgical complications. Mitral valve culture was positive for *A. xylosoxidans*.
Catheter-related bacteraemia is the most commonly reported infection by *A. xylosoxidans*. Endocarditis has been only described in five previous cases, but our patient is unique because the patient suffered a catheter related bacteraemia and several bouts of postdialysis fever one year before endocarditis diagnosis. *Alcaligenes* probably colonized the new hemodialysis catheter and led to low grade bacteraemias finally affecting the mitral valve.
Although treatment of *A. xylosoxidans* is not standarized, currently trimethoprim-sulfamethoxazole, cabapenem and antipseudomonal penicillins are considered the agents of choice. Some authors have suggested that combination therapy may be necessary for serious infections. In this patient combination therapy was administered since 3th day of treatment, but blood and valves cultures were persistently positive.

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FATAL ENTEROCCAL ENDOCARDITIS COMPLICATING A *CANDIDA PARAPSILOSIS* ENDOCARDITIS FAILING TO CASPOFUNGIN PLUS FLUCONAZOL

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A 49 year-old man presented with fever and blood cultures positive for *Candida parapsilosis*. He had history of intravenous drug use, HIV infection (CD4 450/mm3, suppressed viral load) and Child-Plough A cirrhosis (HCV). Liposomal amphotericin B was initiated (3 mg/kg). Transthoracic echocardiograms (TE) showed a 31×24 mm vegetation in the mitral valve. At day 5 of treatment he developed acute renal impairment (serum creatinine [SC] 2.5 mg/ml), with nephrotic symdrome. Amphotericin was stopped and a combined therapy with voriconazole and caspofungin (100 mg/day without loading dose) was administered. On day 10th *C. parapsilosis* grew. Heart surgery was refused due to the patient's poor clinical condition. The level of SC increased to 5 mg/dl. Glomerulonephritis was treated with steroids. 10 days after the combined administration of caspofungin and

voriconazole, a negative blood culture was obtained and subsequent blood cultures were consistently negative. Follow-up TE showed partial resolution of the vegetation (1x 0.6 mm). Improvement of the nephrotic syndrome was observed. On the 35th day *Enterococcus faecalis* grew in blood cultures. Catheter was removed and ampicilin was administered. Seven days later, he developed acute infarct in the left middle cerebral artery territory and 48 hours after he developed a contrallateral stroke and he died. Necropsy revealed a large vegetation of 3×2 cm size in mitral valve and embolic damages in cerebral tissue.Vegetation cultures were positive for *C. parapsilosis* and *E. faecalis*. Cultures of cerebral biopsy was positive for *E. faecalis* but negative for fungus.

In this patient, combination caspofungin and voriconazole therapy was an alternative because of the renal insufficiency. The choice of the 100 mg dose of caspofungin has been suggested, with a rationale that a higher daily dose could enhance the concentrations on target sites. The sterilization of blood cultures and the decreasing size of the vegetations showed supports initial efficacy. Surgery was firstly refused due to the poor clinical condition, later it was not performed because of lack of surgical criteria (with the exception of the etiologic agent, a controversial point). A catheter related bacteraemia by *E. faecalis* led to vegetation colonization and probably influenced the embolization, since the higher incidence of embolic events occurs in the early course of endocarditis.

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CARDIAC TUBERCULOMA. A CASE REPORT

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Background: Tuberculosis is a worldwide high prevalent infection that involves most common lungs. Except for pericardial disease, cardiac tuberculosis is very uncommon.

Methods: We described a patient from Pakistan, resident in Spain for the last 6 year, that presents as a cardiac neoplasm but that finally was diagnosed as cardiac tuberculosis (cardiac tuberculoma). We have reviewed the cases of cardiac tuberculosis other than pericardial affectation (PubMed with the topic "cardiac tuberculoma") and we have found 56 references (2 from Spain).

Case: A 48 year old Pakistani woman had been diagnosed of sternal tuberculosis in December 2005. She had fever, weight loss and pain bone for the 3 past week period. A thoracic TAC revealed a breastbone mass and *M. tuberculosis* was isolated by biopsy. HIV infection was excluded and the patient received treatment with RFP + INH + PZ for two months plus RFP + INH for 7 months. After 9 months a new thoracic TAC was performed and no mass was observed. The patient remained fine to June of 2008 that started with anorexia, progressive weight loss and low grade fever. Two days before Hospital admission, she presented palpitations, fatigue and discomfort. EKG showed an atrial flutter. A chest radiography was normal. Amiodarone therapy was administered and she recovered. A transesophageal echocardiography revealed a great and homogeneous mass, located in the atrial right. A cardiac MRI confirmed the presence of a mass adhered to the right atrium wall. A diagnosis of possible lymphoma vs sarcoma was made and a surgical procedure was performed. The surgeon informs that pericardium was infiltrated. The right atrium showed a hard consistency mass of 6×6 cm that infiltrated the walls. Several samples of the mass and the pericardium were obtained. The pathologic examination showed epithelioid and Langhans giant cell granulomas with central caseating necrosis consistent with tuberculosis. *Mycobacterium tuberculosis* was isolated from urine culture sample. The patient started treatment with RFP + INH + PZ + ETB plus prednisone with clinical improvement.

