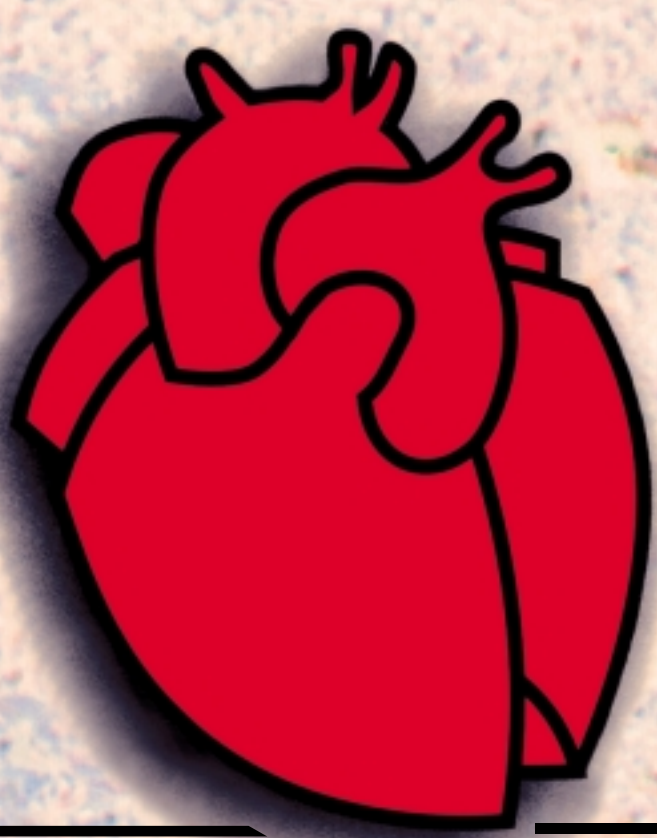

6 SIXTH INTERNATIONAL SYMPOSIUM ON MODERN CONCEPTS IN ENDOCARDITIS AND CARDIOVASCULAR INFECTIONS

June 27 - 29, 2001
Meliá Gran Sitges Hotel
Sitges (Barcelona), Spain

Joia de la Mediterrània

Final Programme and Book of Abstracts

Organised by

The International Society of Cardiovascular Infectious Diseases (ISCVID)

and

Infectious Diseases Services from

Corporació Sanitària CLÍNIC

Hospital Clínic i Universitari, (Barcelona, Spain)

Vall d'Hebron Hospitals

Hospital Vall d'Hebron, (Barcelona, Spain)

Index

Welcome address

Dear colleagues:

On behalf of the International Society of Cardiovascular Infectious Diseases (ISCVID) I take this opportunity to welcome you to the 6th International Symposium on Modern Concepts in Endocarditis and Cardiovascular Infections to be held in Sitges (Barcelona, Spain) on June, 27th -29th, 2001.

This symposium is an excellent opportunity to meet specialists of infectious disesases, cardiologists, microbiologists, pathologists and cardiovascular surgeons to discusss information on basic and clinical research on the pathogenesis, epidemiology, diagnosis, prevention and therapy of infectious endocarditis and other vascular infections, on the prevention and management of infections in cardiovascular surgery and in heart transplantation. In addition, studies of new antimicrobial agents and new surgical techniques, the therapy of multiresistant bacteria, the role of Chlamydia infection in vascular disease and the management of prosthetic and pacemaker infections will be presented. All this information will be given in state-of-the-art lectures, round tables, symposia and original slide and poster presentations. Participants will come away with valuable information to take back to their daily work to improve their research and management of cardiovascular infections.

Sitges, the place where the Symposium will take place, is a beautiful Mediterranean village close to Barcelona (Spain) with an excellent climate, hotel, beaches, golf resorts and gastronomy and with an old history and intensive cultural life you may experience. There will be a shuttle bus service from the Barcelona Airport to the Congress venue on 27th & 29th June. Many social events and tours have been designed for all the participants and for the accompanying persons and hope that all of you will enjoy and experience the sights of this fabulous village of Sitges and the city of Barcelona as well.

We hope that following the success of the previous congress in Amsterdam, the 6th ISCVID Symposium will represent a new highpoint in the international exchange of knowledge and experience in these interesting subjects.

Welcome to Sitges!

The Organizing Committee

Under the auspicies of:

International Societies

International Society for Infectious Diseases (ISID)

European Society of Clinical Microbiology and Infections Diseases (ESCMID)

European Group of Endocarditis of the ESCMID

National Societies

Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC)

Catalan Society of Infectious Diseases and Clinical Microbiology

Spanish Society of Internal Medicine (SEMI)

Catalan Society of Internal Medicine

Spanish Society of Cardiology

Catalan Society of Cardiology

Spanish Society of Cardiovascular Surgery

Catalan Society of Cardiac Surgery

Fundación Máximo Soriano Jiménez

The Spanish Society of Cardiology has sponsorized this Symposium for Continuing Medical Education (CME) to its members (CME credit hours, 14; category 1C).

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Meeting at a glance

Wednesday (27th June 2001)

08:30-18:15 h.	Registration
12:00-13:30 h.	ICE Study Group Meeting
14:45-15:00 h.	Opening Session
15:00-16:30 h.	**First Round Table:** ***Advances in the pathophysiology and prophylaxis of infective endocarditis*** Chairs: **D. Durack** (USA) **M.L. Fernández Guerrero** (Spain)
16:30-17:00 h.	Coffee break & Visit to Poster Exhibition
17:00-18:00 h.	**Special Debate Session: Viewpoints & Counterpoints** ***The role of Chlamydia in vascular disease*** Chair: **E. Gutschick** (Denmark)
20:30-24:00 h.	Welcome party (Sitges, Old town)

Thursday (28th June 2001)

08:30-10:30 h.	**Second Round Table** ***Therapy of infective endocarditis caused by resistant microorganisms: in vivo models and clinical data*** Chairs: **P. Moreillon** (Switzerland) **F. Marco** (Spain)
10:30-11:00 h.	Coffee break & Visit to Poster Exhibition
11:00-13:00 h.	**Third Round Table** ***Role of echocardiography in the management of complications of infective endocarditis*** Chairs: **A. Vahanian** (France) **J. Soler** (Spain) Joint meeting with the Valvular Working Group of the European Society of Cardiology
13:30-15:00 h.	***"Tapas" and Poster Session***

Thursday (28th June 2001)

15:00-17:00 h.	**Fourth Round Table** ***Advances in the diagnosis and therapy of intravascular foreign body infections*** Chairs: **A.W. Karchmer** (USA) **I. Vilacosta** (Spain)
17:00-17:30 h.	Coffee break & Visit to Poster Exhibition
17:30-18:30 h.	Special Conference ***Advances in the surgery of endocarditis*** Moderator: **J.L. Pomar** (Spain) Speaker: **G. Pettersson** (USA)
20:00-24:00 h.	Gala Dinner

Friday (29th June 2001)

08:30-10:30 h.	**Fifth Round Table** ***Prophylaxis and management of postsurgical cardiovascular infections*** Chairs: **E. Rubinstein** (Israel) **J.J. Cuenca** (Spain)
10:30-11:00 h.	Coffee break & Visit to Poster Exhibition
11:00-13:00 h.	**Sixth Round Table** ***Diagnosis and management of heart transplant infections*** Chairs: **C. Paya** (USA) **E. Bouza** (Spain)
12:30-13:30 h.	ISCVID Meeting
13:30-14:00 h.	Closing Remarks & Introduction of the 7th ISCVID Meeting, 2003

Scientific Programme

Wednesday, 27th June, 2001

08.30-15.00 h. Registration

12.00-13.30 h. International Collaborative Endocarditis (ICE) Study Group Meeting
Chairs: **R. Corey** (USA)
C. Cabell (USA)

14.45-15.00 h. Opening Session

15.00-16.30 h. **FIRST ROUND TABLE**

Advances in the pathophysiology and prophylaxis of infective endocarditis

Chairs: **D. Durack** (USA)
M.L. Fernández Guerrero (Spain)

15.05-15.30 h. • *Platelet Microbicidal Proteins in Endocarditis*
A. Bayer (USA)

15.30-15.55 h. • *Aspirin (acetylsalicylic acid) and infective endocarditis*
B. Hoen (France)

15.55-16.20 h. • *Should prophylaxis for endocarditis be reassessed ?*
J.T.M. van der Meer (The Netherlands)

16.20-16.30 h. • *Oral presentations*
Duration, Prevalence and intensity of bacteraemia following dental extraction in children.
V. Lucas (U.K.) (see abstrat # 11)

16.30-17.00 h. Coffee break & Visit to Poster Exhibition

17.00-18.00 h. **Special Debate Session: Viewpoints & Counterpoints**

The role of Chlamydia in vascular disease

Chair: **E. Gutschick** (Denmark)
• For: **S. Gupta** (U.K.)
• Against: **E. Rubinstein** (Israel)

Scientific Programme

Thursday, 28th June, 2001

08.30-10.30 h. SECOND ROUND TABLE

Therapy of infective endocarditis caused by resistant microorganisms: in vivo models and clinical data

Chairs: **P. Moreillon** (Switzerland)
F. Marco (Spain)

08.35-09.05 h. • *Multidrug resistant enterococci*
J. Gavaldá (Spain)

09.05-09.35 h. • *MRSA/GISA/CNS*
J. Entenza (Switzerland)

09.35-10.05 h. • *New pathogens: Bartonella spp, Coxiella burnetii, T. whippelii*
D. Raoult (France)

• *Oral presentations*

10.05-10.15 h. Efficacy of quinupristin-dalfopristin alone or in combination with gentamicin, teicoplanin and imipenem in treatment of experimental endocarditis due to β-lactam and glycopeptide-resistant *Enterococcucs faecium*.
J. Pérez Salmerón (Spain) (see abstract # 21)

10.15-10.25 h. Adding dexamethasone to vancomycin has beneficial effect in the treatment of experimental staphylococcal endocarditis, regarding aortic valve destruction.
M. Giamarellou (Greece) (see abstrac # 22)

10.30-11.00 h. Coffee break & Visit to Poster Exhibition

11.00-13.00 h. THIRD ROUND TABLE

Role of echocardiography in the management of complications of infective endocarditis*

Chairs: **A. Vahanian** (France)
J. Soler (Spain)

11.05-11.30 h. • *Diagnosis and treatment of perivalvular abscess*
A. Mugge (Germany).

11.30-11.55 h. • *Risk of emboli and vegetations*
J. Steckelberg (USA).

11.55-12.20 h. • *Role of echocardiography in the timing of surgery*
A. Evangelista (Spain)

Scientific Programme

12.20-12.45 h. • *Surgical therapy of endocarditis after acute emboli*
P.E. Parrino (USA)

12.45-12.55 h. • *Oral presentations.*
Transesophageal echocardiographic detection of endocardiac valve lesions in experimental endocarditis.
M.S. Rouse (USA) (see abstract # 16)

Joint meeting with the Valvular Working Group of the European Society of Cardiology

13.00-15.00 h. ***Posters Discussion and "Tapas" session at the Auditorium Hall***

15.00-17.00 h. **FOURTH ROUND TABLE**

Advances in the diagnosis and therapy of intravascular foreign body infections

Chairs: **A.W. Karchmer** (USA)
I. Vilacosta (Spain)

15.05-15.35 h. • *Prosthetic valve endocarditis*
R. Corey (USA)

13.35-16.05 h. • *Pacemaker/Defibrillator/left ventricular assist devices infections*
C. Leport (France)

16.05-16.35 h. • *Vascular prosthetic infections*
M. Turina (Switzerland)

16.35-16.45 h. • *Oral presentations.*
Effects of antibiotics on slime producing *Staphylococcus epidermidis* adhered to pacemakers.
L.E. Nilsson (Sweden) (see abstract # 2)

17.00-17.30 h. Coffee break & Visit to Poster Exhibition

17.30-18.30 h. **Special Conference**

Advances in the surgery of endocarditis

Moderator: **J.L. Pomar** (Spain)
Speaker: **G. Pettersson** (USA)

Scientific Programme

Friday, 29th June, 2001

08.30-10.30 h. **FIFTH ROUND TABLE**

Prophylaxis and management of postsurgical cardiovascular infections

Chairs: **E. Rubinstein** (Israel)
J.J. Cuenca (Spain)

08.35-09.05 h. • *Update on antibiotic prophylaxis of cardiac and vascular surgery*
P. Francioli (Switzerland)

09.05-09.35 h. • *Risk factors for surgical wound infections*
M.C. Fariñas (Spain)

09.35-10.05 h. • *Advances in the therapy of post-sternotony mediastinitis*
F. Robicsek (USA)

• *Oral presentations*

10.05-10.15 h. Surgical treatment of infective endocarditis
A. Wang (USA) (see abstract # 89)

10.15-10.25 h. Mediastinitis after cardiac surgery: Microbiological, etiology and pathogenesis
B. Gardlund (Sweden) (see abstract # 95)

10.30-11.00 h. Coffee break & Visit to Poster Exhibition

11.00-13.00 h. **SIXTH ROUND TABLE**

Diagnosis and management of infections in heart transplantation

Chairs: **C. Payá** (USA)
E. Bouza (Spain)

11.05-11.35 h. • *Early diagnosis and therapy of fungal infections in heart recipients*
P. Grossi (Italy)

11.35-12.05 h. • *The role of CMV infections in heart transplantation*
C. Payá (USA)

12.05-12.35 h. • *The role of heart transplantation in the next Millenium*
J.L. Pomar (Spain)

13.00-13.30 h. ISCVID Meeting

13.30-14.00 h. Closing Remarks
Introduction of the 7th ISCVID Meeting, 2003

General information

DATE

27, 28, 29 June, 2001

The Congress will begin on Wednesday 27th June with internal meetings followed by the opening session at 14.45 h. At the end of the day, a welcome cocktail at the beautiful Palau Maricel will be held for all participants. The 6th ISCVID Symposium will close on Friday 29th June, 2001 at 14.00 h.
Please note that the 22nd International Congress of Chemotherapy will be held the following week, 31st June to 4th July in Amsterdam.

CLIMATE

The average temperature in June in Barcelona is 21ºC 70F
Cottom and light clothing is recommended.

THE VILLAGE: SITGES

Few resorts can boast the privileges of Sitges: a breathtaking landscape, seventeen beaches that strech along four kilometres of coastline, well-sheltered by the Garraf massif, a full cultural life and busy festive calendar, first rate tourist facilities and its own dazzling light. Its microclimate (more than 300 sunny days in the year and its prime location (fifteen minutes from Barcelona airport and twenty from the city) make it one of the most delightful spots on the Mediterranean, where you can be sure of finding priceless peace and quiet but at the same time, can enjoy the bustling atmosphere of a cosmopolitan centre.

TRANSPORTATION FROM THE BARCELONA AIRPORT

A shuttle bus service from the airport to the Melia Gran Sitges Hotel will be provided on 27 & 29 June. Bus transportation will be also provided to attend the social events. Please, try to be punctual in order to avoid delays. The Meeting point is always the Main Entrance at the Melia Gran Sitges Hotel.
Information about transportation between the Hotel and Barcelona will be kindly provided at the registration desk.

General information

CUSTUMS

Meal times

In Sitges & Barcelona, like elsewhere in Spain, meals are usually served later than in the rest of Europe. Breakfast is between 9 am and 11am. Families have lunch between 2pm and 3pm and dinner between 9pm and 10.30 pm. In restaurants, the meal times are adapted to the usual working hours and lunch can be had between 1pm and 3pm. and dinner between 9pm. and 11.30 pm.

Shop hours

The shops in Sitges & Barcelona, open their doors at 9 or 10 am and close for lunch at 1.30 p.m. they re-open in the afternoon at 4 or 5pm and remain open until 8 or 8.30 pm. The shopping malls and large retail outlets in the city do not close for lunch. All of them use to open on Saturdays afternoons. Ask the registration desk for more details.

VENUE

Hotel Melia Gran Sitges***
Avda. Port d´Aiguadolç, s/n
08870 Sitges (Barcelona) Spain
Phone (+34) 93 811 08 11
Fax (+34) 93 891 90 34

It is one of the biggest Congress and Leisure Centre in the Mediterranean. It combines the quality and service we have come to expect of Melia Hotels with the latest technology to form an ideal hotel centre for business and holidays.

LANGUAGE

The official language of the Congress is English. No translations facilities will be available.

INTERNET

The congress web site is:

www.geyseco.com/endocarditis2001.htm

Registrations, accomodation and abstract submission can easily be reached by Internet.

BADGE POLICIES

All participants , accompanying persons and exhibitors must wear the congress identification in a visible place. During the congress a control will be carried to gain access to the scientific and social acts or to the exhibition. Therefore it, will be necessary for participants and accompanying persons to wear the identification in order to enter the Congress.

General information

REGISTRATION FEE

Registration on site is 65,000 pesetas/390,66 eur.
The registration fee covers: participation in all scientific session, official congress set, coffee breaks, lunch, welcome party and gala dinner.

CANCELLATION DETAILS

A service charge of 20% will be made if cancellation is received before 1st January, 2001. If the cancellation is made between this date and 30th March, 2001 a service charge of 50% will be applied. Thereafter no refunds are possible.

MESSAGES

Please contact the registration desk for further information regarding messages

VIP´s ROOM

Please, note that all speakers, sponsors and ISCVID Executive Committee members are welcome to the VIP hospitality suite located at **Mestral Room 3** at the Hotel Melia Gran Sitges

RESTAURANTS

In your congress pack, you may find detailed information about the best Restaurants both in Sitges and Barcelona.

TAXIS

Taxis can be easily requested at the Main entrance of the Hotel Melia Gran Sitges
Please, ask registration desk for more information about Mercedes Benz taxis and English speaking drivers.

MUSEUMS

Barcelona is a museum´s lover paradise, as well as Sitges where the following museums can be visited (Cau Ferrat, Maricel, Romantic). Please find out more information at the city´s guide “See Barcelona” enclosed in your delegate pack or ask at the Registration Desk for more details.

Accompanying persons programme

All registered accompanying persons will participate in the accompanying person´s tour programme. All tours will leave from the Hotel Melia Gran Sitges. Tours have limited space and are assigned on a first come-first served basis.

27th June

Classical city tour:

Departure time: 9.30h. Approx. return time: 16.00h.
Meeting Point: Main entrance Hotel Melia Gran Sitges
Dress code: casual

Itinerary:

Once in Barcelona you will see Plaza de Catalunya, Via Laietana, Cathedral and its cloister Gothic Quarter, Plaza Sant Jaume (Generalitat and Town Hall). We continue to the Olympic village and Port which we shall tour on foot. Subsequently we shall go to Monjuic with its panoramic view of the city and port. We shall tour the Stadium, Sant Jordi Palace and the Calatrava Tower. Visit the Spanish Town where the most typical regional architectural styles in Spain are reproduced. Visit MNAC. Lunch

28th June

Artistic city tour:

Departure time: 9.30h. Approx. return time: 16.00h.
Meeting Point: Main entrance Hotel Melia Gran Sitges
Dress code: casual

Itinerary:

Once in Barcelona you will see Paseo de Gracia, Panoramic of “Casa Batllo” and “Casa Mila”. Visit to the Güell Park, declared by the Unesco as an artistic monument and an inheritance for humanity. Return to admire the Holly Family Church, the unfinished masterpiece of the world famous architect, Gaudi. Picasso Museum with works from the “blue and pink” periods of this famous painter. Lunch

Social programme

Wednesday 27th June

19.30 h. Visit to the Maricel Museum
Part of the former residence of Charles Deering now forms the Maricel Museum, which exhibits collections related to Sitges, *Modernisme*, Romanesque mural paintings' and Gothic paintings on wood.

20.30 h. Welcome cocktail at the Palau Maricel
Departure: main entrance of the Hotel Melia Gran Sitges
Dress code: Casual

The Palau Maricel, in the centre of the old town, typifies local people´s conservation of their way of life. It was built in 1910 to house the Art collections of the American millionaire Charles Deering, and still preserves the feel of a "living" stately home.

Thursday 28th June

19.30 h. Departure for Gala Dinner
Finca Mas Soler
Departure: main entrance of the Hotel Melia Gran Sitges
Dress code: Suit & tie, evening gown

Located in Sant Pere de Ribes, this Catalan Renaissance style Palace with splendid gardens is the ideal setting for a relaxed and elegance atmosphere.

Sponsored by

The International Society of Cardiovascular Infectious Diseases (ISCVID) and the Local Organising Committee want to thank the following main sponsors for their highly appreciated support to the ***6th International Symposium on Modern Concepts in Endocarditis and Cardiovascular Infections 2001***:

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Useful addresses and 2003 ISCVID meeting

7th International Symposium on Modern Concepts in Endocarditis and Cardiovascular Infections

June 26th-28th, 2003

Centre de Congrès Le Majestic
Chamonix Mont Blanc, France

Chairs: B. Hoen and F. Delahaye

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Lectures

Lectures

Lectures will be held at the main **Auditorium** of the Melia Gran Sitges Hotel. Slides or diskettes with power point presentations have to be delivered at the **Speakers Preview Room,** located at the **Mestral Room 3,** at least two hours prior your oral presentation. If you bring your computer, please contact with the audio-visual technician in order to prepare your presentation.

Advances in the pathophysiology and prophylaxis of infective endocarditis

PLATELET MICROBICIDAL PROTEINS IN ENDOCARDITIS

Bayer, A.S., Kupferwasser, L.I., Yeaman, M.R.
UCLA School of Medicine. Los Angeles, CA. USA.

Mammalian platelets secrete a family of microbicidal peptides following stimulation by agonists relevant to endovascular infections, such as infective endocarditis (IE) (e.g., following thrombin exposure). These microbicidal peptides have potent in vitro activity against common endovascular pathogens, such a *Staphylococcus aureus* (SA). Recent studies strongly suggest that these peptides contribute to the innate host defense system against endovascular infections. The aim of the present study was to ascertain the contribution of the in vitro susceptibility profile of SA strains to a prototype pletelet microbicidal peptide (tPMP-1) with respect to the induction, local progression, hemotogenous dissemination and cardio-physiologic complications of experimental SA IE. We utilized an isogenic SA strain pair which differed in only their in vitro susceptibility (`S) or resistante (`R) profiels to tPMP-1, to induce experimental IE. Moreover, we employed transthoraric echocardiography to assess the following cardio-physiologic parameters over time: vegetation size, onset of aortic regurgitation, periannular abscess formation, and relative ejection fractions. The two strains did not differ in their capacity to initially induce Ie. However, the microbiologic progression of the infection withiun vegetation, as well as the extent of hematogenous dissemination was significantly less in animals infected with the `S strain as compared to the `R strain. Similarly, the degrees of periannular extension of IE, aortic regurgitation, and congestive heart failure were substantially reduced in animals infected with the `S strain as compared to the `R strain. In conclusion, these investigations emphaize the key role of local secretion of microbicidal peptides from platelets in the innate host defense response to endovascular infections, and suggest that the major impact of such peptides is in modifying the course of the such infections in their post-induction phases.

ASPIRIN AND INFECTIVE ENDOCARDITIS

Hoen, B.
Univ. Med. Center of Besançon, France.

Platelet-bacteria interactions of the endocardium surface are crucial int he initiation of IE. However the role of platelets in the pathogenesis of IE remains debated. Platelets have long been regarded as IE-promoting agents by provindig an adhesive surface for microbial binding. They have also been shown to participate in antimicrobial host defense by the secretion of microbicidal proteins.
Whether antiplatelet drugs might improve the prognosis of IE, by limiting the vegetation growth and/or reducing embolic events is an unanswered question.
Several experimental studies have shown that low-dose but not high-dose aspirin significantly reduces both the weight and the bacterial density of vegetations. In addition, adjunctive aspirin was demonstrated to improve the vegegation sterilization rate as compared with antibiotic treatment alone. In one study ticlopidine given at the dosage of 10 mg/kg/d was shown to decrease the weight of vegetations and to improve the sterilization rate of antibiotic-treated animals while it had no effect on bacterial density, suggesting that the mechanisms of action of aspirin and ticlopidine are not quite similar and not limited to platelet aggregation inhibition. Aspirin and ticlopidine combination even seems to act synergistically to reduce the vegetation weight in a rabbit model of untreated S. aureus IE.
Only very few clinical data are available. In one retrospective study that assessed embolic complications in IE, the rate of emboli was decreased (11% vs. 47%) in patients with native valve IE who had received aspirin because of coronary artery disease.
One prospective observational study examined the effect of low-dose aspirin (75 mg/d) in 9 patients, 4 being randomized to aspirin and 5 to no aspirin. Only 2 patients in the aspirin group and 3 in the control group had documented vegetations. Both patients in the aspirin group showed a decreased vegetation siza while 2 in the control group had increased vegetation size. CT scan showed multiple cerebral infarcts in 2 of the control patients and none of the treated patients.
One large clinical trial assessing the potencial benefits of low-dose Aspirin as adjunctive therapy for IE is ongoing. Other clinical trials aimed at assessing its efficacy and risk/benefit ratio are still needed.

SHOULD PROPHYLAXIS FOR ENDOCARDITIS BE REASSESSED?

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Patients with structural heart disease, a previous episode of infective endocarditis or intracardiac prosthesis are predisposed to encodardial infection. Some of these individuals develop infective endocarditis after a medical or dental procedure that cause bacteremia. Thus, it seems logical to give antibiotics before such procedures in patients at risk for endocarditis, thereby preventing the disease. In the 1940's antibiotic prophylaxis for endocarditis was introduced and quickly became routine medical practice in most countries. However, the results fell short of expectations and prophylaxis has not led to a decreased in the incidence of endocarditis. This might be due to a lack of protective effect. Prophylaxis has repeatedly been reported to fail and no controlled study to demonstdrate it's protective has ever been done, mainly because endocarditis is rare and a large series or patients would be needed. Several case-control studies have been performed with conflicting results. One study, limited by the retrospective recruitment of eight cases over six years, found a protective effect of 91%. Two large studies found a protective effect of about 50%, though not statistically significant. However, the epidemiological data also showed that in the majority of patients with endocarditis the disease did not occur after a medical or dental procedure, and that patients with endocarditis were no more likely than controls to have received dental therapy. This does not rule out that endocarditis occasionally is caused by a procedure. It does, however, rule out a major impact of prophylaxis on the occurrence of endocarditis. It also implies that the efficacy of prophylaxis will be very hard to proof. Irrespective of prophylaxis, the odds are that a patients wil not develope endocarditis as a consequence of a procedure. Sensitivity analyses suggest that prophylaxis might be cost saving under some scenarios for high-risk patients, whereas under other scenarios it might cause net loss of like. Continuing epidemiological studies and more insight in the pathogenesis of endocarditis are needed to earmark the patients that are most likely to benefit from prophylaxis. Untill then low adherence with guidelines for prophylaxis is not a major health problem and resources should be used for other interventions.

The role of Chlamydia in vascular disease

CHRONIC INFECTION, CHLAMYDIA AND VASCULAR DISEASE

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Atherosclerosis is now recognised as an inflammatory disease. Furthermore, conventional risk factors fail to fully explain coronary heart disease (CHD) prevalence and severity in differing populations. Whether 'infectious agents' represent the stimuli for the 'inflammation' and are 'missing risk factors' are intriguing and plausible possibilities.
Of the candidate microorganisms implicated, *Chlamydia pneumoniae* has emerged as the most likely pathogen to have a causal role. Evidence for this is based on sero-epidemiological, pathological, laboratory-based evidence and recent animal models. Direct plaque examination is particularly convincing – with *C. pneumoniae* protein, DNA and 'live' viable organism being detected in vascular tissue, using electron microscopy, immunohistochemical and DNA molecular techniques. Enthusiam for the 'infectious' hypothesis for atherosclerosis has been further generated by small-scale antibiotic studies in CHD. Azithromycin (AZ) and another macrolide antibiotic, roxithromycin were shown to reduce the incidence of further cardiovascular events in patients with CHD. Postulated mechanisms of protection possibly including the suppression of a chronic *C. pneumoniae* infection and/or independent, 'plaque-stabilising', anti-inflammatory effects of macrolide antibiotics. More recently large-scale database analyses showed that antibiotic usage (namely tetracyclines and quinolones) appeared to indirectly protect against first MI.
Prospective antibiotic intervention trials are in progress and include WIZARD, MARBLE, AZACS, ACES and PROVE-IT. The results of such studies will include evidence from over n=20,000 enrolled patients (in total) and should help to determine whether antibiotics have a role in the secondary prevention of the 'epidemic' of CHD.

CHLAMYDIA PNEUMONIAE IN ATHEROSCLEROSIS -AN ETIOLOGIC AGENT OR A HITCHHIKER?

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Although *C. pneumoniae* seems to apparently fulfil the Koch1s postulate, it does so under special circumstances and only in primed or in genetically mutants susceptible animals.
This early observation, of the presence of *C. pneumoniae* in atherosclerotic plaques and the serologic corelation between *C. pneumoniae* and atherosclerotic vascular disease has initiated thousands of therapeutic courses before the rational for therapy, its length, dose and end points have been established.
Many national and international intervention studies have been launched among them: WIZARD trial, MARBLE, STAMINA, CROATS and ACES. In none of those has the code been broken and in none of those the results are known at the present time.
What is known however is that in very short term evaluations (1-2 months) *C. pneumoniae* therapy had some positive effects, but in mid-term studies(6 months) or in follow-up of initial positive study results subsequent results could not confirm the initial salutory therapeutic effect. In addition, in persons with MI the fraction that received anti-chlamydial antibiotic therapy was no different than that not receiving this therapy, and in patients that received antibiotic therapy the rate of MI was similar to those that did not receive antibiotic therapy.
It is beyond doubt that the organism can be seen microscopically or be detected immunologically in atherosclerotic plaques, however its presence there is not unique to the plaque since the organism can be concomitantly detected in many organs as well.
So what is the connection between *C. pneumonaie* and atherosclerotic cardiovascular disease? I believe that we do not know for sure the nature of the connection although a connection may be possible. Few alternative hypotheses include: the similarity between *C. pneumoniae* HSP 60 and the human HSP causing tissue damage or modulating inflammation. The ability of *C. pneumonaie* HSP 60 to induce TNF-alpha and to activate metaloproteinases both associated with inflammatory parameters is another option. It is certainly premature and probably irresponsible at the present time to administer to cardiac patients prolonged courses of antibiotics because of the ecological effects of such an intervention in absence of proof of efficacy.

Therapy of infective endocarditis caused by resistant microorganisms: *in vivo* models and clinical data

MRSA, GISA, CNS

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Together, coagulase-positive and coagulase-negative staphylococci represent > 50% of hospital-acquired bloodstream infections. Since up to 50% and > 60% of them are resistant to methicillin, vancomycin is increasingly used. This has selected for clinically relevant glycopeptide-intermediate Staphylococcus aureus (GISA) that escape virtually any available therapies. Identifying either existing or new drugs effective against both methicillin-resistant *Staphylococcus aureus* (MRSA) and GISA is critical to decrease the vancomycin selective pressure.
Stringent models such as experimental endocarditis proved crucial for such investigation. Among old drugs, combining ampicillin or amoxicillin with penicillinase inhibitors proved effective against MRSA and GISA both in experimental and clinical settings. This correlated with their good affinity for penicillin-binding protein 2A, and maybe with the fact that certain GISA have an altered expression of methicillin-! resistance. Among newer drugs, quinupristin-dalfopristin alone or combined with b-lactams successfully treated MRSA and GISA infections both in experimental endocarditis and in a few cases in man. Likewise, although bacteriostatic in vitro, high dose linezolid exhibited a significant activity in animals with MRSA endocarditis. Combined to surgery, linezolid also proved effective against MRSA endocarditis in man. Still at the preclinical stage, both daptomycin and the glycylcycline GAR-936 were active against experimental endocarditis due to MRSA, and hold promises against GISA as well. On the other hand, newer quinolones are expected to be ineffective, because most multiresistant staphylococci are resistant to these molecules. The data provided by such experimental models offers invaluable information to guide the choice of new treatments that might be further considered for in clinical trials.

Role of echocardiography in the management of complications of infective endocarditis

RISK OF EMBOLI AND VEGETATIONS

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Major embolic events are the most common serious extracardiac complications of native valve infective endocarditis (IE), occurring in as many as 30-40% of patients in some studies. Typically, half of these events occur before IE diagnosis and initiation of antimicrobial treatment and the ramainder after diagnosis. A common but unproven paradigm suggests that emboli represent mechanical detachment of portions of vegetations that embolize to central nervous system, peripheral, or visceral arteries. Thus, numerous studies have attempted to establish a relationship between emboli and echocardiographic characteristics of vegetations. Conclusions from these myriad studies are seemingly contradictory, with some supporting an association and others finding no consistent relationship. Specific elements of study design, echocardiographic techniques, potential biases, populations studied, selection of endpoints and epidemiological estimates (especially risk versus rate estimators) may partially explain apparent inconsistencies.
In addition, analysis of the temporal relationship between antibiotic teharpy, echocardiographic examination, and embolic eventds is critical if study results are to be used as basis for assessing potential candidates for interventions (such as surgery) to prevent future emboli. The etiological microorganism critically influences both embolic rate and the value of vegetations as a predictor of emboli. *S. aureus* native valve IE has a high rate of emboli but vegeatsions have no effect on embolic rate; in contrast, IE due to viridans streptococci has a lower rate of emboli than does *S. aureus*, even in patients with vegetations, but the embolic rate among patients with vegetations is increased approximately 7-fold compared to those without vegetations. Microorganisms are thus a major epidemiological confounding factor, and unless explicitly analyzed, will introduce a potentially major distortion in estimates of relative risk of emboli associated with vegetations.
Also, mitral valve location of vegetations > 10 mm in size has been reported as an important factor increasing future embolic risk. Should patients with large vegetations, as seen on echocardiography, undergo surgical intervention solely on this basis to prevent emboli? Multiple factors bear on this complex decision, including the microorganism and valvular location, the considerable overlap in vegetation size between patients with and without emboli, the declining rate of emboli with time after antibiotic therapy begins, the lack of adquate data that surgical intervention is effective in reducing overall or embolic morbidity, and the risks of surgery, both immediate as well as the prolonged risk of potential embolic or hemorrhagic events related to mechanical valves. Such decisions must be individualized.

ROLE OF ECHOCARDIOGRAPHY IN THE TIMING OF SURGERY

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Doppler-echocardiography , mainly transesophageal echocardiography, provides unique information regarding the intracardiac lesions caused by endocarditis. American guidelines describe as class I surgical indications in the setting of active infective endocarditis acute mitral or aortic regurgitation with heart failure, aortic regurgitation with early closure of the mitral valve, presence of abscesses, fungal endocarditis and persisting sepsis with valve incompetence. In prosthetic valves a class I indication is early endocarditis and heart failure due to periprosthetic leak. Previous speakers have discussed the issue of vegetation size and abscesses, therefore I will phocus on the surgical indications based on the hemodynamic burden caused by the infected valve disease. Data obtained by echo-Doppler are essential in the surgical indication and also help to decide the best timing and in some cases the best surgical treatment. echo-Doppler data can be divided as follows:

1. Echocardiographic diagnosis of the type of valvular disfunction: ruptured cusps, ruptured leaflets, valve perforation, prosthetic dehiscence, prosthetic obstruction
2. Echo-Doppler assessment of the severity of valve dysfunction: quantification of valve regurgitation
3. Echo-Doppler assessment of the hemodynamic status: left ventricular function, pulmonary pressure, cardiac output

This information allows to make a surgical decission and also to decide the best time for surgery. Surgery should be performed immediately, on emergent bases, whenever a severe lesion with severe hemodynamic compromise exist. In cases with severe lesions but moderate compromise surgery can be delayed for a few days under strict clinical supervision, allowing antibiotic treatment to improve the general, septic state. In patients with severe valve lesions but no hemodynamic compromise surgery can be performed electively at the end of antibiotic treatment.
Echocardiographic information is also valuable for the surgeon in order to decide the best surgical approach: in the presence of severe perivalvular dammage in aortic endocarditis a homograft will be the best valve substitute. In some cases of mitral endocarditis the type of valve lesion can help the surgeon to decide the best technique for valve repair.

SURGICAL THERAPY OF ENDOCARDITIS AFTER ACUTE CNS EMBOLI

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Objective: As many as 40% of patients with left-sided bacterial endocarditis will suffer a neurological insult. The significance of a neurological change as an indication or a contraindication for valve replacement remains controversial, as does the timing of surgical intervention.
Methods: We performed a retrospective analysis of the records of 33 patients admitted to the University of Virginia Health Sciences Center between January 1, 1978 and June 30, 1996 with a diagnosis of endocarditis and a neurological change.
Results: All 33 patients had echocardiographic or pathologic evidence of left-sided endocarditis; 23 presented with focal neurologic findings and had a mortality of 22% (5/23), while 10 patients presented with a non-focal neurologic exam and had a mortality of 60% (6/10) ($p < 0.05$). Of the 33 patients, 14 underwent operation and 19 were treated medically. Mortality was 21.4% (3/14) in the surgical group and 42.1% (8/19) in the medical group (p = NS). In 71% (10/14) of the surgical patients, surgery was done within one week of their neurologic event. Of the survivors, the occurrence of additional neurologic deterioration was 18.2% (2/11) in the surgical group and 9.1% (1/11) in the medical group (p = NS).
Conclusions: Choosing therapy for a patient with endocarditis and a neurological change remains a difficult challenge. An initial non-focal, globally dysfunctional exam is a predictor of a poor outcome. By comparing surgical and medical groups derived from the same series of patients, it is clear that patients with bacterial endocarditis and CNS changes face significant mortality regardless of intervention. However, these data demonstrate that when compared to a similar group of medical patients, surgical patients who require and receive operation early in the course of their illness do comparatively well. Improving outcomes by delaying surgery may serve to "select out" hardier patients while other patients who may benefit from surgery expire.

Advances in the diagnosis and therapy of intravascular foreign body infections

PROSTHETIC VALVE ENDOCARDITIS

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Background: Prosthetic valve endocarditis is a serious, often life-threatening infection. Because of its infrequent occurrence, most of the information concerning the diagnosis and treatment of this disease comes from retrospective studies.
Methods: 7 prospective registries from 5 countries were merged. In addition, selected retrospective studies from the past 20 years were reviewed.
Results: From the International Collaboration (ICE): 335 patients with PVE were identified. Mean age was 55 years and 50% were women. Aortic and mitral valves were infected equally. Organisms included *S. aureus* (16%), CNS (16%), Viridans group streptococci (15%), enterococcus (13%), GNR (8%), *S. bovis* (5%), yeast (3%), HACEK (2%), and others/culture negative (22%). Mortality was highest with both *S. aureus* and CNS (50%) though surgery was remarkably different (34% and 67% respectively). Viridans group streptococci had the lowest mortality and surgical rate at 18% and 27% respectively. From the literature: The frequency of PVE in pts with bacteremia and fungemia was 16% and 9% respectively. The Duke Criteria (perhaps with modification) have high sensitivity with unknown specificity. Only 22% of pts with PVE survived with their original valve at 5 years follow-up.
Conclusion: We have made significant progress in delineating the risks, diagnosis, and natural history of PVE. Unfortunately little progress has been made in the area of treatment. Prospective collaborative studies with networks such as ICE provide the best opportunity to decrease the extremely high morbidity and mortality rates that pts with PVE suffer.

Special Conference

ADVANCES IN THE SURGERY OF ENDOCARDITIS

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In a recent article, including patients with active endocarditis operated during 1994-99 an early mortality of 12% was regarded as “treated successfully”. Presented surgical endocarditis series are small nonrandomized and includes mixed subsets of patients. The objects of surgery are to eradicate the infection, to prevent embolism, and/or to correct a hemodynamic problem. The first two objectives require radical removal of the pathology and the third a reliable method of reconstruction. Secondary objetives are to minimize the risks of reoperation for recurrent infection, prosthetic valve dehiscence and prosthetic valve or homograft/autograft degeneration and failure. Understanding the pathology, radical removal of the active infection and recognition of the anatomical landmarks are the keys to success more than the choice of any particular valve or conduit for the reconstruction. Even in the most advanced cases of aortic valve and root endocarditis the LVOT is usually well preserved. The literature favors valve repairs for the same reasons as in patients without valve infection. Valve repair for endocarditis is durable and associated with a low risk of persistent or reucrrent infection. When valve replacement is requiered mechanical prosthesis, bioprosthesis, homograft and autograft are all good choices with their own merits, disadvantages and risks. Surgeons familiar with homografts and autografts recognize their particular qualities with regard to easy and safe reconstruction of the LVOT and low risk of persistent and recurrent endocarditis. Xenograft roots are used by some surgeons when homografts are not available. The use of homografts for tricuspide and mitral valve replacement remains experimental. The treatment of endocarditis can still be improved. Early recognition of complications and optimal timing of surgery are crucial, particularly in patients with prosthetic valve, an aggressive, invasive and difficult to treat organism, advanced pathology by echo, and/or who remains septic after institution of adquate antibiotic treatment. Advanced pathology differs between patients with regard to hemodynamic compromise, anatomical severity and infectious activiy. Surgery to prevent embolism in patients with vegetations remains a less well defined indication. The management of patients with neurological deficits remains a difficult issue. Sound judgement and experience are important as the patients become increasingly complex and severe.

Prophylaxis and management of postsurgical cardiovascular infections

RISK FACTORS FOR SURGICAL WOUND INFECTIONS

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Sternal wound infections are a major cause of morbidity and mortality in patients undergoing cardiac surgery, leading to prolonged hospitalisation and increased hospital expense. The occur in 0,8% to 8% of patients who undergo open-heart surgery and carry a 20 to 40% mortality rate. Sternal infections can range from minor, superficial infections to deep sternal wound infection, or mediastinitis with invasion of the sternum, heart, and great vessels. Staphylococcus splp are responsible for the majority of sternal infections, but environmental sources can cause infections by other organism. The development of seternotomy infections is multifactorial. Numerous prospective and retrospective studies have pointed to a multitude of clinical and perioperative variables as being causative, with as many other studies presenting evidence of the contrary. This has led to confusion about which clinical variables should be modified so as to minimize the individual patient’s risk! for developing this severe complication. Diabetes mellitus, obesity, the use of both left and right internal mammary arteries, and use of staples for skin closure are factors associated with an increased risk for sternal wound infection. Some simple procedures help limite the development of sternal infections in certain patients. The multiple risk factors of median sternotomy infection will be described and treatment options briefly discussed.

ADVANCES IN THE THERAPY OF POST-STERNOTOMY MEDIASTINITIS

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Postoperative sterno-mediastinitis is a life-threatening complication that occurs in about 0.75 to 1.4 percent of all open-heart operations. The result of treatment largely depends on timely diagnosis and appropriate surgical management. Risk factors for infection should be corrected preoperatively whenever possible. Among other preventive measures, meticulous asepsis, atraumatic surgical technique, preserving the blood supply and the mechanical integrity of the sternum, prevention of sternal instability and correction of the same if it occurs are the most important. The management of sterno-mediastinitis should be tailored to the individual clinical features of the patients. Clearly cases with nonpurulent sternomediastinitis and no soft tissue or bone necrosis (type I) may be treated with reopening, drainage, sternal stabilization, and primary closure. Virulent infections with tissue necrosis (type II) may be best handled with reopening, several days of open management, and debridement then secondary closure with viable tissue (usually muscle) flaps. Chronic, smoldering infections (type III) are usually managed with debridement and muscle-flap coverage.

Diagnosis and management of infections in heart transplantation

THE ROLE OF CMV INFECTIONS IN HEART TRANSPLANTATION

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Cytomegalovirus (CMV) infections remains the most common infectious complication following orthotopic heart transplantation. While significant advances have been made in the diagnosis, prevention, and treatment of this infection, it remains a major cause of short- and long-term morbidity in the cardiac transplant recipient. In the absence of antiviral prophylaxis, CMV leads to symptomatic infection (CMV disease) in around 30% of patients during the first 6 weeks. Fisk factors for CMV disease include the absence of CMV immunity in patients receiving an organ from a previously CMV infected donor. In addition, the use of anti-T cell antibodies for induction or treatment of allograft rejection are major risk factors for CMV disease. Initial randomized controlled trials indicate that short (4 weeks) I.V. ganciclovir was only partially effective and did not significantly benefit the hign risk patients outlined above. Recent progress in this field has demonstrated that the oral formulation of ganciclovir, while not perfect, still reduces CMV disease by 85% in high risk patients, when administered for the first 3 months post-heart transplantation. Unfortunately, around 15-20% of patients still develop CMV disease upon discontinuation of prophylaxis which can have the same impact in morbidity and potentially mortality. An improved formulation of ganciclovir, valganciclovir, provides higher absorption rates and is now perceived to be as effective as prolonged I.V. ganciclovir administration.

One unique situation to heart transplantation with regard to CMV is its relationship with chronic allograft rejection. In this type of transplant, cardiac allograft vasculopathy (CAV) occurs in 10-15% of patients in the first year leading to graft dysfunction in up to 50% of patients in 5 years. While the pathogenesis is multifactorial (prolonged ischemia time during allograft harvest, acute allograft relejction, and lipid abnormalities), CMV remains a main stem risk factor for this complication. Animal data using experimental heart transplantation clearly demonstrates the ability of CMV in causing CAV.

Epidemiological data links CMV to CAV in heart transplant recipients and post-hoc studies demonstrate that administration of I.V. ganciclovir protects the onset of CAV at 5 years-post-heart transplantation. The ability of CMV to not only infect endothelial cells and smooth muscle cells, but also to upregulate chemokine receptors that are critical for cell proliferation and inflammation are the likely explanation as to how CMV contributes to this complication.

Altogether, while significant advances in the field of CMV have been achieved in heart transplantation, a number of challenges remain including the suppression of the long-term allograft rejection using antivirals.

Oral & Posters Presentation

Oral presentations

Oral presentations will be held at the main **Auditorium** of the Melia Gran Sitges Hotel. Slides or diskettes with power point presentations have to be delivered at the **Speakers Preview Room,** located at the **Mestral Room 3,** at least two hours prior your oral presentation. If you bring your computer, please contact with the audio-visual technician in order to prepare your presentation.

Poster presentations

Posters will be displayed throughout the Symposium at the **Auditorium Hall**. Posters should be hung between 15-19 h. on June 27th and they should be removed between 13-14 h. on June 29th. Please, mount the poster on the board numbered as confirmed to the presenting author. The numbers on the posterboards correspond with the abstract numbers in the book of abstracts. Materials for hanging the poster will be provided on site. Discussion of posters will take place at the "**Tapas" Session and Poster Discussion** scheduled between 13-15 h. on June 28th. Presenters are required to stand at their posters during this session.

Pathophysiology and prevention of endocarditis

P 001

IN VIVO BACTERIAL ADHERENCE TO INTRACARDIAC PROSTHETIC MATERIALS: A NEW EXPERIMENTAL MODEL

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Objective: Since bacterial colonization of inert artificial materials is a critical variable in the appearance of foreign body centered infections, we evaluated a new experimental endocarditis model that enables quantitative *in vivo* testing of bacterial adherence tot prosthetic materials.
Methods: In 43 rabbits, different patches (Dacron/DAC n = 14; glutaradldehyde-fixed pericardium/GAP n = 14; cryopreserved allograft/AG n = 15) threaded on a prolene suture were-lead through a stitch incision at the left atrium to the ventricle, perforating the mitral valve and leaving the heart at the outside of the left ventricle. The patch gets caught in the valve tissue, creating mitral insufficiency. Six hours postoperatively 6×10^6 colony forming units (CFU) of *Staphylococcus aureus* were administed intravenously. Postmortem examination and further analysis was carried out 48 h after bacterial inoculation.
Results: The animals (2 DAC; 4 GAP; 4 AG) died and were therefore excluded. We found 6/14 sterile patches in the DAC-, 9/14 patches in the GAP-group and the AG unit showed 9/15 germ-free patches. Mean number of cultured organisms in the remaining patches were 2.3×10^6-7.6×10^6 CFU/mg (DAC), 1.8×10^4-6.7×10^4 CFU/mg (GAP) and 4.9×10^5-1.0×10^6 CFU/mg (AG). Mean quantity of CFU/mg in the adjacent vegetation material was 5.9×10^5-1.1×10^6 CFU/mg (DAC), 8.5×10^4-3.2×10^5 CFU/mg (GAP) and 3.2×10^6-1.2×10^7 CFU/mg AG-vegetation. Differences in the number of CFU were not significant for all groups.
Conclusions: The above described model allows reliable quantitative *in vivo* testing of bacterial adherence to different prosthetic materials within a short time period. Our results suggest that there is no advantage of biomaterials compared to Dacron concerning the development of bacterial endocarditis.

P 002

EFFECTS OF ANTIBIOTICS ON SLIME PRODUCING *STAPHYLOCOCCUS EPIDERMIDIS* ADHERED TO PACEMAKERS

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Bacteria adhered to foreign bodies are often more resistant to antibiotics than bacteria of the same strain growing planktonically. Some strains also encapsulate themselves in slime consisting of extracellular biopolymers.
Objective: The aim of this study was to investigate the biofilm formation on pacemakers and the antibacterial effect by rifampicin alone and combinet with ofloxacin on a slime producing strain of *Staphylococcus epidermidis*.
Methods: *S. epidermidis* ATCC 35984 was adhered to Microny® pacemakers (St Jude Medical) in supplemented Mueller Hinton Broth (MHB) for 24, 48, 72, 96 and 120 h, respectively. Adherence and slime production were studied in an evironmental scanning electron microscope (ESEM). The adhered bacteria were washed and exposed to rifampicin (8 mg/L) alone or in combination with ofloxacin (16 mg/L) for 20 h at 37 ºC. The bacterial numbers on the pacemakers were determinated by bioluminescence assay of intracellular bacterial ATP after extraction of ATP in boiling Tris/EDTA-buffer.
Results: After 24 h incubation of the pacemakers in broth containing a start inoculum of 1×10^4 CFU/mL ESEM showed adhered bacteria. The intracellular ATP level on these pacemakers was 2.0×10^9 moles ATP corresponding to 2.0×10^9 bacteria. After further 24 h incubation of the pacemakers in fresh borth ESEM showed adehred slime producing bacteria. The intracellular ATP level on these pacemakers was 2.6×10^8 moles ATP corresponding to 2.6×10^{10} bacteria.
The minimal inhibitory concentrations (MICs) of ofloxacin and rifampicin were 0.125 and 0.008 mg/L, respectively. During treatment of the pacemakers with rifampicin alone development of rifampicin resistance occurred with a MIC increase to > 256 mg/L. Development of rifampicin resistance was provented when rifampicin was combined with ofloxacin. The reduction of intracellular ATP on pacemakers with bacteria adhered for 24 h was 1.4 $\log^{10}$ (meaning 101.4) after explosure to rifampicin in combination with ofloxacin. After the same treatment of the 48 h slime producing bacteria corresponding figure was 0.87 $\log^{10}$.
Conclusions: This study shows that ofloxacin can prevent development of rifampicin resistance. Furthermore the bactericidal effect was more pronounced on adhered bacteria prior slime production. This indicates the importance to assess the age of the biofilm and whether slime production occurs or not in models studying antibacterial effects on bacteria adhered to foreign bodies.

P 003

SPECIFIC INTERACIONS BETWEEN PATHOGENIC BACTERIA, VASCULAR ENDOTHELIAL CELLS AND MONOCYTES ORCHESTRATE FIBRIN FORMATION IN THE EARLY PHASE OF BACTERIAL ENDOCARDITIS

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In bacterial endocarditis (BE), intravascular infection with *Staphylococcus anureus, Streptococcus sanguis,* or *Staphylococcus epidermidis* can lead to formation of a fibrin clot, called vegetation, on the inner surface of the heart and cause heart dysfunction. To activate the clotting system and to maintain fibrin deposition the procoagulant molecule tissue factor (TF) is required. Our *in vivo* and *in vitro* experiments revealed that in an established vegetation the TF molecules are generated by monocytes settling on the fibrin of a growing (infected) clot.
Objective: However these studies do not explain how coagulation starts in the early phase of BE in patients with normal heart valves covered with structurally intact endothelial cells. This question is explored in our current studies.
Methods: In an vitro model of endovascular infection we recently demonstrated that cultured human endothelial cells (EC) upon binding and internalization of *S. aureus,* but not *S. sanguis* or *S. epidermis,* express TF surface antigen and TF-dependent procoagulant activity (TFA).
Results: The results of our successive study show that infecion of EC with these three pathogens induces surface expression of intracellular adhesion molecule 1 (ICAM-1) and vascular cell adhesion molecule 1 (VCAM-1) and monocyte adhesion. Subsequent coculture of these cells synergistically enhanced TFA, which was exclusively dependent on TF molecules that were expressed on EC during coculture. TFA induction required direct contact between monocytes and bacterium-infected EC, but the signals for this response were not generated by the binding of monocytes through their β_2-or α-integrins to ICAM-1 or VCAM-1, respectively, on infected EC. The mechanism by

which monocytes induce TFA in bacterium-infected EC was partly mediated by the proinflammatory cytokine interleukin-1 produced by the cells during coculture. Endogenous tumor necrosis factor-alpha was not involved.
Conclusions: This modulating effect of monocytes on the species- and strain-dependent TFA of bacterium-infected EC supports our hypothesis that in an early stage in the pathogenesis of BE, as well as other intravascular infections that lead to detrimental fibrin formation, the coagulation cascade can be activated on the surfaces of ED as a consequence of specific interacions between pathogenic bacteria, EC and monocytes.

P 004

A RECOMBINANT THROMBOCIDIN-DERIVED PROTEIN WITH POTENT BROAD-RANGE MICROBICIDAL ACTIVITY, AND LACKING NEUTROPHIL CHEMOTACTIC ACTIVITY

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Thrombocidins (Tcs) are microbicidal proteins isolated from human blood pllatelets (Krijgsveld et al, J. Biol. Chem. (2000) 275: 20374). TC-1 and Tc-2 are derived from CXC-chemokines NAP-2 and CTAP-III, respectively, by C-terminal deletion of 2 amino acid residues.
Objective: To investigate whether Tcs may provide design templates for the development of novel antimicrobial drugs.
Methods: In this study we produced Tcs as well as N- and C-terminal variants recombinantly in *Escherichia coli*, and analysed their microbicidal, neutrophil attracting, and hemolytic activity.
Results: We identified rH-TC, a His-tagged variant of TC-1 and NAP-2 es a potent microbicidal protein (MBC 0.4 to 2 µM) with broad-range activity against Gram-positive and Gram-negative bacteria, uncluding strains (multi) resistant against conventional antibiotics. In addition rH-TC was fungicidal for *Cryptococcus neoformans*. We present evidence that the micobicidal activity of rH-TC is at least partly due to the His-tag. The cidal activity of rH-TC partially depended on the presence of a membrane potential in bacteria, but not on ionic interactions with the target organism. In contrast to TCs and NAP-2, rH-TC was not chemotactic for neutrophils. RH-TC also lacked detectable hemolytic activity.
Conclusion: Collectively, rH-TC offers attractive characteristics for further development towards a clinically applicable antimicrobial agent.

P 005

DISTINCT ROLES OF *STAPHYLOCOCCUS AUREUS* CLUMPING FACTOR

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Objective: *S. aureus* harbor multiple surface adhesins mediating colonization and infection of host tissues. To analyse their individual pathogenic we established a system allowing the functional expression of specific adhesins by the less pathogenic *Lactococcus lactis*. The surrogate bacterium was then tested for a gain of function *in vitro* and *in vivo*.
Methods: The clfA and fnBPA genes from *S. aureus* Newman and 8325-4 were cloned into *L. lactis* as described (I&I, 2000; 68: 3516).
Results: Northern blots, Western blots, FACS analysis with specific antibodies, and adherence to immobilized fibrinogen and fibronectin indicated that both adhesins were constitutively and functionally expressed by the recipient lactococci. Rats with EE were inoculated with increasing bacterial numbers and infection was followed. The minimal inoculum infecting 90% of rats (ID_{90}) with the parent *L. lactis* was 10^7 CFU. In contrast, the ID_{90} of both clfA+ and fnBPA+ lactococci was 100x lower. After infection, the clfA+ lactococci were progressively cleared from the valves. In contrast, fnBPA+ lactococci increased over time and rendered the rats sicker. This correlated with the ability of fnBPA+ lactococci to invade both the vegetations and the neighboring endothelium, and was confirmed by immunohistochemistry and internalization in cultured endothelial cells.
Conclusions: This study identified distinct roles for the clfA and fnBPA gene products in EE: one limited to colonization of the damaged endothelium, for clfA, and one extended to both colonization and invasion, for fnBPA. This original gene transfer technique into *L. lactis* might prove useful to study other pathogenic factors as well.

P 006

IN SILICO IDENTIFICATION OF A PH-RESPONSIVE REGULATOR OF *STREPTOCOCCUS GORDONII*

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Oral streptococci that cause endocarditis will experience a shift from low pH towards neutral pH upon entering the bloodstream. Previously, a neutral pH-inducible promoter of *S. gordonii* was identified using a reporter gene.
Objective: To identify the role of the gene regulated by the neutral pH-inducible promoter using bioinformatics tools.
Methods: The partial *S. gordonii* genome was obtained from The Institute for Genomic Reasearch (TIGR), and used as a database on a local BLAST server. The partial genome was searched using the BLASTN algorithm. Homology searches were performed using the BLASTX and TBLASTN algorithms. Sequence motifs were identified with the BLOCKS and PROSITE programs. Promoters were predicted using a neural network promoter site recognition program.
Results: Sequences flanking the neutral pH-inducible promoter were obtained from the partial genome sequence. The translated open reading frame governed by the promoter showed significant homology to regulatory proteins of the LysR-family of bacterial regulators. Therefore, the gene was termed pphR (putative pH-responsive regulator). Scanning the promoter region for sequences that fulfilled criteria for regulator binding sites identified putative regulatory elements in the pphR promoter.
The PphR regulatory protein possibly regulates the expression of a gene that encodes a protein of unknown function, PphX. Analysis of the incomplete genome sequences of other Gram positive bacteria, revealed that homologues of the pphR and pphX genes are present in the *Staphylococcus aureus* genome.
Conclusions: The combined application of experimental data with bioinformatics tools identified a regulatory protein that is induced upon a shift from low pH to neutral pH. This protein possibly regulates expression of a protein of unknown function that is also present in *S. aureus*.

P 007

TOLERANCE TO PENICILLIN AS WELL AS RESISTANCE TO THROMBOCIDINS IS HIGHLY PREVALENT AMONG VIRIDANS STREPTOCOCCI CAUSING ENDOCARDITIS

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Objective: To assess the relationship between the susceptibility of viridans group streptococci to penicillin and to thrombocidin prepared from human platelets.

Methods: Viridans group streptococci (VGS) were recovered from blood cultures from patients with native infective endocarditis (73 strains) and from neutropenic patients without infective endocarditis (22 strains). Also, VGS were isolated from the gingival sulcus from endocarditis patients (20 strains) and patients without endocarditis (294 strains). MIC and MBC values were determined by the broth dilution susceptibility test. Thrombocidins were obtained from platelets recovered from fresh human blood. Bacterial susceptibility to thrombocidins was measured as the percentage of surviving CFU after 30 minutes incubation with thrombocidins.
Results: Among the 73 VGS strains causing endocarditis, 57 (78%) were tolerant to penicillin, and 4 (5%) were resistant to penicillin. Significantly lower frequencies of penicillin-tolerant strains were observed among strains isolated from blood cultures from neutropenic patients ($p < 0.001$) or cultured from the gingival sulcus ($p < 0.001$). Similarly, the majority of 73 endocarditis isolates showed decreased susceptibility to thrombocidins, in contrast to 84 gingival sulcus isolates tested ($p < 0.001$). Analysis of the reduction of viable counts after exposure to thrombocidins and penicillin showed a linear relationship.
Conclusions: Endocarditis causing VGS isolates are more tolerant to penicillin and less susceptible to thrombocidins, than VGS strains isolated from the gingival sulcus or from patients without endocarditis. The degree of penicillin tolerance coincided with the decrease in thrombocidin susceptibility, suggesting that these properties may be associated mechanistically.

P 008

PENICILLIN-DEPENDENT DECREASE OF CELL WALL-ASSOCIATED AUTOLYSIN ACTIVITY OF PENICILLIN TOLERANT VIRIDANS STREPTOCOCCI

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The standard therapy for viridans streptococcal (VS) endocarditis includes prolonged treatment with penicillin. VS can be tolerant to penicillin, which way comlicate treatment. The mechanism underlying this penicillin tolerance is unknown. For the related species *Streptococcus pneumoniae* and *Enterococcus faecalis* penicillin tolerance has been linked to lack or reduced autolysin activiy.
Objective: To study the autolysins of penicillin-susceptible and tolerant VS, and the influence of penicillin on their autolysin activity.
Methods: We analysed the autolysins of penicillin susceptible and tolerant VS isolates using zymograms with *Micrococcus luteus* cell walls as substrate. Subsequently, we compared autolysin activity in cell wall protein preparations from two penicillin-susceptible and two penicillin-tolerant VS isolates, after incubation with of without 100x MIC penicillin for 1 hour.
Results: Compared to a *Lactococcus lactis* strain used as reference, the VS isolates had low autolytic activity. The number of autolysin bands and their migration in the zymograms of secreted and cell wall-associated proteins differed among the VS isolates. No relationship was found between specific autolysins or autolysin patterns and the susceptibility to penicillin. Exposure to 100x MIC penicillin decreased the activity of the major autolytic protein band of the 2 tolerant strains 64-fold, whereas the activity of the major autolysin band of the penicillin-susceptible strains was decreased 4-fold.
Conclusion: Exposure to penicillin decreased the autolytic activity of the penicillin-tolerant VS. This decrease of autolytic activity may contribute to their penicillin tolerance.

P 009

ORAL HEALTH STATUS IN PATIENTS AT RISK OF INFECTIV

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It has been recognized that bacteraemias associated with acute or chronic oral infections may provoke Infective Endocarditis (IE), this being the route of entry of microorganisms in 8-10% of cases.
Objective: The aim of this study was to determine the oral health status and oral hygiene habits in patients with cardiac conditions “at high risk” of IE.
Methods: Fifty patients with previous IE or with a prosthetic cardiac valve were recruited. An oral examination was performed including: periodontal status (spontaneous gingival bleeding, periodontal sockets and/or dental mobility), and dental status (active caries). A questionnaire based in oral hygiene habits and visits to the dental practitioner, was also collected. Results were compared with those obtained in an age and sex matched control group.
Results: Periodontitis was found in 52% of patients versus 20% of controls. Active caries was detected in 52% and 78% respectively. More than one third of the patients brushed their teeth less than once a day, this figure corresponding with 17% in the control group. Almost 40% of both, patients and controls, had not attended a dental practice for more than 2 years.
Conclusions: This study showed a high prevalence of chronic oral infections and poor oral hygiene habits in patients considered “at risk” of IE. An educational program for patients “at risk” based on routine oral checks and regular dental treatment should be designed, where both physicians and dental practitioners should be involved.

P 010

ORAL BACTEREMIA OR INCREASED BLOODSTREAM IL-1 LEVELS ENHANCE SUSCEPTIBILITY FOR VIRIDANS STREPTOCOCCAL IN AN EXPERIMENTAL NATIVE VALVE ENDOCARDITIS RABBIT MODEL

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Periodontal disease is by far the most common oral infection, giving rise to chronic inflammation characterized by raised blood levels of pro-inflammatory cytokines such as IL-1, and to frequent bacteremia. Oral bacteremia also occurs after various dental manipulations. Due to the bacteremia originating from the oral microflora, bacterial endocarditis (BE) particularly by viridans streptococci (VS), can occur in those persons having vegetations at the endocardial surface or heart valves. In the experimental endocarditis rabbit model, such vegetations are induced by the presence of an intracardiac catheter. Although this model enabled studies on BE, the pathogenesis of native BE cannot be studied correctly.
Objective: To assess the influence of oral bacteremia or IL-1 on the susceptibility for BE due to VS in an experimental native valve endocarditis rabbit model.
Methods: We removed the catheter 24 or 48 h prior to the intravenous challenge with 10^5 CFU of 2 VS test strains. Rabbits received an i.v. injection with a mixture of oral bacteria involved in periodontal disease, with IL-1 (10 U/kg), or no injection 2 h prior to bacterial challenge.
Results: In rabbits that had not been injected with the mixture of oral bacteria or with IL-1, VS test strains 1 and 2 did not induce BE. Challenge with *Streptococcus oralis* strain 1 after iv injection with the mixture of oral bacteria induced BE in 5/16 rabbits, and after injection with IL-1 in 6/12 rabbits. Rabbits injected with the mixture of oral bacteria and challenged with *Streptococcus mitis* strain 2 had no BE, whilst

after injection with IL-1, 4/12 rabbits developed BE. The difference in the frequency of BE due to strain 1 and strain 2 in the rabbits injected with the mixture of oral bacteria may be due to the high susceptibility of strain 2 to microbicidal proteins from platelets.
Conclusion: The presence of oral bacteria in the bloodstream, or administered IL-1, enhanced the susceptibility for BE in an experimental native valve BE rabbit model. These studies suggest that raised pro-inflammatory cytokine levels in the bloodstream due to chronic periodontal inflammatory disease, or associated with the traumatizing effect of dental procedures, enhance the susceptibility for native BE in humans with cardiacVGs having bacteremia due to VS.

P 011

DURATION, PREVALENCE AND INTENSITY OF BACTERAEMIA FOLLOWING DENTAL EXTRACTION IN CHILDREN

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Bacteraemia is well documented following dental extractions.
Objective: The purpose of this work was to investigate the duration, prevalence (%) and intensity of bacteraemia after dental extractions (CFU/mL) in children.
Methods: Children and adolescents attending the Eastman Dental Institute for dental treatment under general anaesthesia were recruited. Following attainment of anaesthesia, a Y cannula was inserted into an antecubital fossa vein using aseptic technique. Thirteen mL of blood were withdrawn. Three mL were inoculated into BACTEC PAEDS aerobic and anaerobic respectively A second blood sample was taken at a randomly allocated time between 10 seconds and 60 minutes after dental extractions.
Results: 500 subjects aged between 3 and 16 years were recruited. Fifty subjects were randomly allocated into a post extraction time group.

	BACTEC		Lysis Filtration			
	Base %	PE %	Base %	PE CFU/mL	%	
CFU/mL						
10 Seconds	8	68	32	0.48	66	1.57
30 seconds	10	66	24	0.06	60	0.41
1 minute	8	60	26	0.06	66	2.67
2 minutes	4	60	30	0.19	50	1.35
4 minutes	14	58	20	0.06	46	0.28
7.5 minutes	6	52	28	0.07	54	0.20
15 minutes	8	42	40	0.29	40	0.31
30 minutes	2	18	14	0.05	32	0.11
45 minutes	12	26	22	0.06	24	0.37
1 hour	2	19.6	32	0.14	35.3	0.35

Base = Baseline, PE = Post - Extraction

Conclusions: Statistical analysis of this data suggests that the bacteraemia is quenched by 11 minutes post-extraction.
This work was supported by the British Heart Foundation.

P 012

IMPACT OF AMOXICILLIN ON THE INCIDENCE AND NATURE OF BACTEREMIA FOLLOWING NASAL INTUBATION

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The literature suggests that bacteremia does not occur following nasotracheal intubation. American Heart Association and British Society of Antimicrobial Chemotherapy guidelines do not address nasotracheal intubation as a risk factor for bacteremia and subsequent distant site infection.
Objective: The purpose of this prospective, double blind, randomized, placebo-controlled study was to determine the impact of antibiotic prophylaxis on the incidence and nature of bacteremia in children undergoing nasotracheal intubation in the operating room setting.
Methods: One hundred children (55% males) were randomized evenly to amoxicillin (50 mg/kg) or a placebo 1 hour before surgery. Two minutes following initiation of nasal intubation, 6 mL of blood were drawn and divided between aerobic and anaerobic pediatric BACTEC bottles and incubated for 10 days. Standard bacterial identification methods were utilized.
Results: Eleven of 97 (11.3%) evaluable subjects, ages 1 to 8 years (mean = 3.4), had a positive blood culture of at least one bacterial organism. Three subjects had polymicrobial cultures. There was a significant difference in the incidence of bacteremia between subjects receiving amoxicillin (N = 2,4%) vs placebo (N = 9,19%) (p = 0.02). Overall, 9 different organisms were identified, including 5 aerobic, 6 facultative anaerobic, and one anaerobic bacteria.
Conclusions: We have demonstrated that bacteremia does occur during nasal intubation and that amoxicillin significantly reduces the incidence and alters the nature of bacteremia.