Conclusions: Tuberculoma of the heart should be considered as cause (unusual) of cardiac mass.

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ACUTE ENDOCARDITIS DUE TO *PASTEURELLA* SPP. IN AORTIC PROSTHESIS: CASE REPORT

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Introduction: *Pasteurella* genus bacteria are gram-negative coccobacilus that colonize canine and feline oral cavities. In humans, they are associated to soft tissue infections following dog or cat bites, but systemic infection cases such as pneumonia, osteomyelitis and endocarditis were also described. We describe a severe case of aortic prosthesis endocarditis due to *Pasteurella* spp. complicated by perivalvular abscess.

Report: A 32 year-old patient, cowboy, living in Jordânia-MG, with previous biological aortic prosthesis due to rheumatic cardiopathy. At hospital admission, he had fever for 8 days, myalgia, jaundice, abdominal pain and diarrhea. He had been in direct contact with a litter of cats 10 days prior to the onset of the condition. During the physical exam he was jaundiced, with tachycardia and tachypnea, had systolic murmur (4+/6+) and pain to palpation of the right hypochondrium. A transesophageal echocardiogram did not show vegetations and empiric ceftriaxone and oxacillin were prescribed. He had partial improvement in the first week, maintaining daily febrile peaks. *Pasteurella* spp. was identified in 4 hemocultures and the antibiotic was changed to ampicillin/sulbactam. After 10 days, still febrile, he showed onset of orthopnea. A new ECG revealed a 1st degree ventricular atrium blockade (VAB), and a transesophageal echocardiogram showed an image compatible to perivalvar abscess. He underwent surgery for valvar replacement leading to the remission of the fever and dyspnea. He was discharged from hospital after 6 weeks of ampicillin/sulbactam treatment by intravenous route.

Discussion: In literature, there are 33 cases descriptions of endocarditis due to *Pasteurella* spp. but only four in valve prosthesis. The described lethality is 35% and the need for valvular replacement 29%. In 50% of the previous reports, a prior close contact with cats or bites was described. Probably, the therapeutic success in this case was due to the association of early specific antibiotic therapy with valve replacement surgery. Although rare, *Pasteurella* spp. must be considered as an etiology for infectious endocarditis, particularly when faced with a suggestive epidemiologic antecedent.

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RELAPSING ENDOCARDITIS DUE TO *GRANULICATELLA ADIACENS*

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A 75-year-old woman, with mild COPD, osteoporosis and hypertrophic cardiomyopathy presented a history of fever and cough during the last few days. The clinical findings at the emergency ward included fever >38.0ºC, somnolence, tachypnea (20/minute), a systolic heart murmur and infra-scapular crepitations to the left. A raised CRP, 88 mg/L was noted. After samples for blood cultivation were taken, she was given cefuroxime IV. Preliminary diagnosis was pneumonia and a subsequent bedside chest X-ray confirmed a left dorsal infiltrate. On the day of transferral to the geriatric clinic, gram-positive cocci were observed in each of the four blood cultivation bottles. The condition was now reassessed as an infective endocarditis. The patient quickly recovered clinically, a trans-thoracic echocardiography was performed 12 days after admission, showing no vegetations. The gram-positive cocci were identified by PCR/16 S rRNA as *Granulicatella adiacens* (MIC for benzylpenicillin = 0.125 μg/ml). The patient returned home with advanced home care providing with ceftriaxone. The IV antibiotics were discontinued after a total of four weeks.

At follow-up after two months, samples of blood culture was performed and gram-positive cocci were later isolated. The patient was transferred to the Clinic of Infectious Diseases. On admission her temperature was 37.8ºC, a systolic heart murmur was noticed,

C-reactive protein was 15 g/l. Antibiotic treatment in form of benzylpenicillin (MIC 0.125 μg/ml) and gentamicin was initiated. Transesophageal echocardiography revealed a vegetation 0.5 cm in diameter on the mitral valve. In total 6 of 6 blood culture bottles grew gram-positive cocci, identified by PCR/16 S r RNA as *G. adiacens* (MIC for benzylpenicillin = 0.125 μg/ml). Combination antibiotic treatment with benzylpenicillin and gentamicin was continued for 2 weeks at with benzylpenicillin alone for another 2 weeks. Dental examination revealed a periapical osteitis and dental extraction was made. At follow-up three weeks after antibiotic treatment was completed the patient had no fever and blood cultures showed no growth. *G. adiacens* is a member of nutritionally variant streptococci (NVS) It is related with high bacterial failure a high rate of relapse after therapy and higher mortality. This patient with hypertrophic cardiomyopathy, a risk factor infective endocarditis, relapsed on single treatment with ceftriaxone; this shows that combination therapy is needed.

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