P 013

IV ANTIBIOTIC REGIMENS FOR ENDOCARDITIS PROPHYLAXIS

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Children with congenital heart disease undergoing dental treatment require antibiotic prophylaxis against oral streptococci.
Objective: The regimens currently used at The Great Ormond Street Hospital for Children were tested for their efficacy.
Methods: The subjects were children receiving dental treatment comprising fillings and extractions under general anaesthesia. At anaesthetic induction the antibiotic prophylaxis prescribed was administerd via an indwelling catheter. The choice of antibiotics and the nature of the dental treatment was recorded. The percentage prevalence of bacteraemia was estimated using BACTEC automated broth cultures.
Results: The percentage of positive blood cultures in children with congenital heart disease who received ampicillin alone was not significantly different from that in children receiving a combination of amikacin and teicoplanin (16.7% v 22.2% respectively, Chi Square 0.385, df = 1, p = 0.535) When compared to multiple extractions 1 both ampicillin alone and amikacin with teicoplanin were effective in reducing the prevalence of odontogenic bacteraemia.
Conclusion: In children with congenital hear disease bacteraemia after dental treatment is reduced by antibiotics but is still detected on 16% of occassions. Teicoplanin in combination with amikacin is effective in reducing bacteraemia inchildren who are allergic to penicillin or who have received penicillin within the the previous month.

P 014

BACTERAEMIA ISOLATES FOLLOWING DENTAL EXTRACTIONS IN CHILDREN

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Bacteraemia following dental extractions is common and the use of sensitive blood culture methods has increased the yield of organisms isolated.
Objective: To compare the main groups of microorganisms isolated from bacteraemia following dental extractions using a conventional broth culture technique (BACTEC) and lysis filtration (LF).

Methods: Healthy children and adolescents undergoing dental treatment under general anaesthesia at the Eastman Dental Hospital were recruited. Following induction of general anaesthesia a Y cannula was placed in either antecubital fossa using aseptic technique and 13 mL of blood withdrawn. Six millilitres of blood were processed using LF, 3 millilitres were each inoculated into BACTEC PAEDS aerobic and anaerobic bottles respectively and 1mL was frozen at –80 °C for molecular analysis. This was the baseline sample. A second 13 mL blood sample was taken 60 seconds after the maximum manipulation of the last extraction. The oral streptococci were characterised using biochemical tests and other bacterial isolates by 16S rRNA gene sequencing.
Results: The bacteria most commonly isolated were the oral streptococci (n = 24 BACTEC and n = 18 LF), Coryneform bacteria. (n = 7 BACTEC and n = 23 LF), coagulase-negative staphylococci (n = 2 BACTEC and n = 21 LF). Other species isolated included Neisseria spp. and Veillonella spp.
Conclusions: Similar bacterial species were identified from LF and BACTEC, although there were few Neisseria spp. or obligate anaerobes isolated using LF compared with the BACTEC technique.

Experimental Models (*in vitro* & *in vivo* studies)

P 015

INFLUENCE OF THE ETIOLOGIC AGENT IN THE VEGETATION WEIGHT AND BACTERIAL DENSITY OF THE EXPERIMENTAL ENDOCARDITIS IN RABBITS

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Differents infectious agents produced differents vegetations in experimental endocarditis regarding weight and bacterial density.
Objective: Our objective in the present study was to compare the vegetation weight and bacterial density in the experimental aortic valve endocarditis in rabbits due *Enterococcus faecalis*, *Enterococcus faecium*, *Streptococcus pneumoniae* and Viridans group streptococci.
Methods: The experimental aortic endocarditis in rabbits was produced by a polyethylene catheter inserted via the right artery and left in place for remainder of the experiment. Thirty-six hours after the catheter insertion into left ventricule, each rabbits was inoculated by ear vein with 10^8 CFU (colony formation unit). On day nine the rabbits were killed and the vegetation of each animal were excised, homogenized and weighed, and 0.1 ml aliquots were quantitatively cultured. 14 rabbits were used in the EE due to *E. faecalis*; 16 rabbits in the *E. faecium*; 16 rabbits in the *S. pneumoniae* and 20 rabbits in the Viridans group streptococci.
Results: The median of vegetation weight for group were: *Enterococcus faecalis* 175.36 ± 80.6 mg; *Enterococcus faecium* 94.06 ± 37.9 mg; *Streptococcus pneumoniae* 121.87 ± 87.2 mg and *Viridans group streptococci* 109.65 ± 71.0 mg. The group of *Enterococcus faecalis* obtained the greatest vegetation weight ($p < 0.05$). There were no differences among the other groups. The median of $\log_{10}$ CFU/g for groups was: *Enterococcus faecalis* 9.88 ± 0.52 $\log_{10}$ CFU/g; *Enterococcus faecium* 9.52 ± 0.8 $\log_{10}$ CFU/g; *Streptococcus pneumoniae* 8.69 ± 0.54 CFU/g and Viridans group streptococci 9.72 ± 0,48 $\log_{10}$ CFU/g. The group of *Streptococcus pneumoniae* obtained the lower bacterial level in the vegetations ($p < 0.001$). There was no differences among the other groups.
Conclusions: The group of the *Enterococcus faecalis* developed the largest vegetacions weigh of all the groups. The group of *Streptococcus pneumoniae* obtained the lower bacterial level in the vegetations compared with the rest of the groups.

P 016

TRANSESOPHAGEAL ECHOCARDIOGRAPHIC DETECTION OF ENDOCARDIAC VALVE LESIONS IN EXPERIMENTAL ENDOCARDITIS

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Objective: Experimental endocarditis models are valuable tools for studying pathogenesis and treatment of infectious endocarditis, but longitudinal observations in individual animals are precluded by the need to sacrifice the animal to access most endpoints. New technology has miniaturized echocardiography transducers to a size small enough (3.3 mm) to be passed intravascularly in humans.
Methods: We used a 5.5-10 Mhz phased vector array echocardiographic transducer mounted in an intravascular catheter to perform daily longitudinal plane, color flow Doppler enhanced, transesophageal echocardiography (TEE) on ten rabbits during the course of catheter associated experimental endocarditis. A post mortem exam was performed immediately following on the last day of the experiment.
Results: TEE performed at the time of catheter placement confirmed the catheter tip to be in the left ventricle, no echo dense masses were seen on the aortic valve and no blood flow anomalies were detected prior to catheter placement. 1+ aortic regurgitation was detected immediately after placement of the catheter. Echo dense masses and aortic regurgitaton were detected in all animals in the daily TEE exams. On post mortem exam we found vegetations ranging in size from 1 to 15 mm in diameter attached to the aortic valve, mitral valve, in the aortic root, and adherent to the ventricular wall. TEE performed on day 4 detected all vegetations larger than 1 mm on the aortic valves. Vegetations in the aortic root were detectec in 4 of 10 exams, vegetations on the left ventricle wall were detected in 9 of 10 exams. Doppler enhanced TEE imaged mild to very severe aortic regurgitation in all 10 animals and mild mitral regurgitation in 2 of 10 exams. The animals tolerated the daily TEE exam well.
Conclusions: This technology allows serial evaluations of cardiac valve abnormalities and vegetation morphology in individual study animals.

P 017

INCIDENCE OF RESISTANCE TO BETALACTAM ANTIBIOTICS AND TOLERANCE TO GLYCOPEPTIDES IN VIRIDANS GROUP STREPTOCOCCI AND S. BOVIS ISOLATED IN PATIENTS WITH ENDOCARDITIS IN BARCELONA SINCE 1990 TO 2000

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The prevalence of penicillin-resistant VGS has notably increased in the last years in Europe and USA.
Objective: The objective of this study was to know the real incidence of resistance to penicillim and related antibiotics as well as the activity of the glycopeptides antibiotics in VGS isolated in patients with endocarditis since 1990 to 2000.
Methods: A total of 85 strains of VGS were included in the study. The antimicrobial agents tested were: penicillim (PN), ampicillin (AMP), amoxicillim (AMX), ceftriaxone (CRO), cefotaxime (CTX), cefepime (CFP), cefditoren (CDT), imipenem (IMP), vancomycin (VAN), teicoplanin (TEI), linezolid (LZ), gentamycin (GEN), clindamycin (CL), erythromycin (ERI) and quinupristin/dalfopristin (Q/D).
Results: Among the 85 strains isolated, the following species were identified: 39 *S. mitis*, 20 *S. bovis*, 15 *S. sanguis*, 6 anginosus group and 5 *S. mutans*. MICs 50/90 (mcg/mL) and % of susceptibility for the 85 strains were as follows: PEN (0.06/0.25) 83%, AMP (0.12/0.5) 90%, AMX (0.06/1) 81%, CRO (0.06/0.5) 91%, CTX (0.06/0.5) 94%, CFP (0.12/1) 91%, CDT (0.06/0.25) 96%, IMP (0.015/0.06) 97%,

VAN (0.5/1) 100%, TEI (0.03/0.25) 100%, LZ (1/1) 100%, GEN (4/16); CL (0.12/>128) 61%, E (0.03/>128) 54%, Q/D (0.5/1) 95%. IMP was the antibiotic with higher activity. Resistance to penicillin was higher in *S. mitis* isolates (26%). All *S. bovis* isolated were susceptible to penicillin. In the first five years we have found 4 strains resistant to betalactam antibiotics (14%) and 9 strains in the period 1996-2000 (15%). Tolerance to VAN and TEI was observed in 71% and 73% respectively.
Conclusion: Decreased susceptibility to betalactam antibiotics was detected approximately in one fifth of the VGS isolated from patients with endocarditis. The rates of resistance did not increase over time during the last decade in Barcelona (Spain). Tolerance to glycopeptides was very high in VGS as well as in *S. bovis* isolates.

P 018

EFFICACY OF AMPICILLIN (A) PLUS CEFTRIAXONE (C) AND GENTAMICIN (G) IN THE TREATMENT OF *ENTEROCOCCUS FAECALIS* (EF) EXPERIMENTAL ENDOCARDITIS IN RABBITS

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Objective: To compare the activity of this combination and also the combination of A+C+G, to the treatment with A+G of experimental EF endocarditis in rabbits.
Methods: MICs/MBCs to A, C, and G for E91 strain were 1/4, 64/> 256 and 32/128 mg/L respectively. Synergy was demonstrated by time-kill curves for A+C at concentrations of 1 mg/L of A and 10, 20 mg/L of C. 24 h after induction of non-thrombotic aortic valve endocarditis, 10^8 CFU of E91 were injected by i.v. route. 24 h. later the animals were treated for three days with either A, A+G, A+C or A+G+C, given with a computer-controlled infusion pump system which simulates the human serum kinetics of either A (2 gr/4h iv), G (1 mg/kg/8h iv) or C (2 g/12 h iv). Mean peak and trough serum levels (mg/L) were: A: 86.4 an 4.3; C: 242.7 and 21.6; G: 4.4 and < 0.5 Animals were sacrificed 6h after the end of treatment and valve vegetations were quantitatively cultured. Results were given as mean ± SD of $\log_{10}$ CFU/g of vegetation and compared using Scheffe's test.
Results: The results obtained of the different therapeutics groups are expressed in the Table.

Treatment group	n survivors / n total	$\log_{10}$ E91 / g
Control	15 / 18	9.2 ± 0.4
Ampicillin	13 / 16	6.9 ± 0.9*
A + G	11 / 14	5.7 ± 1.1*
A + C	11 / 15	5.2 ± 0.5*
A + C + G	13 / 15	5.1 ± 1.1*

* $p < .05$ vs control; $p < 0.05$ vs ampicillin alone.

Conclusions: The combination A+C was as effective as A+G to treat experimental endocarditis due to EF91. A+C may be an alternative in patients with enterococcal endocarditis and risk factors that preclude the use of aminoglycosides.

P 019

TEICOPLANIN ALONE OR IN COMBINATION WHITH CEFTRIAXONE, LEVOFLOXACIN AND IMIPENEM IN THE TREATMENT OF EXPERIMENTAL ENDOCARDITIS DUE TO AMINOGLYCOSIDE-RESISTANT *ENTEROCOCCUS FAECALIS*

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Recent studies reveal an alarming increase in the number of aminoglycoside-resistant *Enterococcus faecalis* endocarditis.
Objective: Our objective in the present study was to compare the therapeutic efficacy of teicoplanin alone or in combination with ceftriaxone, levofloxacin and imipenem in a experimental model of aortic valve endocarditis in rabbits due to aminoglycoside-resistant *Enterococcus faecalis*.
Methods: An experimental aortic valve endocarditis due due to aminoglycoside-resistant *Enterococcus faecalis* was produced in 70 rabbits (14 controls and 56 treated) The MIC (minimum inhibitory concentration) of teicoplanin, ceftriaxone, levofloxacin and imipenem was determined by microdilution and E-test methods. Fourteen rabbits were treated with teicoplanin 20 mg/kg/12h im; 12 with teicoplanin + ceftriaxone (30 mg/kg/12h im); 18 with teicoplanin + levofloxacin (30 mg/kg/12h im) and 12 with teicoplanin + imipenem (60 mg/kg/8h im). The response to therapy was determined by the overall survival rate, the sterilization of blood cultures and vegetations and the number of CFU/g *E. faecalis* in each vegetation
Results: The median of $\log_{10}$ CFU/g (colony formation unit/gram) for groups was: Control group 9.88 ± 0.52 $\log_{10}$ CFU/g; teicoplanin 7.47 ± 0.38 $\log_{10}$ CFU/g; teicoplanin + ceftriaxone 6.82 ± 0.78 $\log_{10}$ CFU/g; teicoplanin + levofloxacin 7.48 ± 0.77 $\log_{10}$ CFU/g and teicoplanin + imipenem 5.43 ± 0.68 $\log_{10}$ CFU/g.
Conclusions: All the treatments used in this study have been shown to be efficacious in reducing the concentration of *Enterococcus faecalis* of the aortic vegetation compared to the control group ($p < 0.001$). Teicoplanin + imipenem was the most efficient treatment and it was shown to be superior to the rest of the groups in reducing bacterial level in the vegetations ($p < 0.001$). Teicoplanin + ceftriaxone was shown to be superior to teicoplanin alone ($p < 0.05$) and to teicoplanin + levofloxacin ($p < 0.05$) in the reduction of the bacterial content of the vegetations. There was no differences when teicoplanin was used alone or in combination with levofloxacin.

P 020

QUINUPRISTIN-DALFOPRISTIN ALONE OR IN COMBINATION WITH LEVOFLOXACIN IN TREATMENT OF EXPERIMENTAL ENDOCARDITIS DUE TO β-LACTAM AND GLYCOPEPTIDE-RESISTANT *ENTEROCOCCUS FAECIUM*

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The appearance of b-lactam and glycopeptide resistant strains of *Enterococcus faecium* has been followed by increasing cases of experimental endocarditis (EE) due to this m.o. The addition of ciprofloxacin to quinupristin-dalfopristin has had different results.
Objective: Our objective in the present study was to compare the therapeutic efficacy of quinupristin-dalfopristin alone or in combination with levofloxacin in a experimental model of aortic valve endocarditis in rabbits due to b-lactam and glycopeptide-resistant *Enterococcus faecium*.
Methods: An experimental aortic valve endocarditis due to b-lactam and glycopeptide-resistant *Enterococcus faecium* was produced in 41 rabbits (17 controls and 24 treated) The MIC (minimum inhibitory concentration) of quinupristin/dalfopristin, and levofloxacin was determined by microdilution and E-test methods. Twelve rabbitss were treated with quinupristin-dalfopristin 30 mg/kg/8h im and other 12 with quinupristin/dalfopristin + levofloxacin (30 mg/kg/8h im). The response to therapy was determined by the overall survival rate, the sterilization of blood cultures and vegetations and the number of CFU/g *E. faecium* in each vegetation

Results: The results of MIC was: Quinupristin-dalfopristin 2 mg/ml and levofloxacin 1 mg/ml. The median of log_{10} CFU/g (colony formation unit/gram) for groups was: Control group 9.52 ± 0.8 log_{10} CFU/g; quinupristin-dalfopristin 7.31 ± 0.56 log_{10} CFU/g and quinupristin-dalfopristin + levofloxacin 4.04 ± 1.12 log_{10} CFU/g.
Conclusions: Quinupristin-dalfopristin has been shown to be efficacious in reducing the concentration of *Enterococcus faecium* of the aortic vegetation compared to the control group ($p < 0.001$). Quinupristin/dalfopristin + levofloxacin was superior to quinupristin-dalfopristin alone in reducing bacterial level in the vegetations ($p < 0.001$).

P 021

EFFICACY OF QUINUPRISTIN-DALFOPRISTIN ALONE OR IN COMBINATION WITH GENTAMICIN, TEICOPLANIN AND IMIPENEM IN TREATMENT OF EXPERIMENTAL ENDOCARDITIS DUE TO β-LACTAM AND GLYCOPEPTIDE-RESISTANT *ENTEROCOCCUS FAECIUM*

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The appearance of β-lactam and glycopeptide resistant strains of *Enterococcus faecium* has been followed by increasing cases of experimental endocarditis (EE) due to this m.o.
Objectives: Our objective in the presente study was to compare the therapeutic efficacy of quinupristin-dalfopristin alone or in combination with gentamicin, teicoplanin and imipenem in a experimental model of aortic valve endocarditis in rabbits due to β–lactam and glycopeptide-resistant *Enterococcus faecium*.
Methods: An experimental aortic valve endocarditis due to β-lactam and glycopeptide-resistant *Enterococcus faecium* was produced in 68 rabbits (17 controls and 51 treated). The MIC of quinupristin/dalfopristin, gentamicin, teicoplanin and imipenem was determined by microdilution and E-test methods. Twelve rabbits were treated with quinupristin-dalfopristin 30 mg/kg/8h im; 15 rabbits with quinupristin/dalfopristin + gentamicin (6mg/kg/12h im); 12 rabbits with quinupristin/dalfopristin + teicoplanin (20 mg/kg/12h im), and 12 with quinupristin/dalfopristin + imipenem (60 mg/kg/8h im), 12 rabbits. The response to therapy was determined by the overall survival rate, the sterilization of blood cultures and vegetations and the number of CFU/g *E. faecium* in each vegetation
Results: All the antibiotics used in this study have been shown resistant *in vitro* to *Enterococcus faecium*. The results of MIC was: Quinupristin-dalfopristin 2 mg/ml (intermediate), Gentamicin resistant high level, teicoplanin > 32 mg/ml (resistant), and imipenem > 16 mg/ml (resistant). The median of log_{10} CFU/g for groups was: Control group 9.52 ± 0.8 log_{10} CFU/g; quinupristin-dalfopristin 7.31 ± 0.56 log_{10} CFU/g; quinupristin/dalfopristin + gentamicin 7.16 ± 0.47 log_{10} CFU/g; quinupristin/dalfopristin + teicoplanin 7.06 ± 0.6 log_{10} CFU/g and quinupristin/dalfopristin + imipenem 4.38 ± 0.69 log_{10} CFU/g.
Conclusions: All the treatments used in this study have been shown to be efficacious in reducing the concentration of *Enterococcus faecium* in the aortic vegetation compared with the control group ($p < 0.001$). There were no differences when quinupristin-dalfopristin was used alone or in combination with gentamicin and teicoplanin. Quinupristin/dalfopristin + imipenem was the most potent combination of all the treatments groups in reducing bacterial level in the vegetations ($p < 0.001$).

P 022

ADDING DEXAMETHASONE TO VANCOMYCIN HAS BENEFICIAL EFFECT IN THE TREATMENT OF EXPERIMENTAL STAPHYLOCOCCAL ENDOCARDITIS, REGARDING AORTIC VALVE DESTRUCTION

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Objective: Adding dexamethasone (Dexa) to antibiotics has been reported to have beneficial effect in studies of meningitis, arthritis and endophthalmitis. The aim of this study was to determine whether the administration of Dexa has any beneficial effect in the treatment of experimental aortic valve endocarditis (EAVE) due to a methicillin-resistant strain of *Staphylococcus aureus* (MRSA).
Methods: Rabbits with catheter-induced aortic valve vegetations were randomly assigned to a control group, and groups receiving Dexa 0.5 mg/kg, iv, b.i.d, or vancomycin (Van) 30 mg/kg, iv, b.i.d., or Dexa plus Van, for a total of 10 doses (5 d).
Results: Results were as follows:

	Survival (d)* mean ± SD	no. of vegs sterile/total	log_{10} CFU/g mean ± SD	Valve destruction mild/mod/ severe/no
No treatment[a]	2,6 ± 1,7	1 / 12	8,83 ± 3,12	1 / 0 / 8 / 3
Dexa[b]	4,5 ± 1,2	0 / 14	9,86 ± 1.86	0 / 1 / 10 / 3
Van[c]	5,9 ± 0,5	7 / 16	5,23 ± 3,35	1 / 4 / 10 / 1
Van + Dexa[d]	5,6 ± 0.9	12 / 18	4,32 ± 3.66	11 / 3 / 0 / 4

no: Not appropriate specimen for histopathological evaluation. NS: not significant.
* Maximum survival from MRSA challenge to sacrifice: 6 days.

Statistical comparisons regarding:
i) Survival **a** *vs* **b**, $p < 0.015$; **a** *vs* **c** or **d**, $p < 0,001$; **b** *vs* **d**, $p = 0,029$ **c** *vs* **d**, p = NS (Long rank test).
ii)Sterile *vs* non-sterile heart valve tissue: **a** *vs* **d**, $p = 0.002$; **b** *vs* **c**, $p = 0.007$; **b** *vs* **d**, $p < 0,001$; **c** *vs* **d**, p = NS (Fisher exact test).
iii) Log_{10} CFU/g veg: **a** *vs* **c**, $p = 0.009$; **a** *vs* **d**, $p = 0.002$; **b** *vs* **c** or **d**, $p < 0,001$; **c** *vs* **d**, p = NS (Kruskal-Wallis text).
iv) Severity of heart valve tissue damage: **a** *vs* **d**, p z 0,001; **b** *vs* **d**, p z 0,001; **c** *vs* **d**, $p < 0,001$ (chi-square test).
Conclusions: Adding Dexa to Van for 5 days has beneficial effect in the treatment of EAVE due to MRSA regarding the severity of valve tissue destruction, affecting neither survival nor blood (dat not shown) or vegetation sterilization rates.

P 023

IN VITRO ACTIVITY OF VANCOMYCIN OR LINEZOLID PLUS OXACILLIN OR IMIPENEM AGAINST METHICILLIN-RESISTANT AND GLICOPEPTIDE INTERMEDIATE *STAPHYLOCOCCUS AUREUS* (GISA)

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Vancomycin is the most common antibiotic agent used to treat MRSA infections.
Objective: The description os strains with intermediate resistance to this antibiotic is a matter of concern and an alternative treatment is clearly needed.
Methods: *In vitro* activity of vancomycin (Van) or linezolid (Lz) plus oxacillin (Oxa) or Imipenem (Imi) was tested against the Mu 50 and Mu 3 strains. MICs and MBCs were performed according to the NCCLS methodology. Time killing curves with several concentrations of antibiotic were done in duplicate using Mueller Hinton Broth supplemented with 2% NaCl and an

inoculum of 10^5 CFU/mL. In addition, sinergy studies for the combination of fosfomycin (Fos) plus Imi were realized with the chessboard method.
Results: MIC/MBC in mcg/ml of Van, Lz, Imi, Oxa and Fos, were respectively, 1/1, 4/> 64, 128/128, > 1024, > 1024 for Mu 3 and 4/> 128, 4/> 64, 64/64, 512/512, > 1024 for Mu 50. Overall, no bactericidal activity was observed with any concentration against both strains. The combination of Van plus Oxa or Imi was synergistic for Mu 50 strain, but indifferent for Mu 3. For both strains, a synergy effect was observed with the combination of Lz plus Oxa or Imi. Fos + Imi combinations showed indifference.
Conclusions: A synergistic activity was observed with the combination of Van/Oxa, Van/Imi, Lz/Oxa and Lz/Imi against Mu 50 strain. For mu 3 strain only the combination of Lz/Oxa and Lz/Imi was synergistic. None of the combinations studied showed bactericidal activity. Additional studies are clearly needded to find an alternative treatment against these strains.

P 024

COMPARISON OF VANCOMYCIN (VAN), FLUCOXACILLIN (FLU) AND AMOXICILLIN/CLAVULANATE (A/C) IN THE TREATMENT OF EXPERIMENTAL ENDOCARDITIS DUE TO METHICILLIN-RESISTANT AND GLYCOPEPTIDE-INTERMEDIATE *STAPHYLOCOCCUS AUREUS* (GISA)

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The emergence of GISA in the clinical environment warrants the search for new treatments. A/C was previously shown to be effective against experimental endocarditis due to methicillin-resistant *S. aureus* (MRSA). Moreover, the development of glycopeptide resistance in MRSA was shown to be paralleled by a decrease in methicillin-resistance expression. This phenomenon was recently referred to as the «seesaw» effect (J. Bacteriol. 1997;179:2557) and suggests that A/C and maybe other betalactams might represent an alternative against GISA.
Objective: To test the *in vitro* and *in vivo* efficacy of VAN, FLU and A/C against the two well characterized strains MRSA PC2 and its GISA derivative PC-3* (NEJM 1999;340:517).
Methods: The parental MRSA PC2 and its GISA derivative PC3* were used. The MIC of VAN, FLU and A/C for these organisms was 2 and 16 mg/L, 4 and 2 mg/L and 4 and 2 mg/L, respectively. In population analysis profiles, PC2 and PC3* grew on plates containing either 8 and > 16 mg/L of VAN, 250 and 32 mg/L of FLU or 64 and 4 mg/L of A/C. This underlines the above-mentioned «see-saw» effect. Rats with aortic vegetations were challenged with 10^5 (PC2) or 10^6 (PC3*) CFU and treated for 5 days with human-like kinetics of either VAN (1 g i.v./12 h), FLU (2 g i.v./6 h) or A/C (1.2 g i.v./6 h). Control rats were killed at the start of therapy and treated rats 12 h after the last dose.
Results: Infected rats/total numer of rats (median [range] log CFU/g of vegetation]):

	PC2	PC3*
Controls	13/13 (7.7 [4.7-8.6])	9/9 (7.3 [5.8-8.1])
VAN	13/13 (7.4 [3.5-9.4])	8/8 (8.2 [2.9-9.5])
FLU	12/12 (8.8 [4.6-9.7])	9/12 (5.5 [2.0-8.1])*
A/C	4/13 † (2.0 [2.0-4.6])†	1/13† (2.0 [2.0-5.9])†

*[†, P < 0.05 versus controls, VAN and FLU; *, P < 0.05 versus FLU therapy of PC2].*

Conclusion: Compared to controls killed at the start of therapy, VAN was only bacteriostatic against PC2 and failed to inhibit growth of PC3*. FLU was ineffective against PC2, but significantly decreased vegetation bacterial counts against PC3*. In contrast, A/C was successful against EE due to both PC2 and PC3* GISA isolates. This confirme the decreased ability GISA to express methicillin-resistance, and highlights the good activity *of A/C* against both the MRSA parent and its GISA derivatives *in vivo*.

P 025

EFFICAY OF SYNERCID AND/OR CEFPIROME IN THE TREATMENT OF EXPERIMENTAL ENDOCARDITIS DUE TO GLYCOPEPTIDE INTERMEDIATE *STAPHYLOCOCCUS AUREUS*

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The emergence of glycopeptide intermediate *Staphylococcus aureus* (GISA) has prompted the search for new therapeutic alternatives.
Objective: In this study, we tested the efficacy of synercid (SYN) and/or cefpirome (CP) in experimental endocarditis (EE) due to a well characterized isolate of GISA named PC-3* (N Engl J Med 1999; 340:517).
Methods: The organism was resistant to vancomycin (MIC = 16 mg/L) as, well as to erythromycin, clindamycin, gentamicin and ciprofloxacin. On the other hand, it was susceptible to SYN (MIC 0.5 mg/L), and had relatively low MICs of CP (MIC = 8 mg/L) and other beta-lactams, in spite of both penicillinase and PBP2A production. Both SYN and CP were bactericidal when usted at therapeutic concentrations in time-kill experiments (loss of ≥ 3 log CFU/mL/24 h). Rats with aortic vegetations were treated for 5 days with human-like kinetics of SYN (7.5 mg/kg i.v. 3-times/day), CP (2 g i.v. 2-times/day), SYN combined with CP, or vancomycin (1 g i.v. 2-times/day). Treatment (Rx) with the SYN/CP combination was attempted because it demonstrated synergism against methicillin-resistant staphylococci in previous experiments. Rx was started 12 h after bacterial challenge. Controls were killed at the start of therapy.
Results were (infected rats/total numer of rats [median log CFU/g of vegetation]):

Controls	SYN	CP	SYN/CP	Vancomycin
10/10 [5.8]	2/12 [2.0]†	2/10 [2.]†	0/14 [2.0]†	7/8 [8.1]

[†, P < 0.05 versus controls and vancomycin-treated rats]. Note: 2.0 log CFU/g = limit of detection.

Human-like kinetics of both SYN and CP, alone or combined, successfully treated EE due to the GISA isolate PC-3*. Since monotherapy was effective, the possible advantage of combination Rx did not appear in this setting. In contrast, vancomycin failed and could not inhibit bacterial growth in the vegetation. Importantly, no Rx failures in the SYN of CP groups grew resistant organisms, whereas 3/7 vancomycin failures contained variants that grew on plates containing 32 mg/L of the drug.
Conclusions: SYN and CP represent potential Rx alternatives against problematic GISA infections.

P 026

DAPTOMYCIN PHARMACODYNAMICS IN ENDOCARDITIS: A SIMULATION OF POTENTIAL EFFICACY USING A MONTE CARLO PREDICTION MODEL

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Objective: Daptomycin is a novel lipopeptide with activity against a large number of drug resistant gram-positive pathogens including MRSA, VRE and GISA. Recently, it has

been shown that AUC/MIC is predictive of daptomycin success in an animal model.
Methods: We derived the pharmacodynamic parameters for daptomycin administered as a once-daily 6 mg/kg dose against staphylococci in an *in vitro* pharmacodynamic model that utilizes simulated cardiac vegetations. Optimal AUCfree/MICs (99.9% kill) for staphylococci were generated from model killing curves over 72 h. Daptomycin MICs were then determined for 150 clinical isolates of *S. aureus*: (MSSA and MRSA n = 100) and coagulase-negative staphylococci; (MSSE, MRSE = 50) and combined with patient AUCs derived by varying volume of distribution, weight and renal function (range 30-100 ml/min). The resulting AUCs, MICs and their distribution were imputed into a Monte Carol Prediction Model (MCPM) to determine the probability of achieving the desired PD endpoints.
Results: MICs ranged from 0.03-0.5 mcg/ml. AUCfree/MIC that generated maximal kill ranged from 91.2-1520 for daptomycin at 6 mg/kg q 24 h. Optimal kill (99.9% CFU/g reduction) in the models was associated with an AUCfree/MIC = 142-365. MCPM simulations for 6 mg/kg q 24 h predicted the probability of achieving a 142-365 ratio of AUCfree/MIC as 81-97% for MSSA, MRSA, MSSE and MRSE.
Conclusions: Daptomycin has reliable activity against drug resistant staphylococci and may provide a viable treatment option for endocarditis.

P 027

THE INFLUENCE OF ADJUNCT CLARITHROMYCIN (CAM) ON THE TREATMENT (RX) OF RABBIT *PSEUDOMONAS AERUGINOSA* (PA) EXPERIMENTAL ENDOCARDITIS MODEL (EEM) WITH THE COMBINATION IMIPENEM-TOBRAMYCIN (IMP-TOB)

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Left-sided PA endocarditis has a low medical cure rare. The exopolysaccharide (alginate) produced of mucoid strains of PA seems to be one of the main reasons. It has been proved that if this alginate was removed, the clearance of bacteria from the vegetations is enhanced. Recent data demonstrated the ability of CAM to inhibit the production of glycocalyx.
Objective: The objetive of this work was to determine the influence of adjunct CAM on the Rx of PA EEM with IMP-TOB.
Methods: We used the rabbit model of left sided endocarditis. One day after the catheterization we injected 10^8 CFU of bacteria.48 hours after bacterial challenge, animals were randomized to treatment or control (no treatment) groups. MIC/MBCs for the test strain of IMP and TOB were 1/ 4 and 1/ 2 (in mcg/ml). Doses employed (given for five days), were 25 mgr/kgr IMP bid I.V plus 4 mgr/kg TOB bid I.M. Halft of the animals of the treatment group recieved also CAM 15 mgr/kg bid IV. All animals were sacrificed at least 8 hours following the last dose of drug and the cardiac valve vegetations were aseptically removed and cultured quantitatively.
Results were as follows:

Regimens	Mean ± SD $\log_{10}$ CFU/gr veg. (n. of rabbits)
Controls	9.07 ± 0.8 (9)
IMP/TOB/CAM	4.38 ± 2 (9)
IMPT/TOB/CAM	4.50 ± 1.4 (9)

Conclusions: In the rabbit PA EEM the combination of IMP/TOB reduces bacterial vegetation counts significantly compared to controls ($p < 0,001$). The association with CAM doesn't enhance the efficacy of this regimen in this model.

P 028

TDHE POTENCY OF *ACINETOBACTER BAUMANNII* (AB) TO PRODUCE ENDOCARDITIS IN THE RABBIT EXPERIMENTAL MODEL (REM)

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AB is now recognised as a common cause of nosocomial infections. It accounts for up to 4.8% of clinically significant bacteremias and is the third most common Gram(-) isolated from positive blood cultures. IR spite of these only twenty cases of endocarditis from the opportunistic bacterium have been recorded.
Objective: We tried to evaluate the potency of *AB* to produce endocarditis in the REM of left sided endocarditis.
Methods: We used a strain of *AB* isolated from the blood of a bacteremic patients in the ICU. The serum sensitivity of this train was determined in human and rabbit serum and a high degree of serum resistance was proved. One day after the catheterization ten of the rabbits were injected with 10^{10} CFU of bacteria. Six of them died of sepsis (4 on day 6 and 2 on day 7). Post mortem examination revealed only small vegetations. Twenty rabbits were inoculated with 10^9 CFU and were sacrificed on day 8. Twelve of them had sterile vegetations (1.4 $\log_{10}$). The mean bacterial titer in vegetations (mean ± SD $\log_{10}$ CFU/gr veg.) was 2.04 $\log_{10}$ ± 0.9.
Conclusions: *AB* has an extremly weak potencity to produce bacterial endocarditis in this experimental model. This becomes obvious comparing these results with the bacterial titers in vegetations of other studies with bacteria classically producing endocardits. These results are also in agreement with the clinical data in humans where high and rising rates of bacteremia are opposed to only twenty cases of endocarditis. The inability of adhesion of the bacterium to the sterile vegetations is the possible cause.

Series of infective endocarditis

P 029

CHANGING PROFILE OF INFECTIVE ENDOCARDITIS: RESULTS OF A ONE-YEAR SURVEY IN FRANCE

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Objective: Eight years after a previous similar study, we conducted a prospective survey in order to update the knowledge on epidemiologic, clinical, microbiologic and outcome characteristics of infective endocarditis (IE) in France.
Methods: We collected data of all adult patients hospitalized for IE in 1999 in the 3 regions that participated in the previous study and in 3 new regions, accounting for a total of 16 million inhabitants, i.e. 26% of the whole French population. For each patient, a case report form was filled out by the patient's attending physician (clinical and echocardiographic data) and by the microbiologist. A validation committee reviewed all the forms. Only Duke definite cases of IE were analyzed.
Results: Of the 819 cases that were reported, 496 occurred within the time and area frame of the study, 390 of which were Duke definite, accounting for a crude annual incidence of 29 cases/million. Age- and sex-standardized incidence was 31cases/million/year. Incidence peaked in men between 70 and 80 years of age. IE occurred in patients with no previously known heart disease in 43% of the cases. The frequency of prosthetic valve IE was 16%. Blood cultures were negative in 9% and no

microorganism could be identified in 5% of the cases. In the remaining 95%, the distribution of causative microorganisms was as follows: streptococci 50% (*Streptococcus bovis* 25%; oral streptococci 17%, other streptococci 8%); enterococci 8%, staphylococci 32% (*S. aureus* 24%; coagulase-negative staph 8%); and other pathogens 8%. A major echocardiographic criterion was present in 355 cases (91%), including 336 vegetations, 66 abscesses, and 15 prosthesis dehiscences. Valve surgery was performed in 49% of the patients during the initial hospital stay. In-hospital lethality was 16%.
Conclusion: As compared to 1991, several new trends were recorded: 1) the increase of percentage of IE in patients with no previously known heart disease; 2) the increase of IE due to staphylococci and to *S. bovis*; 3) the increase of valve surgery during the initial hospitalization; and 4) the decrease of in-hospital lethality.

P 030

INFECTIVE ENDOCARDITIS: RISK FACTORS, CLINICAL AND EPIDEMIOLOGICAL FEATURES

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Objetive: To evaluate the clinical and epidemiological features, risk factors and outcome of the cases of infective endocarditis (IE) attended at our hospital.
Methods: We analyzed cases of IE with definite diagnosis (Duke criteria) presenting to Cabueñes Hospital from 1992 to 2000. Cabueñes Hospital is a local hospital with 500 beds that serves a population of 300.000 people.
Results: During the study period, there were 73 cases, of which 69 were Nature Valve Endocarditis (NVE) and 4 Prosthetic Valve Endocarditis (PVE). Thirty four cases were left-sided (18 aortic and 16 mitral) and 23 were right-sided (all tricuspid in VDVP patients). Fifty three patients were male (72.6%) and there were 20 women (27.4%) with a mean age of 51 ± 2.6 years. The main risk factors found were VDVP (31%), previous IE (15%) and rheumatic disease (9.6%). The predominant symptoms were fever (92%), new murmur (48%) and dyspnea (37%). Eleven patients suffered peripherical embolies and 17 had lung embolies. Echocardiography was done in 69 cases (94%) and mayor echocardiographic criteria were found in 59 (83%) of them. In NVE, the most frequent isolated pathogen were *S. aureus* (39%), *Streptococcus spp* (23%) and *Enterococcus spp* (15%). In PVE, *S. epidermidis* (66%). Overall mortality was 15%, surgery was required in 15% of cases and 70% of cases were discharged.
Conclusions: *S. aureus* (probably related to the high percentage of VDVP) and *Streptococcus spp* are the most frequent pathogen in our serie, although the increasing importance of *Enterococcus spp* must be taken into account. Mortality was similar to that described in other series in general.

P 031

INFECTIVE ENDOCARDITIS: 10 YEARS EXPERIENCE

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Objective: We reviewed 110 consecutive cases of infective endocarditis diagnoses from 1991 to 2000 and we analyzed the variables related with mortality.
Methods: A retrospective case study that examinates the general characteristics, risk factors, clinical course and survival of 110 patients who fulfilled the Duke criteria for IE between 1991 to 2000.
Results: Patients: 82 (75%) males, 29 (25%) females. Age 50 ± 19 years (20-83), Underlying heart disease was present in the 43% of the cases. Primary focus: Evidence in 49 cases, 9 dental, 9 endoscopy or abdomir surgery, 9 post-cardiac surgery, 7 in skin and joints, 5 inmunosuppresion, 5 central vein catheters, 4 hemodialysis, 2 urological procedures. Location: Aortic valve 33 cases, mitral valve 28, prosthetic aortic valve 10, prosthetic mitral valve 5, aortic and mitral valves 5. Abscesses 11 cases and embolic phenomena in 49 (29 mayor arterial emboli). Microorganisms: 33 *Staphylococcus aureus*, 13 *Staphylococcus epidermidis*, 34 *Streptococcus spp*, 6 *Enterococcus spp*, 8 Gram negative bacterium, 4 fungus, 7 blood cultures negative. HACEK group microorganisms 5 cases. Clinical course: 57 acute (< 6 weeks), 49 subacute. Echocardiographic diagnosis: 93 Vegetations (84%). Treatment: 39 cardiac surgery (36%), 71 medical treatment (64%). In-hospital mortality: 26%. Univariate analysis of the variates that increased the mortality: 1-females 12/28 (42,8%) *vs* 16/80 (20%); $p < 0.05$. 2- Acute course 37% *vs* 14%; $p < 0.01$. 3- Mayor arterial emboli 42% *vs* 20%; $p < 0.05$. 4- Negative echocardiogram 47% *vs* 22%; $p < 0.05$. 5- Prosthetic or native mitral val involved 42% *vs* 16%; $p < 0.05$. 6- Virulence microorganism. 7- Medical treatment 32% *vs* cardiac surgery 13%; $p < 0.05$. 8- Abscess present 41% *vs* 24%; $p < 0.05$. 9- Older than 70 years old 16/27 (59%) *vs* 13/83 (15.6%); $p < 0.001$. Multivariate analysis, the only variate that worsened the prognosis with statistical significance was to be older than 70 years old.
Conclusions: Infective endocarditis have an obscure prognosis in patients older than 70 years old.

P 032

INFECTIVE ENDOCARDITIS: ANALYSIS OF 117 CASES

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Objective: To evaluate the clinical and prognostic features of infective endocarditis (IE).
Methods: A retrospective case study that examinates the general characteristics, risk factors, clinical course and survival of 117 patients who fulfilled the Duke criteria for IE between January 1994 and December 2000.
Results: Of 117 patients identified, 80 were male (68%) with a mean age of 48 ± 18 years. Hypertension was present in 23%, diabetes in 16%, hyperlipidemia in 7% and the 60% were smokers. We identified 45 patients (38%) with intravenous drug-addiction. A 21% had previous heart disease, and 39% had some valve abnormality, being the more frequent the degenerative valve disease (50%). A 13% of patients had a previous episode of IE. Positive blood cultures were present in 86%: *Staphylococcus aureus* the most common organism (48%), and *Streptococcus spp* in 19%. Transthoracic echocardiography (TTE) established the diagnosis in 70% of the overall serie, but only in the 28% in case of prosthetic endocarditis. A transesophageal echocardiogram (TEE) was perfomed in 42%. Ninety-seven patients (87%) had native valve IE, affecting the mitral valve in 28%, aortic valve 24%, mitro-aortic valves 7%, tricuspid valve 36%, and one case of pulmonar valve IE. Forteen (13%) had prosthetic valve endocarditis: 50% affecting an aortic prosthesis and 43% mitral. 75% of patients developed some type of complications (clinical and echocardiographical) during hospital stay: heart failure in 36%, embolic events in 45%, moderate or severe valve insufficiency in 59%, abscesses in 13%, fistulas 4%, pseudoaneurysm 4%, prosthesis dehiscence 36%, arrithmias in 7% and pulmonar arterial hypertension in 27%. 35 patients (31%) underwent cardiac surgery during the active phase. The in-hospital mortality rate was 22%, the majority due to heart failure, stroke or septic shock. Only 4 patients (11%) of those who underwent surgery died.
Conclusions: The clinical profiles of IE have changed in recent years, owing to the advent of TEE, the introduction of new diagnostic criteria, and the increased frequency of intravenous drug users. IE has still a high morbimortality during the active fase. As in other series, we have a high

prevalence of IE caused by *S. aureus*. The TTE diagnoses the majority of vegetacions in native valve IE, but has a low sensibility to detect complications and prosthetic valve IE, where is essential the TEE. In one third of cases requires cardiac surgery in the active fase, having those patients a low in-hospital mortality rate, so the surgical interven-tion should not be delayed in the presence of complications or parcial response to medical treatment.

P 033

INFECTIOUS ENDOCARDITIS: A STUDY OF 105 CASES

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Objective: The authors present two different series of patients with Infectious Endocarditis (IE) hospitalised in the same ward of Curry Cabral in Lisbon are presented and compared.
Methods: The two series were separated by a 13-year period – the first included patients seen from 1970 to 1976 and the second form 1988 to 2000. In the first series (20 patients) IE occurred mainly in patients with previous cardiac valvular lesion, the course was sub acute and *Viridaris group stretpcocci* was the predominant agent.
Results: In the last series (85 patients), most of the patients were young and didn't have previous valvular lesions. Right side endocarditis predominated and the course was acute. Most of the patients were drug addicts and had HIV infection. *Staphylococcus aureus* was the predominant agent.
The difference of ages of the two series was significantly different. The diagnostic value of echocardiography; transthoracic and transesophageal is stressed. Details of evolution of patients with HIV infection are presented according the values of CD4+ lymphocyte counts.
Conclusions: The relative good prognosis of antibiotic treated IE, of drug addicts, even with HIV infection is presented.

P 034

RISK FACTORS AND OUTCOME IN 53 CASES OF NATIVE VALVE STAPHYLOCOCCAL ENDOCARDITIS

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Over the last decade, the incidence of staphylococcal endocarditis has increased and represents 23-35% of all cases.
Objective: Investigate the risk factors and outcome of native valve staphylococcal endocarditis in Slovak Republic.
Methods: Between 1992 and 1996 all cases of native valve infective endocarditis of stapylococcal origin were prospectively evaluated using a protocol which was submitted to all medical departments in the Slovak Republic. No cases of prostethic endocarditis were included. Major and minor Duke criteria of the Duke Endocarditis service were recorded for definition of infective endocarditis as definitive or possible. The subgroup of staphylococcal endocarditis with a fatal outcome was compared with the subgroup of patients that survived, to determine the risk factors for death in univariate analysis.
Results: There were 53 cases of staphylococcal endocarditis within the 5-year period studied. Thirty of 53 patients had predisposing heart disease (39,6% rheumatic fever) but only 3 were on dialysis, only 2 had central venous catheter, only 2 intravenous drug abuse but 7 had prior cardiosurgery. Mortality was 39,6%. Statistical anlysis revealed that attributable mortality was significantly associated with systemic embolisation ($p < 0.02$), inappropriate therapy ($p < 0.001$) either because of too short therapy ($p < 0.03$) or wrong antibiotic therapy ($p < 0.01$). Surgical therapy was associated with better outcome ($p < 0.04$).
Conclusions: Native valve staphylococcal endocarditis has a high morbidity and mortality. Cardiac surgery improved the outcome of this disease.

P 035

EPIDEMIOLOGY OF PATIENTS WITH ENDOCARDITIS IN NIS, YUGOSLAVIA

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Objective: The aim of this study was to determine the epidemiological characteristics of patients with Bacterial Endocarditis (BE) treated in University cardiology clinic in Nis, Yugoslavia.
Methods: Blood culture confirmed BE in 10 patients with fever and echocardiographic findings of cardiac valve vegetation.
Results: The mean age was 52.3 years (range from 41 to 68 years), and there were 5 male and 5 female patients. Input of infection was: complications of surgical procedures in 30%, complications of cardiovascular interventions in 20%, acquired heart disease in 10%, dental procedures in 10% and unknown in 20%. The mitral valve was involved in 30%, the aortic valve in 30%, both valves in 30%, and the mitral and tricuspid valve in 10% patients. 30% patients were found to have mitral valve prolapse. Echocardiography showed vegetations on aortic valve in 30%, mitral valve 30%, both valves in 20% and implantation aortic valve in 20% patients. *Enterococcus faecalis* was cultivated in 40%, *Streptococcus β-haemoliticus* in 40%, *Staphylococcus epidermidis* in 10%, and both, *Enterococcus faecalis* and *Staphylococcus epidermidis* in 10% patients. 77 blood cultures from patients who were hospitalized shown that 75% was positive, and results of tests for antibiotic susceptibility were analysed for resistance among isolates: *Enterococcus faecalis* resistant on Tetracycline 100%, Penicillin G (high dose) 76%, Gentamicin 57%; *Streptococcus β-haemoliticus* resistant on Amikacin 100%, Gentamicin 92%, Trimetroprim + suf. 67% and *Staphylococcus epidermidis* resistant on Lincomycin 100%, Penicillin G (high dose) 71%.
Conclusions: Bacterial Endocarditis is responsible for substantial morbidity and high rate of mortality. Prophylaxis measures should be used in high risk patients with acquired or congenital heart diseases, during diagnostic and therapeutic procedures associated with bacteremia.

P 036

RISK FACTORS INFLUENCING CLINICAL OUTCOME IN PATIENTS' WITH INFECTIVE ENDOCARDITIS

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Objectives: to asses the risk factors for early lethal outcome in patients with infective endocarditis.
Methods: Retrospective study in an intensive care unit of a university hospital for infectious diseases of 69 patients with infective endocarditis according to the Duke criteria. The following variables were evaluated: a) general patient's characteristics such as gender, age, chronic disesaes, predisposition for IE; b) clinical presentation (subacute and acute, severe sepsis with multiple organ dysfunction, shock), duration of illness until hospitalisation, length of fever (> 37.5 °C) after the start of appropriate antimicrobial therapy, type of affected valve, localisation, specification of maior and minor Duke criteria; c) complications such as central nervous affection, cardiac failure; d) interventions (antibiotics, timing of appropriate antimicrobial therapy, need for mechanical ventilation, surgical procedure); e) outcome.
Results: Twenty-two of 69 patients died during hospitalisation (31.9%). Univariate analysis identified duration of illness, timing of optimal antibiotic therapy, length of fever after the start of appropriate treatment, severity of the disease, mechanical ventilation, developement of cardiac failure and CNS complications as factors associated with increased risk of

death. The multivariate forward stepwise logistic regression analysis identified mechanical ventilation as the most important risk factor of lethal outcome (p = 0.0043; OR = 3.03). Cardiac failure (p = 0.0162; OR = 3.014) and CNS complications (p = 0.0371; OR = 3.012) were also identified as significant independent predictors of death.
Conclusions: Mechanical ventilation of patients with infective endocarditis as well as cardiac failure and neurologic complications significantly increases risk of death.

P 037

ENDOCARDITIS CAUSED BY MULTIRESTANT BACTERIA

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Objectives: To study the etiology and clinical aspects of endocarditis in order to monitorise its therapy.
Methods: We studied the etiological agents, the predisposing factors, the symptoms, the imagistical results and the complications of the patients admitted between 1990 and 1999.
Results: We evaluated 76 patients: 43 suffering from subacute endocarditis and 33 suffering from the disease at its highest peak (sepsis); there were 42 male, 34 female, among of all the patients, adults (61 cases) were mainly involved.
In 2/3 of the patients we noticed one or more predisposing factors. The mitral valve was affected in 64% of the cases. Of those 33 patients above mentioned, apart from endocardites there have been notice multiple involved organs. The bacteriological strains were: *Staphylococcus sp*. (27 cases-25% of which were metiresistant, SMR), *Streptococcus sp*. (9 cases), E. fecalis (7 cases of which 44,3% were ampicillin- and erithromicin- resistant and 26,21% were gentamicin- resistant), BGN (*K. pneumoniae, Ps. aeruginosa, B. fragilis*) –3 cases; mixed bacteriological agents– 2 cases (all of the strains were resistant in 8 to 10 tested antibiotics). The antibiotic treatment was bacteriologically and clinically performed. The mortality occurred in 9 of 33 (27.27%) sepsis cases and in 2 of 43 (4.34%) subacute endocarditis.
Conclusions: The etiological treatment of endocarditis is dependent upon the diversity of the involved strains and upon their susceptibility to antibiotics.

P 038

INFECTIVE ENDOCARDITIS IN CHILE: A PROSPECTIVE STUDY

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In Chile Infective Endocarditis (IE) still has a high morbidity and mortality despite new diagnostic tools and modern treatment.
Objective: To determine the frequency and type of germs causing this disease, its complications and the outcome of medical and surgical treatment along the country and compare these results between regions.
Methods: Prospective non randomized study. 29 secondary and tertiary hospitals in the 13 regions of Chile. 211 consecutive patients were studied prospectively during 1998-2000 referred from Northern regions of the country (NR), Southern regions (SR) and Metropolitan region (MR)-the capital-, that fullfilled the Duke diagnostic criteria for IE. Statistical analysis by Anova, ttest and chi-square. Significance level p < 0.05.
Results: Mean age ± SD = 52.4 ± 16.1 years; men = 76%, Geographical distribution: MR = 59%, NR = 14% and SR = 27%. Duke criteria for definitive IE = 81%.

Results: (In brief)	TOTAL n (%)	MR n (%)	NR n (%)	SR n (%)	p
CLINICAL:					
Subacute form	128 (71)	79 (72)	22 (73)	23 (65)	NS
COMPLICATIONS:					
Embolism	60 (24)	42 (28)	7 (24)	11 (20)	NS
Cardiac failure	126 (63)	65 (62)	20 (69)	41 (64)	NS
Renal failure	49 (18)	29 (18)	10 (34)	10 (15)	NS
MICROBIOLOGY:					
Str. Viridans	37 (40)	24 (37)	4 (20)	11 (52)	< 0.05*
S. aureus	44 (41)	27 (42)	11 (55)	6 (29)	< 0.05*
Enterococcus	7 (8)	6 (9)	1 (5)	4 (19)	NS
Fungi	5 (4)	2 (3)	3 (15)	0 (0)	NS
Miscellanea	11 (3)	6 (9)	1 (5)	4 (19)	NS
Negative culture	76 (38)	46 (41)	10 (33)	20 (49)	NS
ECHOCARDIOGRAPHY:	(*) NR vs SR				
Vegetations present	135 (71)	82 (69)	26 (86)	28 (79)	NS
SUCCESSFUL MED. TREAT:	82/139 (59)	42/73 (58)	12/23 (52)	27/43 (62)	NS
SURGICAL TREAT:	101 (57)	62 (58)	16 (55)	23 (53)NS	
MORTALITY:	39 (23)	26 (25)	5 (19)	8 (20)	NS

Conclusions: Among the three regions of Chile studied: 1) There is no statistical difference in frequency of clinical manifestacions and complications. 2) Nationwide, the average incidence of negative blood cultures, streptococcal and staphylococcal infections are not significatly different. In NR staphylococcal IE predominate and in SR Strep. Viridans. 3) Vegetations in echocardiography, succesful medical treatment, surgical interventional frquency and mortality rates are similar.

P 039

IE AT AUB-MC, A TERTIARY CARE CENTER IN LEBANON

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Objective: Infective Endocarditis (IE) remains a disease associated with high morbidity and mortality. Many studies have been reported worldwide; however, data from the Middle East region is scarce.
Methods: We conducted a retrospective review of all recorded cases of IE in adult patients admitted between Jan 1986 and April 2001 to the American University of Beirut-Medical Center (AUB-MC), a tertiary care center in Lebanon.
Results: The total number of cases was 91.
The mean age was 47 ± 18 years. 59% of patients had a predisposing cardiac condition, the most common of which was rheumatic heart disease (33%). Transesophageal echocardiography was performed in 36 patients (40%), of which 32 showed positive findings (89%). When applying the revised Duke criteria, 82% of the patients were classified as definite and 17% as possible. Mean hospital stay was 37 ± 19 days. Endocarditis occurred on prosthetic valves in 20%, rheumatic valves in 37%, congenital lesions in 13% and on normal valves in 18% of the patients. Blood cultures were positive in 76% of the cases: the most commonly isolated organisms were *Streptococcus spp*. (54%; 40% Streptococcus group viridans) and staphylococci (36%; 10% coagulase negative staphylococci and 26% *S. aureus*, 28% of which were methicillin-resistant.) There was no significant change in the distribution of organisms recovered before and after 1991. The mean duration of therapy was 41 ± 45 days. Surgery was performed in 29% of cases mostly for valvular regurgitation, followed by heart failure. The complication rate was 69% with congestive heart failure (27%), new valvular regurgitation (18%), systemic embolization (14%), stroke (12%), and intracardiac abscess formation (11%) being the most common. The overall mortality rate was 17%.
Conclusions: Our results indicate that the rate of complications from IE is higher than that reported in the literature. Unlike studies reported from USA, Northern Europe and the Middle East, we continue to have a predominance of streptococci as etiologic agents in IE, and rheumatic heart disease as the most common underlying heart condition. Application of the revised Duke criteria was useful in confirming the diagnosis of IE.

P 040

RATE OF BACTERIA ISOLATED FROM INF. ENDOCARDITIS

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This descriptive study was carried out in 1998-1999 at Shaheed Beheshti University hospital.
The diagnosis of endocarditis is based on the clinical features, laboratory tests and echocardiographic imaging. The most precise examinations of patients with infective endocarditis are transesophageal echocardiography and blood culture.
Medhod: The blood samples were transfered in to the culture bottles. The blood cultures were sent to the laboratory and were placed in the incubator for 24 h. If no growth was seen, the media were incubated for a longer period.
Results: In 97 patients (38 female, 59 male) suspected to have infective endocarditis, causative organisms were: *S. sanguis I* (9%), *S. sanguis II* (7%), *S. mitis* (3%), *S. mutant* (3%), *S. pneumoniae* (3%), *S. bovis* (2%), *S. salivarius* (2%), *Enterococcus fecalis* (2%), *Staphylococcus aureus* (12%), *S. epidermidis* (10%), *Brucella melitensis* (6%), *Escherichia coli* (5%), *Klebsiella pneumoniae* (5%), *Pseudomonas aeruginosa* (2%), Neisseria mucosa (1%) and the rest of cultures (28%) were negative.
Conclusions: Viridans group streptococci, Styaphylococcocci and *Gram-negative Bacilli* were the most common etiological agents. Almost one thrid of the cases had negative blood cultures.

P 041

FACTORS PREDICTING LONG-TERM OUTCOME IN NON-ADDICT PATIENTS WITH INFECTIVE ENDOCARDITIS. A 14 YEAR STUDY (1987-2000)

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Most studies on infective endocarditis (IE) only evaluate short term, active phase results. Long-term outcome are less well known.
Objective: To study long-term evolution of non-addict patients with IE and the possible factors associated with prognosis.
Methods: We have reviewed our series of 217 consecutive patients dignosed of IE in our two centers between 1987 and 2000. Von Reyn and Durack's criteria were used for diagnosis.
Results: Mean age was 48 ± 19 years; 60% of patients were male. Causal microorganisms were *Staphylococcy* (36%), *Streptococci* (34%), other (19%) and non-identifyed) 11%). IE was prosthectic in 32% of cases (early prosthetic IE 50%, late prosthetic IE 50%) and native in 68% of patients. Early mortality was 18%. Early surgery during the active phase of disease was performed in 48% of patients. Ten-year survival was 88% for patients surviving the active phase of IE. Overall probability of survival, including early mortality, was 70% at 10 years. Long-term survival was not affected by gender (male 68% and females 70% at 10 years, NS), existence of not of underlying heart disease (68 *vs* 72%, NS), mitral or aortic involvement (64 *vs* 74%, NS), causal microorganisms (*Staphylococci* 68%, *Streptococci* 79%, other 76%, NS) or subtype of IE (native IE 75%, prosthetic IE 67%, NS). Four features were associated with a lower survival at 10 years: age > 65 years (21% *vs* 76%, $p < 0.001$), unidentifyed causal microorganism (17 *vs* 72%, $p < 0,001$), need for early urgent surgery (57%) *vs* 78% for elective surgery and 70% for non-operated atients, $p < 0.01$), and early prosthectic IE (42% *vs* 74% for late prosthetic IE and 75% for native IE, $p < 0.05$). Highest 10-year survivan was for patients undergoing earley elective surgery (78%), age < 65 years (76%), native IE (75%) and late prosthetic IE (74%).
Conclusions: Some phase active clinical features can predict long-term outcome in patients with IE. Age, type of IE and type of early surgery are the main prognostic predictors, while gender, causal microorganism, involved valve or underlying heart disease do not seem to affect long-term prognosis.

P 042

RELAPSING VS. RECURRENT INFECTIVE ENDOCARDITIS: THE DUKE EXPERIENCE

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Previous studies evaluating recurrente infective endocarditis (IE) have not taken into account the important difference between a relapsing infection and a new infection. In addition, the current clinical definition of recurrent IE may not be sufficient to exclude those cases of relapses that occur greater than 6 months after the primary episode.
Objectives: The first phase of this study was designed to evaluate the characteristics and outcomes associated with multiple episodes of IE. The second phase involves using special microbiological techniques to more accurately separate relapses from recurrences.
Methods: Using the Duke criteria, 40 patients with 46 recurrent episodes of definite or possible IE were identified from the Duke University endocarditis databases.
Results: Twenty-six patients (65%) were male, and 20 patients (50%) were black. The average ages for the primary and secondary episodes were 52 years (age range, 22-83) and 54 years (age range, 28-83), respectively. Nine patients (23%) were knows intravenous drug users, shile 13 patients (33%) were on chronic hemodialysis. Twenty-five patients (63%) had a confirmed history of prior valvular disease. The mean interval between episodes was 16 months (range = 0 to 84 months). Following our newly revised clinical definition for recurrent endocarditis, 3 episodes (11%) were categorized as «relapsing IE», 11 episodes (24%) as «recurrent IE,» while the remaining 20 episodes (65%) were determined to be «new infection IE.» Valve affected, organism isolated and complication rates were similar between episodes. Patients were more likely to go to surgery during the first episode (n = 14, 35%) than during the subsequent episodes (n = 9, 20%). The overall mortality rate in our cohort reached 45% (mean follow-up = months).
Conclusions: These data suggest that multiple episodes of IE are clinically similr to the first episode of IE. We are using pulse-field gel electrophoresis (PFGE) to genotype the different strains of each organism. This will allow us to determine precisely whether a second episode of IE is either a relapse (i.e. same strain) or a true recurrence (i.e. different strain or new organism). We will then use these results to ascertain the sensitivity and specificity of our new clinical definition of recurrent endocarditis.

P 043

THE ACTUAL DIAGNOSIS DELAY OF LEFT SIDE ENDOCARDITIS

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Objective: To describe the actual delay diagnosis of left side endocarditis and factors associated to the time of diagnosis.
Methods: 189 episodes of definitive left side infective endocarditis by Durack criteria concurrent and prospectively collected from 1996 to 2000 are analyzed.
Results: Delay of diagnosis was: > 3 months in 24 (12,1%), 1-3 months in 47 (23,7%), 1 month-15 days in 36 (18,2%), < 15 days in 82 (41,4%). Factors associated to an early diagnosis

were septic shock, alcoholism, infections caused by *Staphylococcus aureus* and *Streptococcus* other than viridans.; cardiac presentation also showed a lineal distribution not statistically significant. Factors associated to a late diagnosis were diabetes mellitus, constitutional syndrom as initial presentation, a history of rigors, previous antibiotic treatment and infection due to Strep. viridans, polimicrobial or culture negative.
Conclusions: 1. Delay of diagnosis is still high nowdays, but it is lower than in previous decades. 2. Constitutional syndrom and rigors with focus unknown should be emphasized as a clue for suspecting infectious endocarditis. 3. Type of microorganism remains as a strong determinant for the time of diagnosis.

P 044

DIFFERENCES IN PATIENTS WITH ENDOCARDITIS TREATED IN LOCAL HOSPITALS *VS.* REFERRAL CENTERS: REPORT FROM THE ICE INVESTIGATORS

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Objective: Referral bias is well documented in infective endocarditis (IE) yet few studies have examined differences between IE patients treated primarily in local hospitals compared to those treated predominantly at referral centers. This study was designed to identify differences between a local hospital cohort and referral center cohort of IE patients.
Methods: A multi-national consortium, The International Collaboration on Endocarditis (ICE), was formed to study IE. Of the 25 ICE centers, 7 have large existing IE detabases representing >3000 cases of IE from 5 countries..
These databases were combined using a core set of variables with standar definitions. IE patients treated predominantly in local hospitals were compared to those treated at referral centers.
Results: After combination and application of standard definitions, the database used in this study contained 2268 cases of definite IE. 859 IE patients were treated primarily in local hospitals, while 1409 patients were treated primarily in tertiary care medical centers. There were distinct differences in these populations. Patients treated locally were older (63 years *vs* 54 years, p < 0.001), and less likely to have a history of IV drug use (9.0% *vs* 17.6%, p < 0.001) and previous valve surgery (14.3% *vs* 54.7%, p < 0.001). *Staphylococcus aureus* was less common in the local cohort (27.2% *vs* 31.4%, p=0.04) while viridians group Streptococci were more common (28.8% *vs* 20.0%, p<0.001). Aortic valve IE was more common in the local hospital patients (45.3% *vs* 35.9%, p=0.0001) while tricuspid walve IE was less common (12.0% *vs* 20.0%, p<0.001). Surgery was less common in the local hospitals (29.5% *vs* 39.9%, p<0.001) but, IE patients in local hospitals has a lower overall mortality, rate (12.1% *vs* 31.2%, p<0.001).
Conclusions: Differences in patyient characteristics are found when IE patients treated in local hospitals are compared with those treated in referral centers. In addition, variability is found in microbiologic, cardiac, and outcome characteristics. Future studies need to consider and adjust for these influences. In addition, studies are needed in large populations of IE patients representing diverse groups to mmore fully understand the differences in distinct IE popularions and how these differences affect outcome.

P 045

INFECTIVE ENDOCARDITIS IN NON-INTRAVENOUS DRUG USERS: A COMPARISON OF HIV-POSITIVE AND HIV-NEGATIVE PATIENTS A REPORT FROM THE ICE INVESTIGATORS

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Infective endocarditis (IE) in HIV-positive patients has been shown to be associated predominately with intravenous drug use (IVDU). No previous study of HIV-positive patients with IE has attempted to characterize the non-IVDU population.
Objecte: This study of non-IVDU patients was designed to determine the differences between HIV-positive and HIV-negative patients with IE in a large multinational cohort.
Methods: A multi-national consortium, The International Collaboration on Endocarditis (ICE), has been formed to study IE. Of the 25 ICE centers, 7 have large existing IE databases representing more than 3000 cases of IE. These databases were selectively combined to establish a single large database for analytic purposes. Each database was mapped to a core set of variables with standard definitions. Non-IVDU, HIV-positive IE patients were compared with non-IVDU, HIV-negative IE patients.
Results: The databases included 647 non-IVDU patients with definite IE and documented HIV status from 3 sites in 3 countries (France, Spain, USA). 14 (2.2%) IE patients were HIV-positive while 633 IE patients were HIV-negative. The predominant organism isolated from both groups was *Staphylococcus aureus*, which occurred in 36% of HIV-positive patients and 24% of HIV-negative patients. Prosthetic valves were more common in HIV-negative IE patients compared to HIV-positive IE patients (22% *vs* 7%). HIV-positive IE patients were less likely to go to surgery during the episode (7.2% *vs* 38.6%, p = 0.022). The occurrence of left-sided IE was comparable between both groups. Recorded in-hospital mortality for HIV-positive and HIV-negative patients was similar (14.3 *vs* 14.5%). However, HIV-positive IE patients had a higher follow-up mortality (78.6% *vs* 40.1%, p = 0.005).
Conclusions: There are significant differences between HIV-positive and HIV-negative patients with IE when examining the non-IVDU population. Most importantly, HIV-positive patients had the same in-hospital mortality, even though they were more likely to be treated conservatively. Further studies are needed with larger populations of non-IDVU, HIV-positive IE patients to determine the reasons for these differences.

Nosocomial infective endocarditis

P 046

NOSOCOMIAL INFECTIVE ENDOCARDITIS

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Objective: To describe the incidence and epidemiology of nosocomial infective endocarditis (NIE) at a tertiary-care hospital.
Methods: Prospective study of infective endocarditis (IE) in non-intravenous drug users (IDU) from January 1993 to December 2000.

Results: During this period 162 episodes of IE in non-intravenous drug users were documented; 31 (19%) of them, were identified as NIE and other 5 associated with cardiac surgery. In the retrospective review from 1980 through 1992 at the same hospital, 303 non-IDU episodes of IE were reported and 24 cases (8%) were identified as NIE ($p<0.05$; OR 2.7; 95% CI 1.4 to 5.2). According to the Duke criteria, 22 of the 31 episodes of NIE were categorized as definite and 9 as probable. Twenty (64.5%) were male with a median age of 59.1 ± 15.8 years. Left- sided infection was the most frequent (83%) and only 4 cases involved right-sided valves (3 tricuspid and 1 pulmonary valves). The endocarditis was the result of bacteremia associated with intravenous catheterization in 18 cases (58%), instrumentation of urinary tract in 5 (16%), pacemaker infection in 5 (16%), arterio-venous fistula infection in 2 (6%), and peritoneal-venous shunt related-infection in 1 (4%). The predomminant organisme were *E. faecalis* (13 episodes), *S. aureus* methicillin-susceptible (7) and *S. epidermidis* (6). One polymicrobial NIE was observed (*S. intermedius* and *S. lugdunensis*). When 31 NIE episodes were compared with 126 cases of non-NIE, a significant association was found between chronic underlying disease and NIE (19% *vs* 42%; $p<0.01$). The overall NIE mortality rate was 42% (13/31) and 32.5% (41/126) for non-NIE episodes (p=NS). Significant association was found between NIE mortality and elderly patients (p=0,03), underlying native valve abnormalities (p=0.02) and the episodes with development of embolic lesions (p=0.02).
Conclusions: We observed an increase in the rate of NIE over the past eight years. In our serie. *E. faecalis* was the most frequent causative organism and the chronic underlying disease was the only risk factor statistically associated with NIE. We recommend the reinforcement of the hospital infection control measures in an effort to reduce the incidence of NIE.

P 047

SERIOUS CONSEQUENCES OF NOSOCOMIAL INFECTIVE ENDOCARDITIS IN PATIENTS WITHOUT CARDIAC PROSTHESIS

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Objective: The aim of this study is to describe the epidemiology, microbiological profile, clinical characteristics and mortality of nosocomial infective endocarditis (NE) in patients without cardiac prosthesis.
Methods: We have analysed patients diagnosed of NE, who fulfilled Duke's criteria of infective endocarditis, between January 1990 and December 1999. Endocarditis in patients with cardiac valve prosthesis, parenteral drugs users and HIV positive patients were excluded.
Results: Twenty-five (14 males) were studied, mean age 58 ± 17 years. An underlying heart disease was present in 24% of them. Valve involvement was mitral in 8 patients (32%), aortic in 6 (12%) and mural (right atrial) in 3 (12%). *Staphylococcus aureus* was the microorganism isolated most frequently (76%), and 37% of them were methicillin-resistant *Staphylococcus aureus*. NE was related to an intravascular catheter in 15 patients (60%), genitourinary procedures in 2 (8%), gastrointestinal endoscopy in 2 (8%) and permanent pacemaker in 1 (4%).
Congestive heart failure complicated 52% of cases, peripheral embolism 48% and cerebral embolism 24%. Seven patients (28%) underwent cardiac surgery. Overall mortality was 25%. There were no deaths in patients with involvement of right cavities. All patients who died were infected by *Staphylococcus aureus*.
Conclusions: In our experience, nosocomial endocarditis in patients without cardiac prosthesis was more frequently caused by «*Staphylococcus aureus*», it was associated with the use of intravenous catheters, left valves were frequently involved, and it was complicated with significant morbidity and mortality. Involvement of right cavities and non-staphylococcal infection seem to have a better prognosis.

P 048

HOSPITAL-ACQUIRED (HA) INFECTIOUS ENDOCARDITIS (IE)

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Hospital-acquired infectious endocarditis (HAIE), defined as IE acquired either > 72 hours admission or in association with a procedure performed during a previous, recent hospitalization, was described in a few series, comprising 9-23% of IE cases. Cases of IE occurring in people recently discharged (< 100 days) from hospital, but without an association with an identified procedure were not hitherto considered to be HA.
Objective: The purpose of this study was to better characterize this group of patients with so called community-acquired IE and recent hospitalization.
Methods: 85 cases of culture-positive IE that fulfilled the Duke criteria of definite or possible IE during 1995-1998 were divided into 3 groups. Group A: 14 patients (16%) with HAIE as defined above (associated procedure: valve replacement, vascular line infection, urologic procedure, etc.). Group B: 22 patients (26%) with recent hospitalization (discharged < 100 days earlier) but without an identified associated invasive procedure. Group C: 49 patients (58%) with community-acquired IE not hospitalized in the preceding 100 days (table).
Results:

Isolate	Group A	Group B	Group C	Total
S. viridans		2 (8%)	18 (36%)	20 (22%)
Enterococcus spp.	4 (29%)	6 (24%)	11 (22%)	21 (23%)
S. bovis	1 (7%)	3 (12%)	10 (20%)	14 (16%)
S. aureus (MS)	2 (14%)	6 (24%)	8 (16%)	16 (18%)
S. aureus (MR)	2 (14%)	2 (8%)		4 (4%)
Staph. coag. (–)	2 (14%)	4 (16%)		6 (7%)
L. monocytogenes	1 (7%)	1 (4%)		2 (2%)
E. coli	1 (7%)	1 (4%)		2 (2%)
E. cloace	1 (7%)			1 (3%)
Other			3 (6%)	3 (3%)
Total episodes	14	22	49	85
Total isolates	14 (100%)	25 (100%)	50 (100%)	89 (100%)

Group B was similar to group A and different from group C with respect to the types and frequencies of bacterial isolates. *S. viridans* was significantly ($p = 0.002$) less common and methicillin-resistant *S. aureus* and coagulase negative staphylococci were significantly ($p = 0.03$ and $p = 0.005$ respectively) more common in groups A+B than in group C. We conclude that patients admitted with IE within 100 days of a recent hospitalization and even without a procedure classically associated with IE (group B), who would have been traditionally classified as community-acquired IE, may in fact have HAIE.
Conclusions: HAIE is more common than previously appreciated (42% in this series) and is caused by microorganisms that differ from those causing community-acquired IE.

P 049

HOSPITAL-ACQUIRED INFECTIVE ENDOCARDITIS UNRELATED TO CARDIAC SURGERY

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Objective: To study the frequency and characteristics of hospital acquired infective endocarditis (IE) not related to cardiac surgery.
Material and methods: All the patients included in the Endocarditis Database of the Department of Infectious Diseases in Ljubljana in the years 1984-2000 were included. The hospital acquisition of the disease was suspected when IE followed immediately after the procedure or when the same causative

agent was isolated from central venous catheter or surgical wound in a patient with definitive IE. The statistical analysis was performed using EpiInfo6 programme.
Results: In the period studied 289 (190 male/108 female) patients with diagnosis of IE were treated at our department. In 228 patients the infection occurred on native valve (NVE) and in 61 cases on prosthetic valves. An invasive procedure that could be directly linked to IE was documented in 39 (13.5%) of the patients. 22 (56%) patients had an underlying heart disease, 21 (53.8%) patients had a serious underlying disease. Central venous catheter was the most frequent focus of infection, present in 13 patients, followed by non-cardiac surgical procedures. Other procedures suspected to be the cause of endocarditis were delivery in 2 patients, abortion in one patient, placement of TIPS in one patient, ERCP in one patient, coronarography in three patients and PTCA in one patient, extracorporeal shock wave lithotripsy in two patients and liver biopsy in one patient. *S. aureus* was the most frequent causative agent, present in 12 patients (three MRSA). The mortality rate of patients with presumed hospital acquired IE was 38.5%. The patients with hospital acquired endocarditis were older than other patients and had significantly higher incidence of underlying serious diseases. In fact in all the patients with end stage renal disease IE was considered to be nosocomial in origin. The mortality rate ot patients with nosocomial IE was higher than in other patients although the difference was not statistically significant.
Conclusions: Patients with hospital-acquired IE constitute more than 10% of the population of patients with IE. The disease carries higher mortality than community acquired disease.These patients represent a group of potentially preventable IE, so special measures should be undertaken in patients with known underlying heart disease known to be at risk for acquiring nosocomial IE.

P 050

THE RISK OF DEVELOPING INFECTIOUS ENDOCARDITIS INK PATIENTS WITH HOSPITAL-ACQUIRED ENTEROCOCCAL BACTEREMIA

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Enterococci are a major leading cause of infectious endocarditis, an infection usually acquired within the community as a consequence of bacteremia from colonized sites. Nowadays enterococci are also a common cause of hospital-acquired bacteremia, which it is not believed to represent a serious hazard for the development of endocarditis.
Objetive: To determine the incidence and risk factors for infectious endocarditis in patients with hospital-acquired enterococcal bacteremia.
Methods: Retrospective analysis of 116 patients with enterococcal bacteremia admitted to medical or surgical wards and followed by members of the Division of Infectious Diseases during a period of 5 years. Clinical and routine diagnostic tests. Echocardiography was performed when indicated by clinical criterial.
Results: Seventy-five (61.4%) episodes were hospital-acquired and forty-seven (38.5%) were community-acquired. Most patients had one or more underlying chronic diseases. Patients with nosocomial infection had major abdominal (58.6%) or genitourinary (38.6%) surgery. The source of bacteremia was determined in most episodes. Seventeen patients (14.6%) developed enterococcal endocarditis. By univariate analysis the risk factors associated with infectious endocarditis were: community-acquired infection (p=0.012); monomicrobial bacteremia (p=0.006); 3 or more positive blood cultures (p<0.001); underlying valvulopathy (p < 0.001); presence of a prosthetic valve (p z 0.001); and age (p 0.012). Six patients (8%) developed endocarditis during hospitalization for other diseases and it was a consequence of hospital-acquired enterococcal bacteremia. In the univariate analysis, 3 or more positive blood cultures (p < 0.01); bacteremia due to *Enterococcus faecalis* (p 0.007); underlying valvulopathy (p < 0.001); and presence of a prosthetic valve (p < 0.001) were associated with endocarditis. By logistic regression, the presence of underlying valvulopathy and 3 or more positive blood cultures were associated with endocarditis (Odds ratio 21.0; C.I. (95%) 1.65-266.9; p 0.019).
Conclusions: The risk of developing infectious endocarditis in patients with hospital-acquired enterococcal bacteremia is significant. Since some cases are associated with urogenital procedures, a more accurate identification of patients at risk, particularly the elderly with degenerative valvulpathy, seems of paramount.

Infective endocarditis in i.v. drug abusers

P 051

INTRAVENOUS DRUG USE AND INFECTIVE ENDOCARDITIS: REPORT FROM THE ICE INVESTIGATORS

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Infective endocarditis (IE) in patients with intravenous drug use (IVDU) has a predilection for the right side of the heart and a better prognosis than endocarditis in patients without a history of IVDU.
Objective: This study was designed to determine differences in epidemiology and outcomes in cases of IE in patients with or without a history of IVDU in a large multinational cohort.
Methods: A multinational consortium, The International Collaboration on Endocarditis (ICE), has been formed to study IE. Of the 25 ICE centers, 7 have databases representing > 3000 total cases. These databases were merged to establish a single large database. Individual databases were mapped to a core set of variables with standard definitions. IE patients with a history of IVDU were compared to patients without any history of IVDU.
Results: This study consists of 2258 cases of definite IE from 7 sites in 5 countries. 14.4% of patients had a documented history of IVDU. This group differed from the group without a history of IVDU in several respects. They were younger (28 years *vs* 62 years, p <.001) and more likely to be HIV positive (53.1% *vs* 1.6%, p <.001 in 1109 patients with documented HIV status). IE was more commonly due to *Staphylococcus aureus* in the IVDU cohort (71.9% *vs* 22.7%, p <.001). Septic pulmonary emboli (22.9% *vs* 3.7%, p <.001) were more frequent in this group, and tricuspid valve involvement was more common (59.2% *vs* 7.0%, p <.001). There was no difference in the rate of heart failure or overall systemic embolization between the two cohorts. Fewer patients in the IVDU cohort underwent surgery (23.4% *vs* 61.9%, p <.001). Recorded in-hospital mortality was lower in the IVDU group (12.2% *vs* 28.3%, p <.001).
Conclusions: The results of our multinational collaborative study are consistent with the published literature on intravenous drug use and infective endocarditis. It usually affects the right side of the heart, *Staphylococcus aureus* is the most common organism, and it carries a better prognosis than IE in non-injection drug users.

P 052

CLINICAL FEATURES AND OUTCOMES OF *STAPHYLOCOCCUS AUREUS* INFECTIVE ENDOCARDITIS IN INTRAVENOUS DRUG USERS

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Staphylococcus aureus (SA) is a common cause of infective endocarditis (IE) in intravenous drug users (IVDU). Data evaluating the clinical and microbiologic outcomes of IVDU with SA endocarditis (SAE) are limited. Recent data suggest the susceptibility of gram-positive organisms in IVDU may be changing.
Objective: Describe clinical features and determine predictors of clinical and microbiological outcomes in IVDU with SAE.
Methods: A retrospective cohort study of consecutive IVDU with SAE was conducted at Detroit Receiving Hospital from 1997-99. Infection-related mortality and microbiologic outcomes were evaluated. Clinical outcomes were assessed at day 3 and day 7 of hospitalization and at end of treatment. Stepwise logistic regression was performed.
Results: Forty nine IVDU with SAE were identified. Basic demographics: mean age 42 ± 7, male/ female (55%/45%), right-sided *vs* left-sided *vs* bilateral (66% *vs* 28% *vs* 6%), MSSA/MRSA (82%/18%), polymicrobial (18.4%). Initial regimens: Vancomycin containing/ beta-lactam containing/ quinolone (41% *vs* 44% *vs* 15%). Median days febrile was 8 (2-12). Median days of bacteremia was 4 (1-21). Median days of effective therapy 22 (2-50). Clinical symptoms improved by day 3 and 7 in 10.2 and 28.6% of patients respectively, and end of treatment success rate was 71%. Microbiologic eradication was documented in 84% of patients. Overall endocarditis related mortality was 18.4%. In the logistic regression, only left-sided involvement was identified as a predictor of end of treatment failure and lack of day 3 and day 7 symptom resolution.
Conclusion: Our data demonstrates a marked predominance of MSSA in IVDU with IE. Left-sided involvement was the only identified parameter that was predictive of end of treatment failure and or slow clinical response to treatment.

P 053

INFECTIVE ENDOCARDITIS IN INTRAVENOUS DRUG USERS: CLINICAL CHARACTERISTICS AND OUTCOME

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Objective: To evaluate clinical characteristics, bacteriologic findings, and outcome of 84 cases of infective endocarditis (IE) in intravenous drug users (IVDUs), compared to 41 cases of IE in non-IVDUs.
Methods: We retrospectively reviewed 125 patients with IE consecutively admitted to the National Institute for Infectious Diseases, L. Spallanzani, Rome, Italy in the period 1990-2000. All cases satisfied the Duke criteria for definite diagnosis of IE.
Results: Eighty four (67%) patients were IVDUs, and 41 (33%) were non-I VDUs. The mean age was 32.5 ± 5.7 years and 49.9 ± 17 years for IVDUs and non-IVDUs, respectively ($p < 0.001$). No difference was found according to gender between the two groups. Forty five (54%) IVDUs and 2 (5%) non-IVDUS were HIV-infected individuals ($p < 0.001$). Among IVDUs, the right heart side was involved in 62% of cases versus 5% in non-IVDUs ($p < 0.001$); the tricuspid valve was affected in 73% of cases in IVDUs. Positive blood cultures were found in 68 (81%) IVDUs and 30 (75%) non-IVDUs. Among IVDUs, the organisms more frequently isolated were staphylococci (50/84, 59%); among non-IVDUs streptococci were isolated in 12/41 cases (29%). Fungi were isolated in 7 (8%) IVDUs and in none non-IVDUs. Nineteen (23%) IVDUs and 5 (13%) non-IVDUs died for IE-associated complications. Among IVDUs, in-hospital mortality was higher in HIV infected patients (14/45,31.1%) *vs* non-HIV infected patients (5/39, 12.8%) ($p = 0.08$).
Conclusions: In our ten-year retrospective study, IE remains a severe manifestation in IVDUs, with high mortality rate, especially in case of HIV-associated disease. In IVDUs, IE involved more frequently the right side of the heart, mainly the tricuspid valve. Etiological organisms more frequently isolated were staphylococci, likely due to behavioural features. Clinicians should maintain a high degree of IE suspicion in IVDUs, in order to establish a timely diagnosis and treatment.

P 054

INFECTIVE ENDOCARDITIS (IE) IN IV DRUG USERS

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Objective: To evaluate the epidemiological, clinical and microbiologic data of IE in IDU's.
Methods: Retrospective study of the cases of IE in IDU, diagnosed between 1993 and 2000.
Results: 42 cases were diagnosed; 37 (88%) patients (pts) were male; age ranged from 19 to 47 y. ($\bar{x}$ = 29,7 ± 6,6); 29 (69%) were HIV-1 infected. Most frequent manifestations were fever in 38 pts (90%), respiratory symptoms in 25 (60%), heart murmur in 13 (31%); 17 (40%) had CHF and 9 (21%) renal failure. Embolic phenomena were found in 14 (33%), 8 of which were cerebral; skin abscesses in 8 (19%). Echocardiographic findings: vegetations in 37 (88%), perivalvular abscess in 1 (2%) other lesions in 4 (10%). The valves involved were tricuspid - 24 (57%), aortic - 9 (21%), mitral - 5 (12%) and in 4 (10%) more than one. Blood cultures positive in 39 (93%) pts: *S. aureus* in 32 (76%), 30 (94%) of which were β–lactamase producers and 27 (84%) methicilin-sensitive; *S. epidermidis* in 2 pts; *Candida spp.* in 2 pts, *Gemella lusitaneae* and *P. aeruginosa* in one each and, in another one, a non-identified Gram + ve coccus. All pts were treated with parenteral antibiotics. Eleven (26%) pts, 7 of whom HIV-infected, were operated because of refractory CHF in 8, persistence of the infection in 2 and a perivalvular abscess in one. Five (45%) out of the 11 operated pts died, 5 (45%) are well without drug abuse and one was lost to follow-up. Eleven (35%) out of the 31 not-operated pts died, 14 (45%) were lost to follow-up, 3 (9%) maintained drug abuse, and 3 (9%) are well and free of drugs. Eleven pts died in the first two months after the diagnosis from IE and 5 died after 3 and 35 months, 3 with AIDS, one with CHF and one of unknown cause.
Conclusions: IE in IDU has been more frequently diagnosed in the last years; the tricuspid valve the most often affected; β–lactamase producer and methicilin-sensitive *S. aureus* was the commonest agent. HIV infection should not contraindicate surgery but drug-addiction treatment should be considered.

P 055

CLINICAL FEATURES OF INFECTIVE ENDOCARDITIS ASSOCIATED WITH VIRAL HEPATITIS IN INTRAVENOUS DRUG USERS

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Objective: The aim of this study was to investigate the impact of viral hepatitis infection on the course of infective endocarditis (IE) in injection drug users.
Methods: 60 intravenous drug users with definite IE by the Duke criteria were observed. Two categories of patients were identified: I. IE associated with viral hepatitis (39 patients); II. IE not associated with viral hepatitis (21 patients).

Results: Hepatitis B virus infection in 15%, hepatitis C virus infection in 57%, hepatitis B and C virus infection in 28% patients was detected. Acute course of IE was in 72% patients in the group I, and in 76% patients in the group II, sub acute course of IE was in 20% patients in the group I, and in 24% patients in the group II. Recurrent course of IE was in 8% of patients with IE associated with viral hepatitis and was not observed among the patients of the group II. Hemorrhagic complications and thromboembolism were more frequent in the patients with IE and viral hepatitis. Skin petechiae were in 28% patients in the first group, and 14% patients in the second, thromboses of the peripheral vessels in 10% patients in the group I, and 4% patients in the group II. DIC-syndrome complicated the course of disease in 25% patients in the group I, and in 14% patients in the group II, myocardial infarction was in 7% patients in the group I, and in 4% patients in the group II. Stroke was observed in 7% patients in the group I, and in 4% patients in the group II.
Conclusions: Thus, viral hepatitis were in 65% intravenous drug users with infective endocarditis. Recurrent course of IE was observed in 8% of patients with infective endocarditis and viral hepatitis. Also, this group of patients had a more complicated course of IE.

P 056

CLINICAL ANALYSIS OF INFECTIVE ENDOCARDITIS CAUSED BY INJECTION OF NARCOTIC DRUGS

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Objective: Study the clinical characteristics of infective endocarditis (IE) caused by injection of narcotic drugs.
Methods: We analyzed 8 addicts with IE, and compared with 21 nonaddicts with IE.
Results: *S. aureus* was main pathogenic bacterium in addicts, its positive rate of blood culture was 62.5%, and significantly higher than nonaddicts (19%) ($p < 0.01$). The fever in addicts was more severe than nonaddicts (39.7 ± 0.4 *vs* 38.5 ± 0.70C, $P < 0.05$, and usually accompanied with shiver and ache of muscle. 4 addicts (62.5%) occurred pulmonary embolism, but only one nonaddict had (4.7%) ($p < 0.01$).9 nonaddicts (42.9%) occurred peripheral embolism, but only one addict had (12.5%) ($p < 0.05$). Echocardiography showed that 6 addicts (75.0%) and 15 nonaddicts (71.4%) had endocardiac vegetation. All addicts were right, but 13 nonaddicts were left vegetation.
Conclusions: IE caused by injection of narcotic drugs has a characteristic clinical picture, being usually right-sided and caused by *S. aureus*.

Infective endocarditis caused by specific pathogens

P 057

COMPARED CHARACTERISTICS OF *STREPTOCOCCUS BOVIS* AND VIRIDANS STREPTOCOCCAL ENDOCARDITIS WITHIN THE INTERNATIONAL COLLABORATION ON ENDOCARDITIS (ICE) RETROSPECTIVE DATABASE

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The incidence of *S. bovis* (Sb) endocarditis has increased over the recent years in some countries. This phenomenon is not well understood.
Objective: In order to explain it, we compared characteristics of Sb endocarditis with those of IE due to viridans streptococci (Sv) within the ICE retrospective database.
Methods: 7 ICE centers from 5 countries had large existing IE databases. These databases were merged using a core set of variables with standard definitions. This formed the ICE database that contained 2268 cases of Duke definite IE. Of these, Sb cases (*S. gallolyticus*, and *S. bovis* I, n = 118) and Sv cases (*S. acidominimus*, *S. gordonii*, *S. mitior*, *S. mitis*, *S. mutans*, *S. oralis*, *S. salivarius*, and *S. sanguis*, n = 281) were extracted and compared to each other for demographic, clinical and outcome characteristics.
Results: Sb patients were significantly older than Sv patients (64 ± 11 *vs* 53 ± 18 years, $p < 0.0001$). Sex distribution was not significantly different between the 2 groups (74% *vs* 69% males, $p = 0.35$). Sb patients had more often a comorbidity (any comorbidity: 8.5% *vs* 1.8%, $p = 0.004$; diabetes: 9.3% *vs* 3.2%, $p = 0.01$), were less often IVDUs (0 *vs* 7.1%, $p = 0.003$), and tended to have more often a prosthetic valve (16.9% *vs* 11.0%, $p = 0.11$). Embolic complications, whatever their sites, occurred at similar rates in the 2 groups. Likewise, the percentages of patients with vegetations and intracardiac abscesses did not differ significantly between the two groups. Although Sb patients developed more often congestive heart failure (33.1% *vs* 21.4%, $p = 0.01$) they underwent valve replacement less frequently (33.1% *vs* 42.7%, $p = 0.07$) than Sv patients. Lethality rates were similar in the 2 groups (12.7% *vs* 10.3%, $p = 0.5$).
Conclusion: Sb endocarditis develops more often in elderly and debilitated patients, is more often complicated with heart failure, but has no higher lethality than Sv endocarditis.

P 058

CLINICAL AND ECHOCARDIOGRAPHIC CHARACTERISTICS OF *S. BOVIS* ENDOCARDITIS: COMPARISON WITH OTHER PATHOGENS

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Streptococcus bovis endocarditis is considered as a relatively benign disease, but some recent studies suggested a more severe illness.
Objective: The aim of our study was to compare clinical, echographic and prognostic features of *S. bovis* endocarditis with those caused by other streptococci and other pathogens.
Methods: Among 203 consecutive pts with definite IE by Duke criteria, 50 (25% [group 1]) were SB IE, and 153 (78% [group 2]) were caused by OP. All patients (pts) underwent multiplane TOE and blood cultures. Gastroscopy and colonoscopy were performed in all pts with positive anamnesis and/or clinical signs of gastro-enteric disease. The clinical characteristics, echocardiographic findings, and incidence of events were compared between the two groups.
Results: Pts with SB IE were older than group 2 pts (63 ± 12 *vs* 55 ± 19 years, $p < .05$). Multiple valve involvement (19%), native valve endocarditis (87%) and large vegetations (> 10 mm) (50%) were more frequently observed in *S. bovis* patients than in other groups ($p < 0.05$). There was a significantly higher occurrence of embolism in *S. bovis* endocarditis (56%) than in other streptococci (18%) and other pathogens (41%), $p = 0,004$. Spleen embolism and multiple embolism in *S. bovis* endocarditis (56%) than in other streptococci (18%) and other pathogens (41%), $p = 0.004$. Spleen embolism and multiple embolisms were also significantly more frequent in *S. bovis* patients (25% and 16% respectively). Gastro-intestinal lesions, anaemia and spondylitis were observed more frequently in *S. bovis* endocarditis than in other patients.
Conclusions: In addition to the known need for gastrointestinal examination in *S. bovis* endocarditis, our study underlines the need for systematic screening for vertebral and splenic localizations, as well as the use of early surgery to prevent the high risk of embolism in these patients.

P 059

THE EMERGENCE OF β-HEMOLYTIC STREPTOCOCCI AS A CAUSE OF INFECTIOUS ENDOCARDITIS: REPORT FROM THE ICE INVESTIGATORS

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β-hemolytic streptococci (β-HS) historically are an infrequent cause of infective endocarditis (IE). However, invasive β-HS are increasing among the elderly and chronically ill.
Objective: This study was designed to determine the frequency and distribution of β-HS in a multinational cohort of IE.
Methods: The International Collaboration on Endocarditis (ICE) includes 25 centers, 7 have large IE databases. These databases were combined for analysis. We compared patient demographics, risk factors, echocardiographic findings, and outcome for patients with definite IE caused by β-HS versus all other etiologies.
Results: Of 2107 cases of definite IE from 7 sites in 5 countries with known bacterial etiology, 83 (3.9%) were caused by β-HS. Group B was the most common β-HS [53 (64%)], followed by groups G [17 (20%)], C [6 (7%)], A [4 (5%)], and F [3 (4%)]. β-HS endocarditis patients were older (65 years *vs* 57 years, $p < 0.002$) and more often female (42% *vs* 32%, $p = 0.05$) than other patients with IE. Pre-existing risk factors were similar; however, right-sided IE was less frequent among β-HS patients (6% *vs* 18%, $p < 0.01$). β-HS patients were more likely to have valve dehiscence (8% *vs* 2%, $p = 0.05$) and signs of heart failure (52% *vs* 37%, $p = 0.02$). Systemic embolization was reported more frequently in patients with β-HS (62% *vs* 48%, $p = 0.02$) However, case-fatality rates were not significantly different (29% *vs* 24%, $p = 0.2$).
Conclusions: β-HS, predominantly group B, remain an infrequent, yet important cause of IE with appreciable morbidity and mortality.

P 060

STREPTOCOCCUS AGALACTIAE ENDOCARDITIS: A FRENCH TEACHING HOSPITAL EXPERIENCE

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Among streptococci, *Streptococcus agalactiae* (group B) is rarely responsible for infective endocarditis (IE).
Objective: We report 11 cases definite cases of IE due to *S. agalactiae* extracted from the IE database of our teaching hospital.
Methods: Our database was started in 1991 and is prospectively provided with information on demographic, clinical, bacteriological, echocardiographic and therapeutic characteristics of all cases of IE. Hospitalized in the infectious diseases and cardiology departments. Study period was censored at the end of 1999.
Results: Eleven patients presented with *S agalactiae* IE (mean age: 52,18 years, sex ratio: 6 M/5F). At least, one underlying disease was present in 6 patients, including hypertension (3), myocardial infarction (2), diabetes mellitus (3), chronic hepatopathy (3), chronic obstructive lung disease (1), breast cancer (1). Three patients had preexisting heart disease (mitral stenosis, aortic stenosis, and mitral regurgitation). A source of infection was evidenced in all but 2 patients: vascular surgery (1), urinary tract infection (2), coronary angiography (1), soft tissue infection (2), and dental procedure (1). IE location was mitral (6), aortic (2), aortic +mitral (1), and tricuspid (2). Extracardiac manifestations were recorded in all cases including emboli events in 6 patients (brain (4), spleen (2), kidney (1), artery (1) and lungs (1)), and arthritis in 4 patients. Echocardiography showed a vegetation in all cases, with a significant valvular regurgitation in 8 patients. Valvular surgery were performed for 7 patients and deaths occurred in 4 cases (lethality rate 36,4%).
Conclusions: *S. agalactiae* IE is a rare but severe condition that most often occurs in debilitated patients, has a complicated course and a high rate of surgical treatment and lethality.

P 061

ENTEROCOCCAL NATIVE VALVE ENDOCARDITIS: A REVIEW OF 37 CASES

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Objective: To review the clinical features of enterococcal native valve endocarditis (NVE).
Methods: Prospectively collected clinical and laboratory data from cases of encocarditis seen at St Thomas' Hospital between 1970 and 2000 were analysed.
Results: Thirty-seven cases of enterococcal NVE were seen over the study period, accounting for 9% of the 441 cases of NVE excluding those in intravenous drug users. The diagnosis of endocarditis was clinically definite in 25 cases (68%) according to the Duke criteria and in 34 (92%) by our published modifications. In the 18 pathologically proven cases comparable figures were 78% and 94%. Enterococcal NVE was predominantly acquired in the community (35/37-95%) whereas enterococcal bacteraemia was predominantly hospital acquired. In the 1990's enterococcal NVE increased from 11% of community acquired NVE to 16% *Enterococcus faecalis* accounted for 92% of the isolates. No penicillin or glycopeptide resistant strains were seen in the patients with endocarditis but in those with bacteraemia there was increase in the incidence of glycopeptide-resistant *E. faecium*. High-level aminoglycoside resistance was first detected in an endocarditis isolate in 1998 and has been seen in 6 subsequent cases, all associated with hospital procedures. Most patients (81%) were male and the average age was 66 years. Underlying valvular abnormalities were detected in half the patients (46%). There was no valvular predominance. Most patients had fever; malaise, night sweats and weight loss were common. A new murmur was documented in only 20% of patients. Recurrences were seen in two cases, neither related to the presence of high-level aminoglycoside resistance. The overall mortality was 14% but all 18 patients who had surgery survived.
Conclusions: (1) Enterococcal endocarditis remains a predominantly community acquired disease. (2) Our modifications, with additional minor criteria, increase the sensitivity of the diagnosis of endocarditis. (3) No recurrences occurred in patients with high-level aminoglycoside resistant strains.

P 062

S. AUREUS ENDOCARDITIS: PROSPECTIVE ANALYSIS OF 29 CASES DIAGNOSED AT AN ISRAELI TERTIARY MEDICAL CENTER

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Objective: To describe the clinical characteristics and outcome of *S. aureus* endocarditis in an Israeli tertiary medical center.
Methods: In the past 4.5 years, 106 cases of IE have been prospectively diagnosed by the Duke criteria in our institution. An etiologic agent could be determined in 100 cases.
Results: *S. aureus* was the single most common pathogen isolated among these patients. Excluding 5 cases of polymicrobial infection, 29 adult patients with *S. aureus* IE were identified. Of this, 7 (24%) were hospital-acquired. Transesophageal echocardiography (TEE) revealed evidence of IE in 18 of 27 patients (66.6%). Of the 9 patients with negative TEE, 2 were intravenous drug users (IVU) with clinical tricuspid valve involvement and 3 had prosthetic valve IE. Of the 22 patients with community-acquired IE, 8 (36.3%) had underlying cardiac lesions, 6 (27.2%) were IVUs and 8 (36.3%) had no identificable risk factor. All cases with a presumed intravascular source of infection and those caused by MRSA (4 each, 13.7%) were hospital-acquired. The overall mortality rate was of 44.8% as compared with a mortality of 9.0% among 66 patients with IE caused by microorganisms other than *S. aureus* ($p < 0.001$).
Conclusions: In contrast with recent published data, our findings show that *S. aureus* IE still remains primarily a community-acquired infection presenting among patients without any identifiable source of infection.

P 063

INFECTIVE ENDOCARDITIS DUE TO UNUSUAL MICROORGANISM

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Objective: To study infective endocarditis (IE) caused by unusual or fastidious microorganisms.
Methods: A prospective 3-year-study in a tertiary hospital and a cardiovascular surgery center of Athens, Greece, with a 3 months follow-up period, concerning 98 cases of IE, 70 men / 28 women, age 54.4 ± 17.1 years.
Results: In 18/98 cases (18.4%) cultures were negative and there was not positive serology. 60/98 cases (61.9%) were caused by staphylococci / streptococci / enterococci. Unusual microorganisms were responsible for the rest 18 cases (14 definite / 4 possible, Durack diagnostic criteria), 12 men / 6 women, age 43.6 ± 17.9 years. 9 concerned native valves (NVE), and 9 prosthetic valves (PVE) or permanent pacemakers (PME) –5 early / 4 late–. They predominantly involved aortic (9/18) and mitral (6/18) valves. HACEK microorganisms were isolated in 2 cases, *Enterobacteria* in 3, zoonotic microorganisms (*Brucella, Coxiella, Listeria*) in 4, *Pseudomonas* / *Acinetobacter* / *Campylobacter* / diphtheroids / Propionibacterium in 1 each and fungi in 4. Prolonged (> 3 months) antimicrobial treatment was required, while surgical intervention (including total pacemaker removal) was performed in 8/18 cases. Case fatality rate was 16.7% Mortality was 30% in medical (nonsurgical) therapy.
Conclusions: 1) In our study group, which included a high proportion of PVE & PME, unusual microorganisms were responsible for 18.4% of cases. 2) Although selection bias cannot be excluded in our study, 44.4% of patients were surgically treated. 3) Mortality of IE remains high (16.7%), especially in nonsurgical treatment (30%). The latter stresses the importance of modern concepts for early surgical intervention in IE.

P 064

PLURIMICROBIAL ENDOCARDITIS CO- OR SUPER-INFECTION

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Infectious endocarditis is a serious pathology with an important mortality and morbidity. In France, annual incidence is 38 cases/million. During the last 10 years, fungal and plurimicrobial endocarditis have increased. Nevertheless, fungal and bacterial plurimicrobial endocarditis have never been studied before.
Objective: To definite specific characteristics of bacterial and fungal plurimicrobial endocarditis.
Methods: We report 27 cases of bacterial and fungal endocarditis collected 1) 7 in our Infectious and Tropical Diseases Department for a period of 8 years and 2) 20 cases from review of literature between 1942 to 1999.
Results: These endocarditis occurred especially in men (16 men/11 females) who were 50 ± 13 years old. Mortality rate was important (37%). Early surgery (valves replacement) was necessary in 66% of cases. Predominant isolated pathogens were: *Staphylococcus spp.* (56%) and *Candida albicans* (54%). Risk factors excluding previous valvular pathology were intravenous drug addiction and cardio-vascular surgery.
Two kind of bacterial and fungal endocarditis can be described. The first one was a concomitant infection with both pathogens in population with risk factors (48%) and the second (52%) was a bacterial endocarditis superinfected with *Candida* after a prolonged antibiotherapy (more than 4 weeks).
Conclusion: These infections are serious. We recommend a systematic search of fungal agent in patients suffering from bacterial endocarditis with risk factors (drug addicts and patients with history of cardiac surgery). Suspected patients with treated bacterial endocarditis may be superinfected by *Candida*, if they are treated at least for 4 weeks and if they have clinic and biologic deterioration.
Although the little number of studied cases and their heterogeneousness (retrospective study, several series), the interest of a probabilistic anti-fungal treatment has to be discussed. It could be proposed right away in this defined population (drug addict and those with previous cardiac surgery) suffering from bacterial endocarditis or if the evolution is pejorative during the first 3 weeks in spite of correct antibiotherapy.

P 065

BLOOD CULTURE NEGATIVE ENDOCARDITIS: ANALYSIS OF 63 CASES

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Objective: To assess the incidence of blood culture negative endocarditis (BCNE) and determinde in how many cases a pathogen can be defined.
Methods: Analysis of prospective data from cases of endocarditis seen at St Thomas' Hospital from 1975 to 2000.
Results: Sixty-three cases of BCNE were seen during the study period; 48 involved native valves (NVE) and 15 prosthetic valves (PVE). During this period BCNE accounted for 12.2% of the 516 cases of endocarditis seen at St Thomas' Hospital. The diagnosis of endocarditis was clinically definite according to the Duke criteria in only 21% of the 34 cases of pathologically proven NVE but in 62% of cases if the St Thomas' modifications of the criteria were used. Comparable figures for the 11 cases of pathologically proven PVE were 45% and 73%. Despite negative blood cultures a causative organism was identified in 31 (49%) of the 63 cases: in 15 by serology (*Coxiella burnetii* 8, *Bartonella* 6, *Chlamydia psittaci* 1); in 9 cases culture of the excised valve yielded the pathogen; in 3 microscopy of the excised valve showed large numbers of Gram positive cocci though culture was sterile; in the other 4 cases the

causative organism was isolated from a site other than the excised valve (respiratory specimens 2, pacemaker tip 1, excised embolus 1). In addition 5 of the 6 cases of bartonella infection were confirmed by PCR on the excised valve. Two thirds of the 32 patients for whom no pathogen was identified had received antibiotics before blood was cultured.
Conclusions: 1. Truly «negative» endocarditis is very uncommon. 2. If blood cultures are negative in patients with definite or suspected endocarditis serology should be done, a detailed history of antibiotic consumption obtained and the excised valve cultured, sent for histology and revelant PCR investigacion. 3. Not surplrisingly since positive blood cultures constitute a major Duke criterion, in BCNE the Duke criteria perform less well than our suggested modifications which incorporate additional minor criteria.

Echocardiography, diagnosis of endocarditis and risk of emboli

P 066

STAPHYLOCOCCUS AUREUS BACTERAEMIA: TRANSFOESOPHAGEAL ECHOCARDIOGRAPHY REVEALS HIGH INCIDENCE OF CLINICALLY UNSUSPECTED ENDOCARDITIS

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Staphylococcus aureus bacteraemia (SAB) is a common occurrence in a tertiary referral hospital and endocarditis is knows to be a common and serious complication. At our hospital a policy to evaluate all medically suitable adults with SAB for endocarditis with a transoesophageal echocardiogram (TOE) has been implemented since December 1998 and a registry 1998 and December 2000 to determine the incidence of endocarditis and to assess the percentage of those not evident on clinical grounds. Endocarditis was determined in the presence of SAB if the findings on TOE met the Duke criteria for definite endocarditis. On clinical grounds endocarditis was considered to be evident if there were embolic phenomena (systemic or pulmonary), a new or worsening cardiac murmur, or there was a prosthetic valve or other known predisposing valvular abnormality.
We analysed 52 patients with 53 episodes of SAB. 70% of cases were male an the mean age of the population was 60 years, range 19-90 years. 55% of the SAB cases were nosocomial. 21% of the SAB cases were due to methicillin resistant *Staphylococcus aureus*. 15 cases of endocarditis were found with an incidence of 28.3%. Of the endocarditis cases 33% were due to right sided endocarditis, 53% were due to left sided endocarditis and 13% affected both sides. Endocarditis was present in 6 of 7 (86%) clinically evident cases. Of the 46 remaining SAB cases in which endocarditis was not clinically evident there were 9 cases of endocarditis (20% incidence). 60% of the endocarditis cases were not evident on clinical grounds.
In conclusion in SAB there is a high incidence of endocarditis identified via TOE, and the majority of cases are not evident on clinical grounds. Therefore TOE evaluation is indicated for all medically suitable adult patients with SAB.

P 067

EMBOLISM IN ENDOCARDITIS: INFLUENCE OF THERAPY

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Embolic events (EE) are a frequent and life-threatening complication of infective endocarditis (IE) and the risk of embolism is correlated with the size and mobility of the vegetations detected by transoesophageal echocardiography (TOE). However, the influence of antibiotic therapy on the occurrence of EE is not known.
Objective: The purpose of this study was to assess the value of TOE in predicting EE in pts with IE, including silent embolism and to assess the influence of antibiotic therapy on the embolic risk.
Methods: In 204 consecutive pts with IE by Duke criteria, the echographic characteristics (localization, size and mobility) of vegetations were correlated to embolic risk. TOE was performed in all pts, and to detect silent embolism, cerebral and abdominal CT-scans were performed in 95% of patients. The clinical and echographic features of EE during therapy were specifically analysed.
Results: Among 204 pts with IE, 74 (36%) had ≥ 1 embolic event. There was no difference between pts with and without embolism regarding age, sex and left valve involved. By univariate analysis, staphylococcus infection, right side valve endocarditis, and vegetation length and mobility were significantly related to EE. By multivariate analysis, the only predictors of EE were vegetation length ($p = 0.03$) and mobility ($p = 0.01$). EE were particularly frequent among 30 pts with both severely mobile and large vegetations (> 15 mm) (83%, $p < 0.001$). Among 74 EE, 17 (23%) occurred after initiation of antibiotic therapy. Incidence of new EE under therapy was 8% among all cases of IE (17/204). Embolism included 6 cases of cerebral, 1 ocular, 1 coronary, 2 pulmonary, 3 limb ischemia and 1 splenic embolisms. Three other EE were silent (1 splenic, 2 renal) and detected by systematic CT-scans. These 17 pts presented with very large (18 ± 5 mm) and mobile vegetations. Vegetation size was > 10 mm in 15 (88%) of thesel 17 pts, and > 15 mm in 11 (64%).
Conclusions: 1. Embolic risk in IE is highly correlated with the size and mobility of vegetations assessed by TOE. 2. The incidence of EE under antibiotic therapy is relatively low (8% of all cases of IE). 3. However, severely disabling EE may occur in IE, even after initiation of antibiotic therapy, especially in pts with large and mobile vegetations. 4. These data suggest that early surgery may be recommended in patients with vegetation size > 15 mm and high mobility.

P 068

MAJOR EMBOLIC EVENTS IN INFECTIVE ENDOCARDITIS ARE ASSOCIATED WITH A YOUNGER AGE

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Clinically overt embolic events occur in 30-40% of cases of infective endocarditis. Identifying patients at higher risk may improve risk among the clinical and laboratory data obtained on hospital admission in patients diagnosed as having definite infective endocarditis according to the Duke's criteria.
Niney-four patients were enrolled in a prospective study. The results of hematological, echocardiographic and microbiological investigations performed on hospital admission were analysed, using statistical methods as appropriate, with respect to the occurrence of major embolic events. Multivariate analysis was applied to variables significantly associated with embolism on univariate analysis.
Ninety-two patients had vegetations. Forty-three (46%) developed a major embolic complication. No association was found between embolism and gender, site of infection or microorganism involved. Patients with embolism were significantly younger (39 *vs* 52 yrs; $p < 0.003$), had larger vegetations (14.3 *vs* 10 mm; $p < 0.003$) and showed a significantly higher level of serum C-reactive protein (62.2 *vs* 29.6; $p < 0.02$) and lower hemoglobin (10.1 *vs* 11.3; $p < 0.002$) and albumin (3.2 *vs* 3.6; $p < 0.001$) concentrations than those without embolism. Young age (< 46.5 yrs, OR 7.04, $p < 0.004$) and a larger vegetation (> 10 mm, OR 6.25, $p < 0.02$) were

independently associated with an increased incidence of embolic events in the multivariate analysis.
According to our data, infective endocarditis patients younger than 46, with vegetations larger than 10 mm, presenting with signs of a stronger inflammatory response are at increased risk of major embolic complications.

P 069

CEREBRAL COMPLICATIONS IN INFECTIVE ENDOCARDITIS – A RADIOLOGICAL AND NEUROCHEMICAL STUDY

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Central nervous system (CNS) embolism is a frequent and serious complication in infective endocarditis (IE).
Objective: To establish the rate of cerebral embolic events and the nature of cerebral injuries before and during antimicrobial therapy of IE. To identify clinical markers correlated to increased frequency of CNS complications.
Methods: Prospective study. Patients with IE were, irrespective of neurologic symtoms, evaluated by magnetic resonance imaging (MRI) of the brain early during treatment and again after 2-3 months. Specific brain damage markers were analyzed in cerebral spinal fluid (CSF) and blood repeatedly during treatment and correlated to the neuroimaging fingigs.
Results: 21 patients were included, 19 with definite and 2 with possible IE according to the Duke criteria. One patient died during therapy, 3 relapsed. 16 had vegetation on TEE examination, 4 had prosthetic valve endocarditis. Symptoms of cerebral emboli were noted in 6/21 (29%) patients while 10/21 (48%) had MRI findings suggestive of CNS involvement. Another 3 patients had increased brain damage markers as the only sign of emboli. Thus, total rate of embolic events was 13/21 (62%) patients. Among 10 patients with MRI pathology, 7 had infarctions, 2 had infarctions with a hemorragic component and one had mycotic aneurysms with bleeding. The 4 patients with MRI pathology without neurologic symptoms all had small infarctions on MRI.
Conclusion: In the present series, MRI of the brain and analysis of brain damage markers in CSF indicated a total rate of cerebral complications of 62% compared to 29% if only symptomatic patients were included. The clinical significance of these findings is still unknown.

P 070

INFECTIVE ENDOCARDITIS WITHOUT VEGETATION

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Vegetation is the primary endocardial lesion of infective endocarditis (IE). However, even with the most recent echocardiographic techniques, a vegetation is found by echo in only 80% of the cases. In order to describe their characteristics and follow-up, we reviewed the charts of 36 pts without echocardiographically detected vegetation in a prospectively created database containing 235 cases of definite IE according to the Duke criteria recorded from 11/1990 to 12/1999. All these pts were hospitalized either in the Cardiology dpt or in the dpt of Infectious Diseases of our University hospital (tertiary referral center for the region and primary care center for the local population).
Of these 36 pts (15% of all the cases), 10 had an other echocardiographic criteria considered as major in the Duke classification: 5 ring abscesses, 5 new valvular prosthesis dehiscence, of whom 5 were surgically treated. Valvular surgery was also performed in 8 other pts: it confirmed the diagnosis in 6 pts (2 undiagnosed abscesses, one tricuspid vegetation due to infection of PM leads, one infected biological prosthesis thrombosis, and 2 unprecised surgical confirmation of IE) and was the circumstance of discovery in 2 pts who had prior history of fever. Three other pts were operated on from 4 to 7 months after the initial hospital stay, without surgical confirmation in 2 pts (one with major calcification of the aorta, one with initial cerebral embolic event). Among the 15 remaining pts, one had IE on pacemaker with positive culture of the leads removed by traction which were thick at echo without individualized vegetation, 7 had IE on valvular prostheses, 3 on native valve disease and 4 had no previously known heart disease. Biological immunological syndrome was present in 9 of the 15 pts, and 2 pts had initial embolism. During the follow-up of these 15 pts (0-7 yrs), 2 died in the acute phase (one with IE due to Coxiella burnetii on valvular prosthesis, one following an initial major cerebral embolism), 2 died during the follow-up (one due to heart failure, one because of colonic neoplasm which was the portal of entry of IE), one had another episode of IE on valvular prosthesis, one had chronic infection due to *Candida* on aortic prosthesis.
In conclusion, echocardiography sometimes fails to demonstrate the initial vegetative lesion in IE, especially in presence of intracardiac devices (prostheses or PM), in cases with initial embolic event, and at a later evolutive level when abscess is present. Event-free survival of pts without vegetation at echocardiography appears to be poor.

Molecular diagnosis (PCR) of infective endocarditis

P 071

ETIOLOGIC DIAGNOSIS OF INFECTIVE ENDOCARDITIS BY BROAD-RANGE PCR AND SEQUENCING

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We have analyzed 97 surgically resected endocardium specimens (60 valves and 37 others) or 73 patients suspected of having infective endocarditis by broad-range PCR amplification of part of the 16S rRNA gene and subsequent sequencing. PCR results were compared with those of culture and Gram staining and, if available, with previous blood cultures. Of 37 samples positive by PCR the etiologic agents were viridans streptococci (16), other streptococci (8), staphylococci (5), enterococci (5), Haemophilus sp. (2), and Tropheryma whipplei (1). Only in 3/37 (8%) PCR-positive specimens bacteria could be detected by culture and in 7/37 (19%) by Gram staining, whereas six and one of 60 PCR-negative specimens were positive by culture and Gram staining, respectively. For 15 of 21 (71%) patients with previous positive blood cultures, infective endocarditis and isolated organisms were confirmed by PCR. In one additional patient *Staphylococcus aureus* grew in the blood culture two months before surgery, but PCR revealed Streptococcus dysgalactiae on the valve. Moreover, in 7 of 22 (32%) patients with negative blood cultures bacterial DNA was found in the resected materials. We conclude that for endocardial specimens broad-range PCR is superior to culture to identify the etiologic agent of (mostly pretreated) infective endocarditis.

P 072

PCR IN DIAGNOSIS OF INFECTIVE ENDOCARDITIS

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Early diagnosis of infective endocarditis is important for the clinical outcome since mortality increases if diagnosis is delayed. The diagnosis of infective endocarditis is based mainly on

clinical features, echocardiography and especially on blood culture findings, but negative blood cultures have been reported in 5% to 15% of proved cases. Polymerase chain reaction (PCR) can detect even small amount of bacterial DNA and is fast and relatively cheap.
Objective: The aim of our study was to investigate possible usefulness of the PCR in the diagnosis of the disease.
Methods: The study group consisted of 28 patients (pts) with acquired rheumatic valvular heart disease and ongoing infective endocarditis. The diagnosis of endocarditis was established according to the Duke criteria by clinical examination, echocardiography, laboratory investigations (inflammatory parameters) and positive blood cultures (in 20 pts). Two control groups consisted of pts with acquired rheumatic valvular heart disease: 10 without infective endocarditis and another 10 pts with active urinary tract infection with significant bacteriuria. To detect bacterial DNA (with no identification of a specific bacteria) in blood of investigated pts PCR was performed with an employment of universal bacterial primers (16S rRNA).
Results: Bacterial DNA was found in all pts with endocarditis and positive blood cultures or negative either. This suggest that sensitivity of the method may exceed traditional culture techniques. No bacterial DNA was found in all controls without endocarditis and in 3 of pts with urinary tract infection. In 2 latter pts PCR was positive. This could occured due to high sensitivity of employed universal primers.
Conclusion: PCR with an employment of universal bacterial primers could be a useful additional diagnostic tool in pts with endocarditis especially when blood cultures are negative.

P 073

RAPID SERODIAGNOSIS OF GRAMPOSITIVE BACTERIAL ENDOCARDITIS

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Lipid S is a short chain length exocellular form of the cellular lipoteichoic acid produced by a wide range of Gram-positive cocci including viridans streptococci and staphylococci.
Serum IgG levels to lipid S were significantly elevated in 34/43 patients with Gram-positive infective endocarditis (IE), confirmed as «definite» or «possible» by the Duke criteria, caused by staphylococci (23/43), streptococci and enterococci (14/43), polymicrobial infection (6/43) as compared to 50 control sera, 1 culture-negative IE and 2 Gram-negative IE patients. The test had a sensitivity of 79% and a specificity of 87%. Positive and negative predictive values were 85% and 84%, respectively. The likelihood ratio of a postive test was 6.08, for a negative test it was 0.24 and the accuracy was 84%. The assay is independent of culture results or endocardial imaging, making it complementary to currently used investigations. The results of this assay may therefore augment the Duke criteria for diagnosing Gram-positive IE, particularly when an organism has not been isolated or when coagulase-negative staphylococci are grown and the significance is uncertain. An algorithm that incorporates lipid S serology into a positive diagnostic strategy is presented.

P 074

DUKE CRITERIA AND GENETIC DETECTION OF PATHOGENS IN IE

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In 35 patients admitted to our institute with diagnosis of infective endocarditis the possible role of molecular genetic approach among standard used criteria for detection of infective endocarditis were analyzed. We weighted the diagnostic value of PCR-AFLP and /or RFLP based detection of pathogens in blood and valve tissue samples by using three different sets of criteria, as follows: (a) Duke criteria, (b) Duke criteria, replacing hemocultivation with molecular detection as a major criterion, and (c) Duke criteria with molecular genetic detection added to the major criteria.
In (a) 20 cases were classified as «possible» and 15 as «definite» IE. In (b) 12 previously «possible» cases were reclassified as «definite». Eight cases remained as «possible» in spite of positive PCR results. In (c) two «possible» cases were additionally reclassified as «definite» IE. From remaining six «possible» cases, 4 patients were PCR negative (in blood) and the diagnosis of IE was confirmed by improvement of clinical status after replacement of infected valve (infection detected by PCR).
Although in this series the number of culture-negative cases was exceptionally high, current molecular genetic approach allow more precise definition of IE and is already valuable in the diagnosis of IE. Duke criteria may achieve enhanced diagnostic power by considering molecular diagnosis among their constituents' criteria.

Antibiotic therapy of infective endocarditis

P 075

CLINAFLOXACIN FOR ENDOCARDITIS: FINAL RESULTS

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Quinolones are potentially attractive for treatment of endocarditis: they are bactericidal, rapidly penetrate vegetations, and can be administerec both IV and orally. Clinafloxacin, an investigational quinolone with Gram-positive and Gram-negative activity, was used in a multi-center study of both native and prosthetic valve endocarditis. These are the final results of that study.
Methods: Patients who met Duke criteria and signed an informed consent were enrolled. After 3 days of IV therapy they could be switched to oral therapy. Follow-up extended to 6 months.
Results: 106 patients were enrolled; 39 were excluded. Reasons for exclusion were: no pathogen isolated (16 pts), adverse events (5 pts), withdrew form study (5 pts) and other (5 pts). Of the remaining 67 patients, 54 had native valve and 13 prosthetic valve infection. Native Valve: The valves involved were tricuspid (20 pts), mitral (15 pts), aortic (8 pts), multiple valves (8 pts), VSD (1 pt) and indeterminate (2 pts). Infecting organisms were Staphylococci (MSSA 17 cases; MRSA 4 cases; Coagulase negative 4 cases), Streptococci (18), Enterococci (8), and Gemella haemolysans (1 pt). There were 5 Gram-negative infections. The median duration of treatment was 31.0 days (IV 14.5 days, PO 23.0 days). The median duration of bacteremia and fever was 3.0 days. 12 patients required surgery, 4 after completing therapy. Valve cultures were negative in all but 1, who had an infected indwelling catheter. 6 pts failed although bacteremia cleared by day 4 in 3 cases. 1 continued to use drugs and had recurrent bacteremia at day 78, another at 3 months, 1 had persistent fever despite negative cultures, G. haemolysans became resistant in 1 case; and 2 remained bacteremiac at day 6 and 8. Prosthetic Valve: 13 pts had prosthetic valve infection (aortic 4, mitral 7, multiple 2). Nine were cured (follow-up 6 months). Two had surgery although blood cultures were sterile after 1 day. Three of 4 who failed presented with typically fatal complications, but blood cultures cleared on day 1, 3, and 6 respectively. Stenotrophomonas maltophilia developed resistance in 1 pt who died.
Conclusion: Quinolones are effective therapy for native- and prosthetic-valve endocarditis.

P 076

FAILURE OF LIPID-COMPLEXED AMPHOTERICIN B IN THE TREATMENT OF FUNGAL ENDOCARDITIS

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The low incidence of fungal endocarditis, and the high rate of related complications and mortality makes therapeutic trials impossible in this condition. Lipid based formulations of Amphotericin B (AmB) allow patients to receive higher daily doses than AmB deoxycholate, with less infusion related symptoms and nephrotoxicity. Several cases of successful treatment of fungal endocarditis with lipidic AmB has been reported in the literature. However, their role in the therapy of fungal endocarditis remains controversial, as some lipid formulations achieve lower serum concentrations than conventional AmB deoxycholate.
Objective: To evaluate the role of new lipid formulations of AmB in the therapy of fungal endocarditis.
Methods: With the aim of evaluating our experience with the new formulations of AmB, we searched the endocarditis data base of our institution (1985-2000), and reviewed the case reports of the patients with endocarditis due to fungi.
Results: There were 16 cases of fungal, endocarditis: 11 due to *Candida* spp, 4 due to *Aspergillus spp.*, and one due to *Scedosporium* spp. Lipid AmB was used in five patients, and only one of them survived (a drug addict with *Candida* right-sided endocarditis). Lipid formulation AmB was used in four additional patients who died of progressive fungal infection. Antifungal therapy was not evaluable in two patients with prosthetic valve endocarditis because of death soon after diagnosis (*Scedosporium spp*, *Aspergillus spp*). In the other two patients with *Aspergillus* prosthetic valve endocarditis, high dose liposomal AmB was started in the first day of surgical valve replacement, with later relapse and prosthetic disfunction due to *Aspergillus* persistent infection.
Conclusions: Prompt valve replacement and high dose liposomal AmB was ineffective in two cases of *Aspergillus* prosthetic valve endocarditis. Medical treatment of fungal endocarditis remains a therapeutic challenge.

P 077

DISCONTINUOUS THERAPY WITH SHORT T1/2 ATB IN IE

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Infectious endocarditis physiopathologic model speculates that the pathogenic organisms are characterized by a slow rate of multiplication due to low metabolic activity. This feature along with the abundance of fibrin in the microbial colony constitutes barriers against the immunologic defense mechanisms as well as against antibiotics intervention.
Objective: To assess the outcome of patients with infectious endocarditis treated with antibiotics with short half-life, which are administered in a 12 hours interval instead of a classical 4-6 hours interval.
Methods: 30 patients diagnosed with infectious endocarditis were enrolled in the study. The etiology in these cases was determined to be: streptococcus viridans, enteroccocus, streptococcus beta hemolytic, *Staphylococcus aureus* and klebsiella. MIC and MBC were determined by dilution method. Patients received treatment with antibiotics with short half-life: penicillin G, ampicillin, oxacillin plus aminoglycoside administered q 12 hours. The measured SBT (at 2 4 6 8 10 12 hours after the IV bolus antibiotics during the first 5 days of therapy) were above MBC near 8h and below MBC until the next dose. The following parameters were evaluated: fever duration, evolution and outcome, rate of recurrence, medical and surgical complications. The results were compared with those that were obtained by using conventional antibiotic therapy. The classic therapy achieves SBT consistently above MIC and MBC of the pathologic agents.
Results: The patients became afebrile in 6.6 days after therapy was started. Persistence of the fever was due to septic emboli or local complications. Seven of the patients (23,3%) had valvular complications requiring emergency surgery. Two of these patients (representing 6.67%) required valvular prosthesis and other two have died. One patient developed severe immunologic complications. 23 patients (76.6%) had a good outcome clinically and pathologically.
Conclusions: Discontinuous therapy of Infectious Endocarditis with short half-life antibiotics administered q 12 hours appears to be as effective as classic therapy. The study supports the theoretical model of IE physiopathology.

Prosthetic valve endocarditis and pacemaker/defibrillator infections

P 078

PROSTHETIC VALVE ENDOCARDITIS

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Objectives: To know the incidence, clinical characteristics and evolution of prosthetic valve endocarditis (PVE).
Methods: We retrospectively studied 130 patients with PVE diagnosed in our hospital from January 1979 to December 2000 (130 PVE / 4087 patients undergoing valve replacement -> incidence: 3.1%).
Results: 56 patients had early PVE (EPVE: < 1 year of valve replacement) (incidence of EPVE: 1.4%) and 74 had late PVE (LPVE: > 1 year of valve replacement). There were 77 males and 53 women with a mean age of 52 years. The prostheses involved were: aortic (33%), mitral (32%) mitro-aortic (27%) and other (8%). Etiologic agents were: S.epidermidis 44 (EPVE: 46.5%, LPVE: 24%), viridans streptococci 20 (EPVE: 3.5%, LPVE: 24.3%), S.aureus 17 (EPVE: 12.5%, LPVE: 13.5%), enterococci 10 (EPVE: 3.5%, LPVE: 12%), gram-negative bacteria 15 (EPVE: 12.5%, LPVE: 15%) and others 19. Five patients had negative cultures. Ninety six patients (88%) had fever, 23% had heart failure and 18% had other complications. Echocardiography was done in 101 patients and revealed vegetations in 34 patients (34%), valvular dysfunction in 24 (24%), dehiscence in 23 (23%) and a ring abscess in 4 (4%). All patients received medical therapy and 29 underwent valve replacement. Overall mortality was 28% (34% in EPVE: and 22% in late disease).
Conclusions: 1) PVE is a rare complication of prosthetic surgery 2) Echocardiography is useful for diagnosis detecting vegetations and local complications. 3) Complications are frequent and mortality remains high even with combined medical and surgical treatment.

P 079

FIRST YEAR PROSTHETIC VALVULAR ENDOCARDITIS (PVE)

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Objective: To determine the differences in the clinical, microbiological and echocardiographic features of PVE ocurring < 61 days (early), and between 61- 365 days (midtern) postsurgery.
Methods: 30 definitive (Duke's criteria) episodes of PVE were concurrent and prospectively collected from 1996 to 2000: 10 early (E) and 20 midtern (M).
Results: Fever was the first clinical symptom in 9 (90%) in E and in 14 (70%) in M. Heart failure at admission was present in 3 (30%) of E and in 5 (25%) of M, being severe in 3 (33%) of E

and in 1 (5.6%) of M. First symptom of PVE appeared 15 days or less before diagnosis in 8 (80%) in E and 9 (47%) in M. Atrioventricular block of any degree was evident in 6 patients (30%) of M, and in none of the E. The most frecuent microorganism E was *S. aureus* (50%) and S.epidermidis (55%) in M. Transesophageal echocardiogram disclosed vegetations in 40% of E versus 85% in M, and pseudoaneurysm in 1 (10%) of E versus 6 (30%) of M. Mortality was 30% in E and 50% in M. Surgery was performed in 50% of E and in 70% of M, being the survival 100% and 42.8% respectively.
Conclusions: 1) E and M PVE have a different clinical, microbiological and echocardiographic profile. 2) E have a more protean clinical picture than M, and at the contrary of the later is mainly caused by virulent microorganism. 3) Extensive cardiac infection is present at diagnosis in M PVE. 4) Mortality is higher in M PVE, even with surgical treatment.

P 080

EVALUATION AND PROGNOSIS IN EARLY PROSTHESIS ENDOCARDITIS

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Objective: Early prosthesis endocarditis (EPE) is a serious disease with high mortality. Medical advances in diagnosis and treatment however may change its poor prognosis. In order to evaluate the prognosis and follow-up for endocarditis in recent implanted prosthesis we performed a retrospective study.
Methods: 33 patients (pt) with EPE were enrolled and divided in two groups: Group A (GA-alive): 15 pt, 6 men, medium age (MA) 36.3±14.8 years; 11 had mitral prosthesis (MP), 3 aortic prosthesis (AP) and 1 mitral and aortic prosthesis (DP); Group D (GD-death): 18 pts, 11 men, MA = 48.6±13.3 years; 5 MP, 9 AP and 4 DP. We compared clinical, echocardiographic and laboratory data between group A and D. Fischer, t-student and Mann-Whitney statiscal analyis were done.
Results: Overall mortality was 54%. *Staphylococcus epidermidis* was the most frequent agent in both groups: 13 in GA e GD (p = ns). GD had more patients with prosthesis in aortic position, (p = 0.011), older age (p = 0.02), early fever during follow-up (start in 3rd day after operation) (p = 0,025), and more immunocompromised pt (6 in GD: 4 advanced liver disease, 1 lung cancer, 1 asplenic, and none in GA) (p = 0.021) than GA. Five pt have aortic abscess in GD and one in GA (p = ns). There were no statistical difference between groups in relation to vegetation size, pt who developed heart failure or stroke.
Conclusion: 1) Overall mortality in EPE remains elevated. 2) Staphylococcus epidermidis was the most frequent agent; 3) Older age, immunocompromised patients and aortic position were correlated with a poor prognosis.

P 081

PROGNOSTIC FACTORS OF *STAPHYLOCOCCUS AUREUS* PROSTHETIC VALVE INFECTIVE ENDOCARDITIS (SAPVIE) ANALYZED WITHIN THE INTERNATIONAL COLLABORATION ON ENDOCARDITIS (ICE) PROJECT

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Objective: SAPVIE has a high lethality rate but its prognostic factors have not been clearly elucidated. This study was designed to search for prognostic factors within the largest series of SAPVIE ever formed.
Methods: Databases from 7 centers in 5 countries were merged using a core set of variables with standard definitions. This formed the ICE database that contained 2268 cases of Duke definite IE, 68 of which were SAPVIE. 2 patients who died within the first 24 hours of hospital admission were excluded from prognostic analysis. Judgment criteria was in-hospital death and explicative variables were age, sex, comorbidity factors, vegetation, intracardiac abscess, prosthesis dehiscence, systemic embolism, stroke, congestive heart failure (CHF), and early valve replacement (EVR). Logistic regression analysis was performed to identify independent prognostic factors.
Results: Patients' mean age was 58 ± 19 years; there were 42 males and 24 females. 6 patients were IVDUs and 11 had a comorbidity (diabetes mellitus, n = 9, HIV infection, n = 1, immunosuppressive Rx, n = 1). 19 patients underwent valve replacement and 29 died during the initial hospital stay (lethality rate 44%). In univariate analysis, only 3 variables had a p value < 0.2: stroke (OR = 7.5, 95%CI: .8–71), intracardiac abscess (OR = 0.38, 95%CI: 0.1–1.4), and vegetation (OR = 0.51, 95%CI: 0.2–1.4). These variables were considered for multivariate analysis, in addition to age, EVR, and CHF, that had been formerly identified by others as potential prognostic factors. Stroke was the only prognostic factor identified after multivariate analysis (OR = 7.3, 95%CI: 0.8–69, p = 0.08).
Conclusions: SAPVIE is confirmed to be associated with a high lethality rate. Stroke was found to be the main factor contributing to prognosis while EVR was not associated with a significant survival benefit.

P 082

NON-STAPHYLOCOCCAL PROSTHETIC VALVE ENDOCARDITIS: REPORT FROM THE ICE INVESTIGATORS

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Objective: Non-staphylococcal prosthetic valve infective endocarditis (NSPVE) is uncommon and not fully described in the literature. This study was designed to describe a cohort of IE patients with NSPVE and to identify differences in NSPVE patients treated medically or with surgery.
Methods: The International Collaboration on Endocarditis (ICE) was formed to study IE. Of 25 ICE centers, 7 have large existing IE databases representing > 3000 cases of IE from 5 countries. These databases were combined using a set of core variables with standard definitions. Descriptive statistics were and comparisons were made between NSPVE patients treated medically or surgically.
Results: After combination and application of standard definitions, the contained 2268 cases of definite IE, of which 213 patients had NSPVE. The mean age for this group was 64.0 years. The patients more commonly male (64%). 18% (40/213) of NSPVE patients had documented congenital heart disease, most often mitral valve prolapse (9/40). The most common microorganisms were: viridans group streptococci (25%), *Enterococcus faecalis* (11%), *Streptococcus bovis* (7%), gram negative organisms (7%), HACEK group (4%); *Candida* spp. (4%). Infected valve distribution was as follows: aortic (52%), mitral (52%), tricuspid (1%), pulmonic (1%). Intracardiac abscess was less frequent than overall systemic embolization (16% *vs* 28%). Heart failure occurred in 30% of NSPVE patients and the overall mortality rate was 25%. When comparing NSPVE patients managed medically versus those managed surgically, patients managed surgically were more likely to be male (74% *vs* 59%, p = 0.03) and have an abscess (31% *vs* 8%, p < 0.001). The mortality rates were similar (28% *vs* 25%, p = 0.62).

Conclusions: Although NSPVE is uncommon, nearly 9% (213/2268) of patients with IE in this large cohort of IE patients from throughout the world had NSPVE. Viridans group streptococci were the most common microorganisms identified, while the aortic and mitral valves were nearly equally affected. Complications such as intracardiac abscess, systemic embolization, heart failure and death were common.

P 083

FUNGAL PROSTHETIC VALVE ENDOCARDITIS

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Objective: To study the incidence, etiology, clinical findings and outcome of fungal prosthetic valve endocarditis (PVE) at our hospital.
Methods and Results: Medical records of 65 patients with a diagnosis of PVE were reviewed, from 1984 to 2000. Blood cultures were performed using the BACTEC 460 system and BacT/Alert (since 1992). Lysiscentrifugation techniques were not used in any case.18 episodes were caused by fungi (28%). The incidence rates were 1.95% and 0.54% respectively, among patients operated for valvular disease. 12 patients were men. Mean age was 52 ± 14 years. Fungi causing PVE were *Aspergillus fumigatus* (10 cases), *Mucor spp.* (6) and *Candida spp* (2). In all cases the microorganisms were isolated from surgical resected material. 12 episodes of PVE occurred less than 2 months after surgery. Mechanical valves were infected in 14 cases, and bioprosthetic valves in the remaining 4. Clinical features included fever (82%), new murmurs (71%), peripheral embolization (12%), and heart failure (71%). Echocardiography imaging showed periprosthetic leaks (27%), paravalvular abscess (16%), vegetations (22%), and mycotic aneurysms (22%). Aortic valve was involved in 12 cases and mitral sites in 6. Blood cultures were negative in all cases but two. All patients were treated with amphotericin B (lipid complex in 7 cases) and cardiac surgery. Surgery was delayed 15 ± 7 days respect to the clinical presentation of endocarditis. Overall mortality was 78%, including 5 patients who received lipid complex amphotericin B.
Conclusions: 1. Fungal PVE entails a high mortality rate yet. 2. New formulations of amphotericin B do not seem improve the outcome. Therefore, early cardiac surgery is advisable.

P 084

CLINICAL OUTCOMES OF PROSTHETIC ENDOCARDITIS

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32 patients operated for prosthetic endocarditis in our institute within a four-year period were analyzed retrospectively for the outcome of the disease. The age of patients ranged from 23 to 78 years. The most frequent affected valve was aortic (21 patients), 10 patients have infection of the mitral and one of the tricuspidal valve. Early infection occurred in 6 and late infection in 37 patients.
Acute operation was done in 14 patients, elective in 29 patients. The most frequent infection agents in early-onset infection was *Staphylococcus epidermidis* and that of late infection was *Staphylococcus aureus*, *S. epidermidis*, Streptococci and also some fungi pathogens. Early after operation died 4 patients, after two years 1 patient. The remaining are in good condition.
Success in detection of causative agent is significantly improved by genetic detection based on polymerase chain reaction (PCR) together with amplification fragment length polymorphism (AFLP) and/or restriction fragment length polymorphism (RFLP).

P 085

SURGICAL TRETAMENT OF PACEMAKER AND DEFIBRILLATOR-LEAD ENDOCARDITIS. THE ROLE OF ELECTRODE LEAD REMOVAL ON OUTCOME

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Objective: The aim of this study was to report our experience with pacemaker (PM) or defibrillator (DEF) endocarditis in order to determine: (1) the clinical and echocardiographic characteristics and (2) the outcome of this population depending on the mode of treatment (medical versus surgical treatment).
Methods: The multidisciplinary team for diagnosis and treatment of infectious endocarditis (IE) from the Hospital Clínic of Barcelona, conducted a prospective, monocentric and consecutive study and identified and followed all patients with IE between 1979 and 2000.
Results: 26 patients (5 women and 21 men, aged 61 ± 15 years) with PM (23 patients, 9 single chamber and 14 dual chamber) or DEF (3 patients) were identified among a series of 669 patients (3.8%) with IE screened during a 21-year study period. During the study period a total of 3768 PM and 460 DEF have been implanted in our institution (incidence of infection of 0.61% and 0.65% respectively). 9 patients (34%) had early onset infection, 17 patients (65%) had late onset infection,and 35% of the patients had experienced a previous surgical manipulation in the pacing system. 15 patients (57%) had two or more implanted electrodes, and only in 5 (19%) a cutaneous ulcer at the generator implantation site with active infection could be determined as a source of infection. Mean number of electrodes was 1,7/patient. Echocardiographic vegetations were detected in 83% of the patients with variable sensitivities for transthoracic and transesophageal echocardiography. Vegetations greater than 10 mm were observed in 30% of patients. The most frequently detected causative microorganisms were staphylococci. Coagulase negative staphylococci were detected in 12 (46%) of the cases (*S. epidermidis* in 30%, *S. lugdunensis* in 11% and *S. hominis* in 4%). *Staphylococcus aureus* were isolated in 27% of the cases. Medical treatment without removal of the pacing system was initially performed in 5 patients, 4 of them (80%) experienced relapses of IE and 1 patient died. Surgical treatment was effective in eradication of the infection in all of them after a mean of 1.6 relapses. The remaining 21 patients underwent surgical removal of the entire device with cardiopulmonary bypass or external counter traction.
3 patients died after surgical treatment and the rest were successfully cured with no relapses after a mean follow-up of 38 ± 9 months. No demographic, clinical, microbiologic or echocardiographic characteristics significantly distinguished patients with successful outcome from those with failure of treatment of death. The only prognostic factor for failure of treatment or mortality was the absence of surgical treatment. Although staphylococcal infection was not statistically associated with increased mortality, all patients that did not survive had staphylococcal endocarditis (1 *S. aureus*, 1 S. lugdunensis, 2 *S. epidermidis*).
Conclusions: Electrode-lead endocarditis presented in < 0.1% of PM and DEF implants. Overall mortality was 15% and the only prognostic factor for failure of treatment or mortality was the absence of surgical treatment.

P 086

PACEMAKER ENDOCARDITIS-PRELIMINARY OUTCOME

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Objective: Clinical characteristics and outcome were reviewed of 17 patients with 19 episodes of pacemaker endocarditis (IE) in Göteborg during the last 16 years. Male/female ratio was 10/9. Age range was 31-90, median 74 years.
Methods: Ten were definite and 9 possible using the Duke criteria modified for pacemaker endocarditis. 9 episodes had no other surgery than primary pacemaker implantation and 7 episodes had 4-6 surgical procedures preceding the diagnosis of IE. Pacemaker surgery within three months before symptoms of IE was noted in 6 episodes, 4 of them had pocket symptoms after surgery. The interval from last surgical procedure to symptoms of IE was 2 days to 8 years, median 10.5 months. The delay from first symptom to diagnosis was 1 to 113 (median 11) days.The most common symptom at admission was temperature above 38 ºC and heart murmur. Tte verified pathological findings in 3/10 and TEE in 12/12 episodes. Microbiology: Blood cultures were positive in 17 episodes, 8 *S. aureus*, 5 *S. epidermidis*, 3 *alphastreptococci* and one mixed. 4 out of 5 electrode cultures were positive, all of them with *S. epidermidis*.
Results: In 12 episodes the pacemaker system (PS) was removed by thoracotomy, traction or laser assisted extraction. 9 had new PS implanted on the contralateral side. Of these 12 patients 2 died, one in a suspected relapse. Of the 7 episodes that kep their PS, 2 had a relapse and among the remaining there is only one alive and available for follow-up. That patients has only been followed for 3 months, which prevents final evaluation. All but for 4 patients had treatment with adequate antibiotics for 28 days or more.
Conclusions: TEE is superior to TTE in diagnosing pacemaker IE. There were on long-time survivals among the patients who kept their PS. Pacemaker IE is a serious disease with high mortality. Further studies are needed to evaluate diagnostic criteria and optimal surgical and medical-treatment.

P 087

PACEMAKER INFECTION. CLINICAL CHARACTERISTICS AND OUTCOME

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Objective: The aim of the study was to determine the clinical characteristics, etiology, therapy and outcome of patients with pacemaker (PM) infection.
Patients: From January 1995 to December 1999, 1.059 patients (p) had a PM implantation (PMI). We retrospectively studied 31 p with PM infection.
Results: 16 p had generator pocket infection and 15 p had bacteriemia. Pocket infection (PI) are caused by *S. epidermidis* (10), *S. aureus* (5) and S. enterica (1) Twelve were early infections (< 6 months after PMI) and 8 (50%) appeared after the initial implantation. All p had local signs and 50% had fever. All p were cured: 8 were treated conservatively with antibiotics (*S. epidermidis*) and the others were treated with antibiotics and removal of the whole PM. Bacteriemic infections (BI) were due to *S. epidermidis* (8), *S. aureus* (5) and gram-negative bacteria (3), 12 were late infections and 10 occurred after two or more replacements. All p had fever, 5 had pocket infection and 5 had endocarditis diagnosed by echocardiography with pulmonary embolism in 3. Eleven p (all p with PI and BI) were treated with antibiotics and surgery and 3 died of unrelated causes. There were 6 relapses in patients with partial explantation, 1 mediastinitis and 1 pericarditis and total removal of PM was necessary for successful outcome. Four high risk p, in whom surgery was contraindicated, were treated with antibiotics for prolonged period and 3 were cured.
Conclusions: Infection remain a relatively rare complication of PM insertion or replacement. Most infections are caused by *Staphylococcus*. Pocket infection are early infections and bacteriemic infections are late infections. In bacteriemic patients echocardiography is useful to exclude endocarditis. When possible treatment should include the removal of the entire system and prolonged antibiotics.

Surgery of endocarditis

P 088

SURGICAL VERSUS MEDICAL TREATMENT IN INFECTIVE ENDOCARDITIS: CRITICAL REVIEW OF A TEACHING HOSPITAL EXPERIENCE

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Objective and methods: In order to evaluate our experience in surgical treatment of infective endocarditis, we reviewed the data of all the patients entered in our prospective IE database between Nov. '90 and Dec. '99 and compared the 128 patients (gr 1, mean age 58 ± 17 years) who were operated on during their initial hospital stay to the 134 patients (gr 2, mean age 58 ± 17 years) who were treated medically only. All these 262 patients had Duke definite endocarditis.
Results: Group 1 patients were more often male (77% *vs* 60%, $p < 0.005$). The two groups did not differ for the following variables: pre-existing native heart disease (49 *vs* 47%), valvular prostheses (14 *vs* 23%), site of IE, multiple valvular location (16 *vs* 10%), extracardiac manifestations (61 *vs* 64%), embolic event (34 *vs* 31%), negative blood culture (9 *vs* 10%), type of causative micro-organism (gr 1: staphylococci: 44 pts, streptococci: 67 pts, other micro-organisms: 5 pts *vs* gr 2 staphylococci: 43 pts, streptococci: 66 pts, other: 11 pts), distribution of streptococci, mortality during the initial hospital stay (21 *vs* 20%). Heart failure was most often present in operated patients (57% *vs* 38%, $p < 0.01$). Echocardiography evidenced features of IE more often in group 1 than in group 2 (vegetation: 89 *vs* 79%, $p < 0.025$; intracardiac abscesses: 16 *vs* 4%, $p < 0.005$; valvular regurgitation grade 3 or 4: 72% *vs* 42% prosthetic dehiscence: 50 *vs* 24% among patients with valvular prostheses, $p < 0.025$). Group 1 patients were operated on with a mean delay of 29 ± 22 days (range 0-105) after the first day of hospitalisation. Among the 116 patients for whom we could obtain precise surgical data, 90 had only one diseased valve (2 valves: 25 pts, 3 valves: 1 pt). Mitral valve was affected in 63 pts, aortic valve in 62 pts, and tricuspid in 19 pts. Macroscopic examination of mitral valve showed vegetation in 43 pts, valvular perforation in 11 pts, abscess in 4 pts, chordal rupture in 13 pts, valvular tear in 5 pts, prosthetic dehiscence in 4 pts. On aortic valve, a vegetation was seen in 44 pts, perforation in 24 pts, ring abscess in 21 pts, valvular tear in 4 pts, and prosthetic dehiscence in 5 pts. A vegetation was present on tricuspid valve in 17 pts (of whom 6 on pace-maker leads) and a perforation in 3 pts. A prosthetic valve replacement was necessary for 51 mitral valves, 61 aortic valves, and 7 tricuspid valves. Conservative surgery could be performed in the other cases. Mean aortic cross clamping time was 62 ± 28 mn.
Conclusion: Surgically treated cases of IE only differ of those medically treated by the severity of cardiac lesions as evidenced by echocardiography and clinical hemodynamic status. Surgery for infective endocarditis still carries a relatively high operative mortality.

P 089

SURGICAL TREATMENT OF INFECTIVE ENDOCARDITIS

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Objective: Cardiac surgery for the treatment of infectious endocarditis (IE) has been reported to be associated with acceptable operative risk and good outcome. However, few studies have evaluated the clinical, echocardiographic, and outcome data of IE patients treated with surgery compared to those treated with medical therapy alone.
Methods: A multi-national consortium, The International Collaboration on Endocarditis (ICE), has been formed to study IE. Seven large existing IE databases representing > 3000 cases of IE were combined to establish a single large database for analysis. Each database was mapped to a core set of variables with standard definitions. IE patients who underwent cardiac surgery during hospitalization were compared to IE patients treated medically.
Results: The combined database included 2217 cases of definite IE by Duke Criteria from 7 sites in 5 countries for whom treatment with or without cardiac surgery was known. 795 (35.9%) patients underwent cardiac surgery whereas 1422 (64.1%) patients had medical therapy only during their hospitalization. In comparison with the medical only group, the surgically treated patients were younger (54 *vs* 55 years, p = 0.014); more often male (75% *vs* 63%, p < 0.001); had fewer co-morbid illnesses (diabetes 9.4% *vs* 14.5%, p = 0.009; history of cancer 5.2 *vs* 10.4%, p = 0.002; intravenous drug use 7.0 *vs* 19.0%, p < 0.001); and less likely to have Staph aureus as the microbiologic cause (20.6% *vs* 35.4%, p < 0.001). Surgical treatment was utilized similarly in patients with prosthetic valve compared to native valve IE, but was less likely to occur in patients treated at North American centers (17% *vs* 40%, p < 0.001). Echocardiographic findings included more left sided IE; intracardiac abscess (23.4% *vs* 4.5%, p < 0.001); and new valvular regurgitation (36.0% *vs* 5.2%, p < 0.001) in patients treated with surgery. Although congestive heart failure was more common and cerebrovascular events similar in patients treated with surgery, this group had better overall survival compared to the medical only group (80.6% *vs* 74.2%, p = 0.001).
Conclusions: Patients treated with cardiac surgery for IE have fewer co-morbid illnesses but more complications of IE. Despite these complications, survival of patients with IE treated with surgery is better than with medical treatment alone.

P 090

DECREASE IN MORTALITY OF PATIENTS WITH INFECTIVE ENDOCARDITIS. POSSIBLE ROLE OF EARLY SURGERY. A TEN YEAR PROSPECTIVE STUDY (1990-2000)

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Infective endocarditis (IE) is a severe disease with high rates of morbidity and mortality. Early mortality remains about 20-25% in most IE series. With the aim to study if lower mortality rates can be achieved and to identify the possible factor associated with this reduction, a prospective study has been carried out in out two centers between 1990 and 2000. All patients with IE, according to the Von Reyn and Durack's criteria, and who were not drug addicts, were included and prospectively followed up for a mean period of 40 months; 183 patients met these criteria. Two groups of patients were stablished and compared: those diagnosed in 1990-1995 (93 patients) and those studied in 1996-2000 (90 patients). Age was higher in the 1996-2000 group (55 ± 16 *vs* 44 ± 21 years, p < 0.001). No differences was found according to gender (male: 66 *vs* 68%, NS), native or prosthetic IE (native: 68 *vs* 72%, prosthetic: 32 *vs* 28%, NS), causal microorganisms (*Staphylococci* 42% in both periods, *Streptococci* 38 *vs* 31%, NS), proportion of non-identified microorganism (11 *vs* 9%, NS), involved mitral or aortic valve, or % of vegetations detected by echocardiography. Early mortality was significantly lower in the period 1996-2000 (12 *vs* 28%, p < 0.001), as well as the rate of severe complications (60 *vs* 81%, p < 0.05). Patients in the 1996-2000 group underwent a higher rate of early (during the active phase of the endocarditis) surgery (58 *vs* 42%, p < 0.05), with a reduction of urgent indications (15 *vs* 21%) and an increase in elective operations (41 *vs* 21%, p < 0.05). Late mortality for patients surviving the active phase of the disease was similar in both groups (86 and 89% at 3 years, respectively). In conclusion, our findings show that it is possible to obtain a reduction in the early mortality of IE, with mortality rates near 10%, in spite of a marked increase in patients age (a prognostic risk factor). This reduction in morbidity and mortality can be explained, at least in part, by the increment of early and elective surgery during the active phase of the disease.

Heart transplant infections

P 091

INFECTIOUS COMPLICATIONS IN HEART TRANSPLANT RECIPIENTS AT THE HOSPITAL CLINIC OF BARCELONA (SPAIN): A THREE-YEAR PROSPECTIVE STUDY (1998-2001).

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Objective: The aim of this study is to describe the characteristics of the infectious complications during the first three years of a new heart transplantation (HTx) program in a tertiary teaching hospital in Barcelona (Spain).
Methods: Prospective study of the first 51 cases included in a new HTx program at the Hosp. Clinic of Barcelona (Spain) from May 1998 until February 2001. All patients received the same initial immunosuppressive therapy (cyclosporine, azathioprine, prednisone and OKT3, <50 mg). Patients received antimicrobial surgical prophylaxis with teicoplanin and netilmicin (48 h.). Trimethoprim-sulfamethoxazole (1 y.), itraconazole and oral acyclovir (8 wks) were given after the first week of HTx. Positive PPD recipients received isonacid for 1 y. Primary T. gondii or citomegalovirus (CMV) prophylaxis was done with pyrimethamine (6 wk) or ganciclovir (2 wk) for D+/R-, respectively.
Results: Mean±SD age was 54±10 years, 39 patients were males (76%). Median (range) time for follow-up was 11 months (1-34). Overall, 22 patients (44%) had 41 infectious complications (0.8 episodes per patient-years of follow-up). 19 patients (38%) had bacterial infections. Gram-negative bacilli were isolated in 9 cases (18%) and Gram-positive cocci in 3 (6%). 13 patients had respiratory infections (25%) and two a surgical wound infection (4%). 11 bacterial infections (58%) developed within the first month after HTx. CMV infection was diagnosed in 14 cases (27%). Three patients had a focal CMV disease (miocarditis, enteritis and anal ulcer) and 11 cases had only isolated fever. Primary CMV prophylaxis (D+/R-) with ganciclovir failed in 2 out of 4 patients. All but one CMV infections appeared between 1 and 6 months (93%). Two patients had herpesvirus infections (*H. simplex*, 1 case and *H. zoster*, 1 case). One patient developed an invasive aspergillosis. One negative PPD recipient had a

prostatic tuberculosis. None of the patients developed pneumocystosis or toxoplasmosis. Post-surgical non-infectious complications (reoperation, acute renal failure-hemodialysis and early allograft dysfuntion) were observed in 15 patients (29%) and were associated with mortality in 7 patients (p=0.001). 26 patients had acute rejection (51%) that was associated with infection in 9 cases (p=ns). Nine patients died (18%). The death was infectious-related in 3 cases (33%). The only independent risk factor associated with mortality was the presence of non-infectious complications (p=0.004).
Conclusions: In this series of HTx, bacterial and CMV infections were the most common etiologies and pneumonia was the most common infection. Post-surgical non-infectious complications were the most important risk factor for mortality. In most cases, prophylaxis was successful except in the case of primary CMV infection.

P 092

UTILITY OF CMV PP67 MRNA IN MONITORING HEART POST-TRANSPLANTATION PATIENTS (PREVIOUS RESULTS)

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Objective: We are conducting a prospective evaluation of the utility of CMV pp67 mRNA in monitoring heart transplant patients and its clinical implication.
Methods: From July of 2000 fifteen heart transplant recipients were enrolled in the study and were monitored weekly during the first 3 months and, if virological signs still were present, the follow-up continued till 6 months every two weeks of till the disappearance of active CMV infection. A total of 206 samples were analysed. We compared NASBA CMV mRNA pp67, qualitative automated method (Nuclisens, Organon Teknika), CMV pp65 antigenemia by indirect inmunofluorescence assay and CMV-Vue and qualitative PCR-CMV (Roche Diagnostics) in EDTA-treated blood samples. The serological status of donors and recipients were evaluated by automated ELISA (COBAS-CORE; Roche Diagnostics).
Results: Serological results: Donor(+), Recipient(+):5; D(+), R(–):5; D(–), R(+):4; D(–), R(–): 1. Active infection: 11 patients, disease: 8/11 developed CMV disease (very high for our normal rate of CMV disease), 4/8 patients had a relapse after antiviral treatment was stopped. Virological results: positive samples: PCR-CMV: 86; NASBA mRNA pp67: 65; Ag pp65 (> 10 cel/250.000): 54 (no differences between both methods). Active infection: Positive NASBA result were obtained earlier than Ag pp65 in 4/11 patients at the same time in 5/11 and in 2/11 Ag pp65 was detected before. CMV Disease: Positive NASBA obtained early than Ag in 3/8 patients, at the same time in 4/8 and in 1/8 Ag was detected earlier than mRNA pp67. After treatment mRNA pp67 and Ag pp65 levels decrease rapidly. In 3 out of 4 patients (relapse) mRNA pp67 remained positive after cessation of therapy and they presented a relapse with Ag pp65 in a few days.
Conclusions: More patients are being included in this study so statistical differences will be evaluated subsequently. 1. Nuclisens CMV mRNA pp67 is an automated assay, rapid, standardised and easy to perform. 2. It have been found similar results between Ag pp65 and Nuclisens CMV mRNA pp67, it seems that mRNA pp67 appears earlier than Ag pp65.3. CMV mRNA pp67 seems to be a good marker of CMV infection and reactivation and in monitoring heart post-transplantation patients.

Post-surgical cardiovascular infections

P 093

BEST GOAL FOR ANTIMICROBIALPROPHYLAXIS IN SURGERY

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Objective: The aim of this study was to obtain the gold standard protocol for antimicrobial prophylaxis in cardiac surgery.
Methods: We have included twelve hospitals with protocols for antimicrobial prophylaxis. Different antimicrobials were evaluated, including regimens during surgical procedures and its quality performance. Finally, theorical economical proficiency –in pesetas (pts) and euros (eu)– was estimated.
Results: Mostly protocols (58%-7 centers) included cefazolin (2g, ev), with a cost of 1,278 pts/7.70 eu, in a single dose. Cefuroxime (1.5g, ev) was used in 33% cases (4 hospitals), which supposed a cost of 1,400 pts/8.43 eu. In allergic hazards or resistance, vancomycin was used in the 75%-9 (cost 3,647 pts/21.97 eu) centers and other, teicoplanin (cost of 10,440 pts/62.89 eu), in two hospitals (17%). No exceptional pathogens were declared to be surveillants in any hospital.
Conclusions: Within the evaluated antimicrobials, a single dose given –just before surgery–, provides adequate concentrations throughout the intervention. Best goal is obtained with preoperatory cefazolin, 2g ev, single dose, or vancomycin, 1 g ev, as an alternative option in allergic patients. Some centers seem not to include costs for standards selection.

P 094

OUTBREAK OF ENDOVASCULAR ASPEGILLOSIS AFTER OPEN HEART SURGERY

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Objective: From June 1996 to January 1997, nine patients developed endovascular aspergillosis after having had a cardiac operation. There were two females and seven males.
Methods: Mean age was 44 (range 12-70). Time of incubation 97 days (8-215). The type of operation was: aortic coarctation 2, coronary artery bypass grafting 2, aortic valve replacement 2, mitral valve replacement 1, mitral valve repair 1, Konno procedure 1. Clinical features were prosthetic valve endocarditis 5, micotic aneurysm 2, pseudoaneurysm of the ascending aorta (cannulation site and/or proximal anastomosis of saphenous vein graft) 4. Cerebral and systemic embolization was the main symptom in 5 patients. Blood cultures were consistently negative. Diagnosis was confirmed at surgery and necropsy. All but two patients were reoperated on: it consisted in removal of pseudoaneurysm and graft interposition and removal of infected prosthetic valve and homograft or bioprosthesis implantation. In one aortic coarctation patient the pseudoaneurysm was excluded from the circulation by way of aortic arch ligation and extraanatomic graft interposition between ascending aorta and the distal descending aorta through the pericardial sac. All patients were treated with lisosomal amphotericin.
Results: 3 patients initially survived the operation (hospital mortality 68%): the single coronary artery graft patient, the mitral valve repair patient and the aortic coarctation patient repaired with the extraanatomic graft. The mitral patient suffered a second episode of aspergillus prosthetic endocarditis despite antimycotic treatment and died three moths later. No attempt for a second reoperation was done. The coronary a. graft patient suffered a second mycotic pseudoaneurysm 3 months after the initial successful reoperation and died in the OR. The only long-term survivor was the coarctation patient in

which an exclusion of the lesion from the blood circulation could be achieved. She is alive and well 4 years after the operation but with oral antimycotic treatment indefinitely. In the rest of the patients necropsic findings showed multiple cerebral emboli with severe brain damage, multiorgan involvement of the infection, recurrence of pseudoaneurysm or endocarditis and extensive myocarditis with fungal microemboli as the mode of death.
Conclusion: Endovascular aspergillosis is a lethal disease with no surgical or medical cure, except the rare case like aortic coarctation where the lesion can be excluded from the blood stream. Prevention of the disease is the only effective approach and this involves architectural measures, strict aseptic technique and proper behavior of the surgical team.

P 095

MEDIASTINITIS AFTER CARDIAC SURGERY: MICROBIOLOGICAL ETIOLOGY AND PATHOGENESIS

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Objective: Postoperative mediastinitis developed after 110 (1.46%) of 7525 consecutive cardiac surgery procedures during a 7 year period, 1992-1998.
Methods: The records of these 110 cases of mediastinitis were reviewed.
Results: The median time from operation or the last reoperation to the development of mediastinitis was 7 days. Sternal dehiscence was seen in 79 patients (72%). Coagulase negative staphylococci (CNS) were isolated in 48% of the cases with a verified microbiological etiology and *Staphylococcus aureus* (S aureus) in 22%. Gram-negative bacteria were found in 18% of the cases. In patients with mediastinitis and sternal dehiscence on reoperation, CNS was isolated in the majority of the patients (42/73, 58%) which is significantly more frequent than in the mediastinitis patients with stable sternum (8/31,26%) ($p = 0.003$). On the other hand, *S. aureus* was more frequently isolated in patients with stable sternum (14/31, 45%) than in patients with sternal dehiscence (9/73, 12%) ($p = < 0.001$). Gram-negative mediastinitis occurred equally often in both stable and unstable sternum. High BMI was associated with CNS etiology ($p < 0.001$) and with sternal dehiscence ($p = 0.008$). COPD was also associated with CNS etiology ($p = 0.03$) and with sternal dehiscence ($p = 0.009$). Patients who had been reoperated before onset of mediastinitis tended to have an increased risk for a gram-negative etiology (32% *vs* 15% in patients not reoperated, $p = 0.12$). The overall 90-day all cause mortality in patients with mediastinitis was 19%. High age, need for reoperation before mediastinitis, a long primary operation time was associated with increased mortality ($p = 0.012$, $p = 0.009$ and $p < 0.001$, respectively), but no specific bacterial etiology.
Conclusion: Three basically different types of postoperative mediastinitis emerge: 1) Mediastinitis associated with obesity and sternal dehiscence and sometimes also with COPD often caused by CNS 2) Mediastinitis following peroperative contamination of the mediastinal space often caused by S aureus and 3) Mediastinitis mainly caused by hematogenous spread from concomitant infections in other sites than the mediastinum in the postoperative period, often caused by gram negative rods. This proposed classification of postoperative mediastinitis and the different pathogenic mechanisms they represent can be useful in planning and launching proper infection control programs.

P 096

HYPERBARIC THERAPY IN CARDIAC SURGERY INFECTIONS

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Objective: To evaluate the efficacy of the treatment of post-surgical sternal infections by hyperbaric oxygen therapy (HOT).
Methods. We retrospectively evaluated the sternal infections complicating the cardiac operations performed between January 1996 and March 2001. The patients have been subdivided in two groups homogeneous regarding wound disinfection and antibiotic therapy. The only great difference was the treatment or not by HOT.
Results: Among 4665 cardiac operations 45 were complicated by sternal infections (0,96%, mean age 66,6 ± 6,8). The group I (19 pz., 42%) wasn't treated by HOT; the group II (26 pz., 58%) was treated by HOT (average of treatment: 15,7 ± 5,3 days per patient). The dominant isolated microorganisms were *Staphylococcus aureus* and *S. epidermidis* (> 90% in both groups). There was no significant difference between the two groups about the time recovery from infection, while the infection relapses and the mean hospital stay were significantly much more in the group I (relapses: 21% versus 3.8%, hospital stay: 65 versus 52 days).
Conclusions: Many studies showed the efficacy of the wound treatment by HOT, without moreover to clarify the exact mechanism of action. Probably the HOT efficacy is depending on local angiogenesis stimulation and by antibiotic therapy boosting thanks to direct bactericide action and/or to more antibiotic afflux and distribution to infection site. In conclusion the HOT permitted a better wound recovery, less relapses and hospital stay with a consequent decrease of costs.

P 097

CATHETER RELATED INFECCTIONS (CRI) IN A POST-CARDIAC SURGICAL INTENSIVE CARE UNIT (ICU). A PROSPECTIVE STUDY

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Objective: The incidence and risk factors of CRI, bloodstream infections (BSI) and catheter related BSI (CRBSI) after heart surgery and its impact on clinical outcomes are not well-known.
Methods: Patients that underwent major heart surgery within a 10-month period were studied. All patients were prospectively followed and all catheter tips cultured with standard semiquantitative microbiological techniques.
Results: During the study period 328 patients were operated on and 1,589 catheters (348 Swan-Ganz; 398 central; 388 arterial; 455 peripheral) were inserted. Mean catheter exposure was 4.6 ± 9.9 days with an overall of 7,148 catheter-days. There were 231 CRI with an incidence density of 32.3/1,000 catheter-days. Most common microorganisms were coagulase-negative staphylococcus (75%), *E. faecalis* (5%) and S. marcescens (2.6%). The duration of catheterization was significantly higher for infected devices (6.2 ± 5.9 *vs* 4.2 ± 10.8; $p < 0.0001$), but the site of the catheter insertion was not found to be a determinant risk factor. There were 34 BSI, 13 of which (38%) were CRBSI. Independent risk factors for BSI were: high ASA (American Society of Anesthesiologist) score, low ejection fraction and prolonged cardiopulmonary bypass time; and for CRBSI were: high CCS (Canadian Cardiac Society) score, needs of BIA (Intra-aortic balloon) and high needs of red cells transfusion. Patients with BSI had significantly longer lengths of stay in the ICU (20.3 ± 24.9 *vs* 3.9 ± 5.1 days; $p = 0.02$) and hospitalization (47.2 ± 34.7 *vs* 11.9 ± 30.4 days; $p = 0.002$). Overall mortality was 7.3%, but mortality in patients with BSI and CRBSI reached 40% and 42%, respectively. BSI was an independent risk factor for mortality with a RR 5.2, 95% CI 1.19 to 23.25, $p = 0.03$.

Conclusions: BSI, but not specifically CRBSI, are independent risk factors for hospital mortality following cardiac surgery, and both are associated with prolonged lengthes of hospitalization.

P 098

THE IMPACT OF POSTDISCHARGE INFECTIONS IN PATIENTS UNDERGOING CARDIAC SURGERY

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Objective: The purpose of this study was to determine the impact of postdischarge infections in patients undergoing cardiac surgery.
Methods: A prospective cohort study was used. During thirteen months (June 1, 1999-June 30, 2000) 513 patients undergoing cardiac surgery were prospectively surveyed for nosocomial infection both before and for 1 month after hospital discharge. Surveillance was based on chart review or phone calls to contact patients. The main outcome measure was nosocomial infection.
Resuls: Postdischarge surveillance was complete in 84% of the patients. During follow-up 158 patients showed evidence of nosocomial infection, 123 in hospital and 35 at home. One hundred eighty eight infections (81.4%) were in-hospital, whereas forty three infections (18.6%) were noted after hospital discharge. The distribution of postdischarge infections was 22 (51.2%) surgical site infections (SSI), 12 (27.9%) lower respiratory infections, 7 (16.3%) bacteremias, and 2 (4.7%) other infections. Postdischarge SSI were 14 sternotomy and 8 venectomy wound infections. The classification was: 11 (50%) superficial incisional, 5 (22.7%) deep incisional, and 6 (27.3%) organ/space. Rehospitalization was required for 59.1% of the patients with SSI and reoperation was required in 45.5%. In-hospital surveillance alone would have estimated the SSI rate to be 6.4%, when the true rate was 10.7%. Thus, more than one third of SSI were detected after hospital discharge.
Conclusions: Postdischarge follow-up of patients who previously have undergone cardiac surgery is necessary to avoid underestimates of the infection rates.

P 099

99M-TC CIPROFLOXACIN IMAGIN OF CVS INFECTIONS

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Objective: The performance of 99mTc-Ciprofloxacin (Infecton), a novel radioimaging agent which binds to living bacteria, in cardiovascular infections was evaluated in an international multi-centre trial.
Methods: 35 patients with suspected cardiovascular infections, endocarditis (n = 26) and sternal wound infection post cardothoracic surgery (n = 9), were referred for Infecton imaging. The infections were classified as definitely infected, probably infected or not infected according to the Duke's or CDC criteria respectively. Causative organisms were identified by standard techniques to enable microbiological correlation. Each patient received 2mg of 99mTc-labelled (300-400 MBq) ciprofloxacin (prepared in-house) intravenously. Whole body images were taken 1, 4 and sometimes 24 hrs later. Each image was reviewed by a nuclear medicine physician, blinded to the clinical information.
Results: No adverse reactions occurred. 35 infecton images were produced, these included 17 true positives, 12 true negatives, 6 false negatives and no false positives. Overall, the sensitivity of Infecton imaging was 62.5% for endocarditis (80% for prosthetic valves) and 100% for sternal wound infection. Several patients underwent serial imaging and positive scans were seen to revert to negative with successful antimicrobial therapy and clinical response.
Conclusions: Infecton imaging has been shown previously to be a highly sensitive (88%) and specific (93% in microbiologically confirmed infection) technique, superior to leucocyte imaging, for the diagnosis of active bacterial infection. The hallmark of endocarditis is vegetation on the heart valve, although it is not always possible to determine the activity of infection from this. Thus using Duke's criteria, which employ echocardiographic evidence, as the gold standard may have accounted for the reduced sensitivity of Infecton imaging in endocarditis. The results in sternal wound infection are particularly encouraging where a typical request is to distinguish infection from pain due to sternal splitting. Bone and leucocyte scans show increased uptake in both conditions. Infecton with no marrow uptake shows linear sternal uptake only when there is bacterial infection. Infecton may also be useful in monitoring the response to and the requirement for antimicrobial or surgical therapy through serial imaging.

Vascular infections. Chlamydia infections

P 100

THE ROLE OF ARTERIAL HOMOGRAFTS IN VASCULAR INFECTIONS. A NINE-YEAR EXPERIENCE

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Objective: To report the experience and mid-term results with the use of large-caliber arterial homografts in the treatment of vascular infections.
Methods: Between 10/92 and 3/01, 22 patients underwent 23 operations because of vascular infection. There were 19 males and 3 females with a mean age of 61.8 years (38-78). Diagnostics were prosthetic vascular infection in 15 (aortofemoral 8, femoropopliteal 3, ascending aorta 2, femoral 2) and primary infection in 7 (aorta 4, femoral 3). Isolated pathogens were *C. albicans* (3), *S. aureus* (2), *C. burnetii* (1), *Salmonella* (2), *P. aerugunosa* (1), *E. faecalis* (2), *E. faecium* (1), Coagulase negative *Staphylococcus* (3) and MRSA (1). Culture was negative in 8 cases. There were 3 polybacterial infections. Operations performed were aortoiliac/femoral graft (11), iliofemoral graft (5), femorodistal in (3), ascending aorta (3) and axillofemoral (1). Emergency/urgent surgery was performed in 15 (65.2%) cases. Cryopreserved homografts from multiorgan donations were used. Single grafts were used in 15 and composite grafts in 8 cases. Two patients were HIV positive.
Results: Hospital mortality was 8 cases (34.8%) because of multiple organ failure (3), uncontrollable sepsis (2), pneumonia (1), ruptured anastomosis (1) and myocardial infarction (1). One patient died at five years because of suicide. Overall survival at 9 years is 59%. Mean follow-up is 42.4 months (1-109). There has been no recurrence of infection among survivors during the follow-up.
Conclusions: Large-caliber arterial homografts show and adequate behaviour as a vascular substitute in cases of complex vascular infection. Reinfection rate on the long-term is almost negligible.

P 101

NON-SURGICAL TREATMENT OF INFECTED VASCULAR PROSTHESIS

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The use of synthetic vascular grafts has supposed an important advance in vascular surgery. However, infection of these prosthesis is a serious complication with high morbidity and mortality and, for most authors, complete extraction of the vascular graft plus parenteral antibiotic treatment are needed for cure.
Methods: We prospectively studied the patients with infected vascular prosthesis attended at our hospital. Only patients with patent prosthesis and without septic shock were included. We tried a conservative approach keeping the graft in place, with surgical or radiological guided drainage plus antibiotic treatment.
Results: Fourteen patients with early prosthesis infection have been included (one of them with periaortic infection, and the others with extracavitary infection). All patients, except one, presented fever and spontaneous purulent drainage. Microorganisms was isolated in seven patients (*S. epidermidis* (n = 4), *S. aureus*, *E. coli* and *B. cepacia*) and mixed flora in the other three patients (*Streptococcus simulans* + *E. faecalis; S. epidermidis* + *E. faecalis* and *S. epidermidis* + *Proteus mirabilis*). Complete clinical, radiological and analytic cure was achieved in 10 patients (71.4%), two other follow in antibiotic treatment today, and in other two (14.3%) the conservative management failed.
Conclusion: Most patients with early vascular graft infections, can be cured without surgical extraction of the prosthesis.

P 102

C. PNEUMONIAE SEROPOSITIVITY & STROKE IN CAMEROON

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Objectives: To determine the relationship between chronic Chlamydia pneumoniae infection and stroke in Cameroon West Africa.
Methods: Fifty consecutive subjects presenting with stroke at the Teaching Hospital and Central Hospital in Yaounde Cameroon, have been enrolled into this ongoing study. We compared IgG (1/64) and IgA (1/16) titres against Chlamydia pneumoniae in these patients with those of 21 age and sex matched case controls, using a micro-immunofluorescence technique (MRL diagnostics).
Results: There was no significant difference between patients and controls with respect to smoking, alcohol intake, and BMI. However, patients had a higher waist-to-hip ratio than controls (0.95–0.01 v 0.86–0.07, p < 0.01). Positive C. pneumoniae serology was detected in 36 (72%) of the patients compared to 10 (48%) of controls (odd ratios 2.83, 95% confidence intervals 1.00-9.25, p = 0.05) for IgG, and 40 (80%) v 10 (48%) respectively (OR 4.4, 1.42-1.9, p = 0.006) for IgA. Thirty of the 50 patients had CT Scan performed, 24 (80%) of whom had ischaemic stroke. When the analyses were repeated using the 24 cases of confirmed ischaemic stroke, the association with C. pneumoniae was stronger than with all cases of stroke for both IgA and IgG.
Conclusions: Our preliminary findings show, for the first time in a West African population, a strong relationship between markers of chronic C. pneumoniae infection and stroke, (especially ischaemic stroke). These findings may have important public health implications in sub-Saharan Africa, where stroke rather than ischaemic heart disease is the major complication of hypertension, and merits larger prospective studies.

P 103

TRACE ELEMENT BALANCE AND INFLAMMATORY REACTION IN HUMAN SCLEROTIC HEART VALVE DISEASE

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Following the decline of rheumatic fever, valve sclerosis is the main cause of aortic stenosis, which often requieres surgery. In non-rheumatic aortic stenosis, as well as in atherosclerosis, inflammation is a conspicuous feature. Furthermore, evidence suggests that *C. pneumoniae* infection may play a role in the valvular sclerotic process. Trace elements are important for the normal immune activation in infections, and some data suggest trace element imbalances to influence microbial virulence and to promote the development of chronic inflammation.
Objective: To investigate whether trace element imbalances exist in the sclerotic value tissue and if there is a correlation to inflammatory activity in patients where *C. pneumoniae* could be detected in the valve, as well as in cases where tests for that organism turned out negative. The following trace elements were determined: Al, As, Cd, Ca, Co, Cu, Fe, Pb, Mg, Mn, Hg, Se, Ag, V and Zn.
Method: Tissue concentrations of the 15 different trace elements were analyzed in the sclerotic valve tissue from 46 patients undergoing surgical replacement of the aortic valve due to aortic stenosis. Fifteen forensic medicine cases without known heart disease served as controls. Trace elements were measured in a ICP-MS (mass spectrometer). All tissue samples from patients and controls were tested by nested PCR for *C. pneumoniae*.
Results: Fe, Cu and Zn, which are importante markers of infection, were greatly increased in the sclerotic heart valves. Fe showed a more marked increase in the *C. pneumoniae*-positive than in the *C. pneumoniae*-negative patients. Ca, which reflects the severity of the tissue lesion, showed a strong correlation to Fe, which is an essential element for *C. pneumoniae* growth. In addition, Se, which is important for an optimal antioxidative and immune function, was decreased. Results of remaining elements will also be presented.
Conclusion: The trace element and *C. pneumoniae* results in sclerotic heart valves support the contention that persistent infection may be one important factor in the pathogenesis in this multifactorial disease.

P 104

CHLAMYDIA PNEUMONIAE IN VASCULAR INFECTIONS

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Chlamydia pneumoniae has been associated with atherosclerotic cardiovascular disease by both seroepidemiologic studies and direct detection of the organism in atherosclerotic plaque by electron microscopy (EM), immunocytochemistry (ICC), and polymerase chain reaction (PCR). Furthermore *C. pneumoniae* has been demonstrated in human monocytes and these circulating blood cells may be a potential reservoir.
The aim of our study was to evaluate by PCR the presence of C. pneumoniae both in peripheral blood mononuclear cells (PBMC) and in tissue specimens obtained from patients undergoing carotid endarterectomy.
Until now, 51 consecutive patients (70 mean age ± 8 years) with carotid lesions of > 70% stenosis were studied. Clinical and demographic data were considered. All patients were examined for the presence of *C. pneumoniae* DNA in PBMC, in atherosclerotic carotid internal arteries, in inflammatory lymph nodes (in front of carotid biforcation) and for *C. pneumoniae* antibodies by microimmunofluorescence (MIF) in serum samples. The PBMC for PCR were processed in accordance with a

method described by Condos et al. DNA was isolated from PBMC and tissue specimens according to the method of Sambrook et al.; *C. pneumoniae* PCR was performed using the *C. pneumoniae*-specific primer pairs HL-1/HR-1 and HM-1/HR-1. IgG and IgA antibodies to *C. pneumoniae* were measured by MIF test (Labsystems-Dasit).
In 12 patients, *C. pneumoniae* DNA was detected in PBMC, in atherosclerotic carotid arteries and in lymph nodes; in 3 patients, in both PBMC and atherosclerotic carotid arteries; in 2 patients, in both PBMC and lymph nodes; and in 5 patients, only in PBMC or in atherosclerotic carotid arteries. MIF serology results indicating exposure to *C. pneumoniae* were found in 39 (76.5%) of 51 patients. Thirteen patients were negative both by *C. pneumoniae* serology and PCR on PBMC, atherosclerotic carotid and lymph node specimens.
Our preliminary results show that *C. pneumoniae* can be mostly detected in PBMC; since examination of specimens of carotid is usually not possible as a routine diagnostic procedure, blood samples could be an alternative in the diagnosis of chlamydial vascular infections.

Case reports, reviews and miscellanea

P 105

ABIOTROPHIA SPECIES INFECTIVE ENDOCARDITIS: ANALYSIS OF FOUR CASES

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The genus *Abiotrophia* has become increasingly implicated in human diseases, particularly in infective endocarditis (IE). *Abiotrophia* species were previously designated as nutritionally variant streptococci and they were included in the viridans group streptococci. Nowadays, genus *Abiotrophia* is considered as an independent genus.
Objective: The aim of this study is to report the incidence, microbiologic, clinical characteristics and outcome of the cases of *Abiotrophia* IE diagnosed in our institution in the last two years.
Methods: A prospective study of consecutive cases of IE was carried out at a 900 bed tertiary hospital in Barcelona, Spain. From January 1999 to December 2000, all patients with a definitive diagnosis of IE according to the Durack criteria were included. Clinical presentation, microbiologic data, diagnostic procedures, antimicrobial treatment and outcome were recorded. Cases of *Abiotrophia* IE were identified and analyzed.
Results: Four cases of *Abiotrophia* IE were detected among 86 episodes of IE (5%). All patients were males. Median age was 42 years (range 30-79). Three patients had a chronic underlying disease. The infection was community-acquired in all cases. The source of the infection was unknown in all cases. Two patients had a native valve IE (one of them had a previous rheumatic valve disease) and the other two had a prosthetic valve IE. Involved valves were the mitral valve in 2 cases, the aortic valve in 1 case and mitral + aortic valves in the other case. Duration of symptoms was > 90 days in 2 cases. Left heart failure developed in 2 cases. *A. defectiva* was isolated in 1 patient and *A. adiacens* in the other 3. MIC for penicillin were 0.03, 0.25, 0.5 and 1 mg/L, respectively. Valve vegetations were detected by TTE/TEE in three cases. Their size was > 10 mm in all cases. Patients received aqueous penicillin G or ampicilin for 4-6 weeks together with gentamicin the first 2 weeks. Valve replacement surgery was performed in all cases. Two patients (50%) died.
Conclusions: Abiotrophia was an infrequent but important cause of IE with significant morbidity, surgical requirement and mortality.

P 106

HIGH LEVEL PENICILLIN RESISTANT PNEUMOCOCCAL ENDOCARDITIS

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Objective: To describe a case of sub-acute infective endocarditis caused by high level penicillin resistant *S. pneumoniae*.
Methods: MICs were determined by the NCCLS recommended broth macrodilution method with in-house prepared Mueller-Hinton (M-H) broth supplemented with divalent cations and 5% lysed horse blood. E-test (AB Biodisk North America, Inc., Culver City, Calif.) was performed following the manufacturer's recommendations with M-H-Sheep blood agar plates (BBL Microbiology Systems, Cockeysville, Md.). In brief, *S. pneumoniae* was grown overnight on blood agar plates, suspended in Trypticase soy broth to a 0.5 MacFarland density, and inoculated for confluent growth onto M-H-blood agar plates. Isolates were designated susceptible to penicillin and ceftriaxone when the MIC was < 0.1 and ≤ 0.25 mcg/ml respectively; intermediately resistant when MIC between 0.1-2.0 and 0.5-1.0 respectively; and resistant, MIC > 2.0 mcg/ml for both antibiotics.
Case Report: A 70-y/o female patient was hospitalized for intermittent fevers of 6 weeks duration following an episode of pneumococcal pneumonia and bacteremia treated with penicillin 6 weeks earlier. Blood cultures grew *S. pneumoniae*. TEE showed a 13 mm vegetation on the anterior leaflet of the MV, ruptured chordae and moderate MR. The isolate was initially reported mistakenly as susceptible to penicillin (by E-test). Intravenous penicillin G at a continuous infusion of 20 million units per day was administered with a slow defervescence. Repeated blood cultures were sterile. However, 3 weeks after initiation of penicillin therapy symptoms of progressive heart failure developed, TEE showed worsening of MR necessitating surgery. Destruction of both MV and AV, as well as an aortic root abscess were found. The patient underwent MV and AV replacements. Gram positive cocci were observed on Gram stain of the MV, but cultures were negative. Repeated MIC by the E-test revealed MIC of 2.0 mcg/ml for penicillin and 0.19 for ceftriaxone. MIC by broth macrodilution was 4 mcg/ml for penicillin and 1.0 for ceftriaxone. The patient completed a 4 weeks course of treatment with ceftriaxone (4.0 gr/day). 2 months after completing antibiotic therapy her condition is stable and blood cultures are sterile.
Discussion: Our case is unusual because penicillin-resistant-S.pneumoniae (PRSP) has so far rarely been the pathogen of endocarditis, and sub-acute presentation is the exception. Moreover, resistance to penicillin does not develop during therapy, thus we believe that the patient was initially infected with PRSP, partially responded to the therapy administered initially, only to have a metastatic infection of her heart that did not adequately respond to penicillin therapy twice.The presence of a positive Gram stain suggests that the bacteria persisted in the tissue. If penicillin therapy would have been sucessful the autolytic enzymes would have rendered the Gram stain negative. Thus, pneumococcal diseases need aggressive therapy and careful monitoring to avoid life threatening complications as endocarditis.

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ENTEROCOCCAL INFECTIVE ENDOCARDITIS. TWO CASES

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We report here two cases of infective endocarditis by microorganisms from genus Enterococcus. First case was a diabetic 67-years-old man with a 15-days progressive course of fever, fatigue and other congestive heart failure signs. *Enterococcus faecalis* were isolated from multiple consecutive blood cultures, that were susceptible to ampicillin, vancomicyn and had positive sinergism with gentamicin and streptomycin. Intracardiac vegetations were found at the aortic valve by echocardiographic study, and severe aortic insufficiency and light mitral insufficiency by cardiac catheterization. Abdominal echocardiographic study showed an isquemic splenic infarction image. Antibiotherapic treatment was carried out with ampicillin and gentamycin for over six weeks, until surgical intervention with aortic valve replacement was performed. Clinical course was postoperatively complicated and patient died eight days after surgery due to cardiogenic shock. Second case was a 27-years-old man, intravenous drug user (cocaine, heroin), serologic test to HIV antibodies negative and HCV antibodies positive, hard smoker and alcoholic drinks consumer, that was admitted in our hospital because of a one week clinic course with remittent fever upto 38ʃC, malaise, fatigue, night sweats, pleuritic chest pain, nonproductive cough and wrist pain. A sistolic heart murmur and a patchy interstitial infiltrate were detected. *Enterococcus faecalis* were isolated from blood cultures, that were susceptible to ampicillin, vancomicyn and had positive sinergism with gentamicin. Intracardiac vegetations in aortic valve and annular abscesse in mitral valve were found by transesophageal echocardiography, so as severe aortic insufficiency and light mitral insufficiency. Antibiotherapic treatment was carried out with ampicillin and gentamycin until surgical intervention with aortic valve replacement was performed. Althoug patient was hospital discharged in two months time he died 9 months after due to congestive heart failure.
Conclusions: Enterococci are able to produce grave infection with high mortality rates. They could suppose a serious problem of medical treatment if they acquire mechanisms of resistance.

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UNFAVORABLE OUTCOME AND INCREASED REQUIREMENT OF SURGICAL TREATMENT IN *STAPHYLOCOCCUS LUGDUNENSIS* INFECTIVE ENDOCARDITIS. A REVIEW OF 54 EPISODES (1988-2000)

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S. lugdunensis was initially described in 1988 as a different species of coagulase-negative staphylococci. The pathogenic potential of this microorganism has been determined in several types infections but *S. lugdunensis* infective endocarditis (IE) has been seldom reported.
Objective: We describe our experience with 5 cases of S. lugdunensis IE and we review the literature.
Methods: The multidisciplinary team for diagnosis and treatment of IE from the Hospital Clinic of Barcelona, conducted a prospective study and identified and followed all patients with IE diagnosed since 1989. All data of *S. lugdunensis* IE were collected prospectively using a previously designed questionnaire that specified the clinical, microbiological, echocardiographical, therapeutical and evolutive variables. To review the cases published in the medical literature since 1988, a computer-based search was made using the terms: «endocarditis» and «*S. lugdunensis*».
Results: A total of 421 consecutive patients with IE were diagnosed between 1989 and 2000. 104 cases were IE in intravenous drug abusers (IVDA) and 317 were IE in the general population: 213 cases had native valve endocaridits (NVE), 75 cases prosthetic valve endocarditis (PVE), and 29 cases pacemaker IE. 5 cases of IE due to *S. lugdunensis* were identified in the last decade. All were in the general population (1.1%) representing 0,9% and 7% of NVE, and pacemaker IE respectively. A total of 49 cases of IE dueto *S. lugdunensis* have been identified after a comprehensive revision of the literature. The combined analysis of these 54 cases showed that 31 patients were male (57%) and mean age was 59 years (range 23 to 85). A preexisting structural heart disease was present in 46% of the patients. NVE, PVE and pacemaker IE was present in 75%, 15% and 10% of cases respectively. Aortic valve IE was present in 21 cases, mitral valve IE in 22, aorto-mitral infection in 6 cases and triple valve infection in one patient. Heart failure was found in 41 patients (76%) and emboli phenomena were reported in 10 cases (18%). Surgical treatment (valvular or pacemaker surgery) was performed in 28 cases (52%). Overall mortality was 52%, dying 19 out of 25 patients from the medical group (76%) and 9 out of 29 cases from the medical plus surgical group (31%).
Conclusions: *S. lugdunensis* IE has an aggressive course with a high mortality. It usually involves native left-sided valves and most patients developed heart failure and/or embolisms. Surgical treatment is often required and seems to be the optimal treatment in order to improve the outcome of this disease.

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STAPHYLOCOCCUS LUGDUNENSIS ENDOCARDITIS. A REVIEW

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Objective: To emphasize the increasing importance of Staphylococcus lugdunensis as a cause of endocarditis.
Method: We describe a case of Staphylococcus lugdunensis endocarditis and we reviewed all cases published in the literature. A Medline search was performed including all cases published in any language.
Results: A total of 52 cases of Staphylococcus lugdunensis endocarditis were found since 1950. Our case was a 43 year- old woman that presented high fever and chills twenty days after a percutaneous pulmonary valvuloplasty for a congenital estenosis of pulmonary valve. A 3/6 pulmonary murmur was detected and 10/10 blood cultures were positive to Staphylococcus lugdunensis. A transparietal echocardiography showed a 0.6x0.6 cm verrucous lesion at pulmonary valve. Cloxacillin 12gr/day plus gentamicin (3mg/kg/day single daily dose) were started with clinical improvement, completing a total of 6 week therapy (with amoxicillin during the last 2 weeks). No embolic events were detected and after two years follow-up the patient is doing well and asymptomatic. In one literature review we found that patients with S. lugdunensis had a high mortality, 52% (27/52); systemic embolic phenomena were reported in 25% of cases. Almost a 60% (31/52) of patients needed surgery because severe valvular dysfunction or cardiac failure. Only one previous case of pulmonary S. lugdunensis endocarditis has been reported. 42/52 (90%) cases were on native valve, 8 were in prosthetic valve and the remaining two cases of endocarditis were related to the presence of a pacemaker device. β–lactam or vancomycin plus an aminoglycosid were the most commonly used antibiotics.
Conclusions: Staphylococcus lugdunensis is a coagulase-negative staphylococcus (CNS) increasingly reported as a cause of endocarditis. Characteristically, in contrast with others CNS, involves most commonly native valves, has an aggressive course,

surgery is needed often, and mortality rate is high. Pulmonary involvement and a favourable outcome with antibiotic therapy were the most prominent features in our case.

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LACTOBACILLUS RHAMNOSUS ENDOCARDITIS IN A DRUG ADDICT

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Clinical history: A 39-year-old woman was admitted for asthenia, dyspnea and bilateral gonalgia. Her medical history disclosed a post-rheumatic aortic valve stenosis, intravenous drug abuse, chronic hepatitis C, and dental extraction without prophylaxis two months earlier. Her temperature was 37oC, the cardiac auscultation revealed an aortic stenosis murmur without regurgitation, there was no signs of peripheral emboli or vasculitis.
Laboratory: The white blood count, the C-reactive protein, the sedimentation rate, and the rheumatoid factor were normal. A transthoracic echocardiogram revealed severe valve remodeling without floating vegetations. Blood cultures grew a Lactobacillus rhamnosus, poorly susceptible to beta-lactams (MIC> 2 mg/L), but susceptible to macrolides, rifampin and quinolones. *in vitro* killing was achieved only with levofloxacin and amoxicillin-gentamicin.
Evolution: The patient recieved levofloxacin, and responded by a resolution of her arthritic signs. After two weeks she developed bilateral Achilles tendinitis and was switched to amoxicillin-gentamicin. After 6 weeks she underwent prosthetic valve replacement. Endocarditis was confirmed by the pathology, but valve cultures remained sterile. The further evolution was uneventful.
Discussion: Lactobacillus spp. endocarditis is rare and primarily described in elderly immuno-compromised patients (Int J Food Microbiol 1994; 24: 179-89; Clin Infect Dis 1997; 25: 1048-55). Among these, L. rhamnosus is the most frequently described. Our patient was younger, HIV-negative, and had no signs of immuno-suppression. However, she was infected with L. rhamnosus. The clinic was torpid and only the pathology fitted the Dukes criteria for endocarditis. A possible origin of the organism was a heavy consumption of yogurts around the time of dental extraction.

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TRICUSPID VALVE ENDOCARDITIS CAUSED BY ACTINOMYCES

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A 40 year-old woman with a history of heroine abuse and a previous tricuspid and aortic valve *Staphylococcus aureus* endocarditis was admitted to hospital with fever, a systolic murmur was noticed from apex to I2 dx. Transesophageal echocardiography identified a vegetation 10 mm in diameter on the tricuspid valve. The blood culture yielded a Gram-negative-staining rod, identified as Actinomyces funkeii; a new species of Actinomyces.
The patient was cured by a prolonged treatment with 22 weeks of antibiotic treatment; where cephalosporins alone failed as therapy, when rifampicin and clindamycin was added the patient slowly improved. Actinomyces is a facultative anaerobic gram-positive, non-acid fast rod that is found in the oral cavity, gastrointestinal, and in women in the urogential region. It usually causes infection in the orophacial region. Septicaemia caused by actinomyces is unfrequent. Endocarditis is rare, less than 20 cases of infective endocardits related to actinomyces are described in literature.
Actinomyces funkeii is a new species, identified at CCUG University of Gothenburg, this is the first described case of Actinomyces funkeii endocarditis.

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METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA) SEPSIS AND RIGHT-SIDED ENDOCARDITIS COMPLICATED BY ASCENDING AORTA ANEURYSM IN A HIV-POSITIVE IVDU PATIENT

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Introduction: To report a case of MRSA-induced endocarditis associated with mycotic aneurysm of the ascending aorta in a HIV+ IVDU, which was successfully treated with early surgical management and prolonged antibiotic therapy.
Case Report: A 24 year-old HIV+ female patient presented to the hospital for evaluation of fever, cardiac arrhythmias and dyspnoea. She also complained of worsening chest pain and arthralgias. She had a history of i.v. drug use anf five years before, she was hospitalized because or right-sided endocarditis and bilateral pneumonia due to methicillin-susceptible *S. aureus*. Repeated blood cultures performed on admission yielded MRSA. The organism was beta-lactamase-positive and was resistant to a variety of antibiotics including penicillin G, cotrimoxazole, mezlocillin, ampicillin, ceftotetan and ceftazidime, and it appears susceptible to choramphenicol, amikacin, erythromycin and vancomycin. Echocardiographic study revealed mild mitral insufficiency, vegetations attached to the tricuspid valve with a severe tricuspid insufficiency, an aneurysm in the ascending aorta, and a mild pericardial effusion. CT angiography confirmed the presence of a moderate-sized aneurysm in the ascending aorta. A successfull combined medical (a prolonged course of vancomycin + ciprofloxacin) and surgical treatment (a complete TV resection with valve replacement along with resection of the aneurysm and aortic rapir with a in-situ graft) was performed.
Conclusion: This is the first reported case of right-sided infectious endocarditis complicated by ascending aorta aneurysm caused by MRSA in a HIV+ patient in Italy. Because the prognosis of infectious endocarditis due to MRSA may be particularly severe in immunocompromised hosts, a high index of clinical suspicion should be considered in HIV+ individuals who present with febrile illness associated with chest pain and bacteremia in order to formulate an early diagnosis and aggressive treatment.

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FIRST CASE OF SPONDYLODISCITIS COMPLLCATING A CAMPYLOBACTER FETUS ENDOCARDITIS

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Campylobacter fetus is an opportunist pathogen which occurs mainly in immunodeficient patients. The predilection for the vascular endothelium can lead to thrombophlebitis, mycotic aneurysm and endocarditis. We report a case of *C. fetus* mitral endocarditis complicated by spondylodiscitis in an immunocompetent host.
In october 2000, a 72-year-old man with a past history of mitral stenosis was hospitalized for an one month history of general malaise, fever, anorexia and a 3-kg weight loss. On physical examination, he had a temperature of 38,7 ºC. The auscultation revealed a pansystolic murmur of mitral regurgitation. The erythrocyte sedimentation (ESR) rate was 100 mm/h, C-reactive protein was 178 mg/L (normal range < 5mg/L), the white cell count was 20.000/mm^3 and the creatinine level was 187 micromol/l. Transesophageal echocardiography (TEE) showed an anterior mitral valve vegetation. After five days of incubation, *C. fetus subspecies fetus* was recovered in two bottles of the three

sets of blood culture. Despite appropriate therapy with intravenous amoxicillin plus clavulanic acid (4 g/day) and gentamicin (120 mg/day) fever reappared and a mitral valve abcess was confirmed by TEE. The patient underwent mitral valve replacement by bioprothesis. Gram staining and culture of the valve were negative. The post operative outcome was complicated by a L4-L5 spondylodiscitis revealed by left sciatica, persistant inflammatory syndrome and magnetic resonance imaging (MRI). Therapy was changed to pefloxacin (400 mg twice daily) and roxithromycin (150 mg twice daily). After three months, the outcome was favourable: the ESR was 24 mm/ h, the CRP was 8 mg/L and an improvement of the vertebral lesion was noted in MRI.
About 28 cases of endocarditis due to *C. fetus* have been reported mainly in debilitated hosts. The aortic valve is predominantly affected and previous valve heart disease is common. Prosthetic location is rarely encounterred. The gastrointestinal tract is the probable portal of entry but most patient had no intestinal symptoms. The diagnosis is made by the positivity of the blood culture which must be incubated for a prolonged incubation time. Due to the intrinsic activity of clavulanic acid against *C. fetus*, the combination of amoxicillin plus clavulanic acid in association with gentamycin is the antibiotherapy of choice due to bactericidal and synergistic effects of the association.
Prognosis seems to be improved by early valve replacement. The association of a spondylodiscitis has never been reported to our knowledge. In this case a prolonged oral antibiotherapy must be necessary with effective and good osseous tissue diffusion antibiotics as macrolides, quinolones, cyclines for a prolonged duration of 3-6 months. Therefore, clinicians should be aware of this infection and microbiologist should accurately isolate this organism by prolonging the incubation time of the blood culture to encompass the growth requirement of *C. fetus*.

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CANDIDA PARAPSILOSIS ENDOCARDITIS: CASE REPORT AND LITERATURE REVIEW

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The case of a 72-year old diabetic man with fungal endocarditis due to C. parapsilosis presented with FUO and pancytopenia is reported. Six months ago he had been operated for colon cancer and had a post surgery course, complicated –among other events– by an episode of fungemia with C. parapsilosis in the presence of a CVC for parenteral nutrition. This episode was managed by CVC removal and a 14-day treatment with high-dose fluconazole. A TEE a month later showed no vegetations. During current illness C. parapsilosis was resistant to fluconazole and a large vagetation was present on a prolapsing mitral valve. Blood cultures remained negative only with high dose liposomal amphotericin B, but after 45 days a new vegetation was detected on the aortic valve. Surgery and replacement of both mitral and aortic valve was decided and successfully performed but the patient succumbed 2 months later, because of a course complicated by renal failure, arrythmias and multiple episodes of sepsis due to multiresistant bacteria and associated with a CVC.
C. parapsilosis, once believed non-pathogenic (< 1940), is now a frequent cause of fungemia in some institutions. Earlier being associated with endocarditis in IVDU, is currently emerging as important pathogen causing nosocomial infections usually associated with invasive procedures of prosthetic de vices. 39 reports of *Candida parapsilosis* endocarditis were retrieved from the English literature (1966-2001). Seventy-five cases are described in total, 21 of them after 1992. There is a trend of decreased incidence in IVDU and increased in patients with prosthetic valves. Two nosocomial epidemics are described. Characteristically, a long incubation period is seen (20-345 days) and infection may result despite effective treatment of the initial episode of fungemia. A murmur, splenomegaly, large vegetations and peripheral emboli ara common and despite the fact that *C. parapsilosis* is less virulent, endocarditis shares a grave prognosis (35% total survival, 50-64% if both surgical and antimicrobial treatment is applied).
Conclusions: *C. parapsilosis* can emerge as an important nosocomial pathogen, threatening patients with central lines and endocarditis must always be kept in mind in order to be early diagnosed and effectively treated.

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PSEUDOANEURYSM OF THE AORTIC ANNULUS AS A COMPLICATION OF PROSTHETIC VALVE ENDOCARDITIS

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Prosthetic valve endocarditis remains an infrequent but serious complication of cardiac valvular replacement. We report the case of a patient who developed a large pseudoaneurysm as a complication of aortic prosthetic valve endocarditis.
A 55-year-old man with a history of aortic staphylococcal endocarditis who required aortic valve replacement, was admitted to our hospital three months later because fever. Physical examination revealed a respiratory rate of 20 breaths per minute, a heart rate of 100 beats/min, an a blood presure of 120/60. He did not show a new murmur. Other findings of physical examination were unremarkable. Laboratory studies revealed a white count of 13.500 / mm3, hemoglobin 9.5 gr/dl and hematocrit 30.8%. ECG and chest-x-ray film did not show specific features. Blood cultures drawn upon admission grew Candida albicans. Transesophageal echocardiography was performed usin a Hewlett- Packard 2.500 Sonos machine with a 5-MHz echocardiographic system transesophageal echocardiographic probe. Close examination of the aortic prosthetic valve revealed a large periprosthetic pseudoaneurysm adjacent to the aortic annulus. A highly mobile vegetation was found in this echolucent region. Color Doppler mapping demonstrated forward flow from the aortic annulus into the pseudoaneurysm. This study demonstrated normal function of the aortic prosthetic valve. Anti-fungic therapy was started but the patient's condition worsened on hospital day 3. He refused operation and died 48 h later due to persistent sepsis.
Despite major advances in cardiovascular surgical techniques and routine use of prophylactic antimicrobial agents, prosthetic valve endocarditis remains an extremely serious complication with very high mortality. Moreover, fungal endocarditis itself has an ominous prognosis. In this case the patient developed a large pseudoaneurysm with an uncommon feature: a highly mobile vegetation floating inside. We present it because of its amazing images.

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INFECTIVE ENDOCARDITIS COMPLICATED BY MYCOTIC HEPATIC ANEURISM CURED WITH ENDOVASCULAR OCCLUSION: A CASE REPORT AND REVIEW OF THE LITERATURE

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Objective: To report a rare complication of infective endocarditis.
Methods: Case report.
Results: The patient, was a 36 years old man with fever, weigh loss for two months and dyspnea for few days before the admission. On examination: temperature was 38.8 ºC. Conjunctival petechiae and Osler's node was observed. A grade 4/6 holosystolic murmur over the mitral area. Dull percussion of Traube's space was noted.

Echocardiography showed large vegetations on the mitral valve with severe regurgitation. Penicillin, oxacillin and gentamicin were started to treat endocarditis. *Streptococcus oralis* grew in blood cultures. Four weeks later the fever persisted. New blood cultures were sterile. Abdominal sonography revealed splenic nodule but no abscess or aneurysm was detected by angiogram. Computed tomographic (CT) scan of the brain showed frontal lobe infarction but angiogram was normal. No reason was found to justify the persistence of fever so mitral valve replacement was performed. On the eighth day of post-operative the fever recurred. CT showed hepatic nodules and aneurysm in the hepatic artery. Sonography revealed splenic infarction, multiple liver abscesses and aneurysm of the hepatic artery. Angiogram confirmed large aneyrism of the hepatic artery.
Successful coil embolization of the aneurysm was performed. Penicillin plus gentamicin completed eight weeks. Recovery was uneventful.
Conclusions: Brain and splenic embolization are not uncommon finding in *Streptococcus oralis* endocarditis but mycotic aneurysm of the hepatic artery is very rare. The coil embolization seems to give good results and should be considered in patients with infective endocarditis with hepatic artery aneurysm.

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INFECTIVE ENDOCARDITIS DUE TO RARE OR FASTIDIOUS BACTERIA IN CENTRAL TUNISIA

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Infective Endocarditis (IE) to unusual or fastidious bacteria can be divided into post operative caused by fungi, legionella ect and community acquired due to bacteria rarely associated with endocarditis or intra cellular bacteria that cannot be routinely isolated.
We report in this study particularities of five cases of community acquired IE due to unusual organisms diagnosed in the two university hospitals of Sousse-Central Tunisia from 1990. The organisms were Corynebacterium diphtheria, 2 cases; Brucella, 2 cases and Coxiella burnetii, 1 case. Representing 5% of community acquired IE, the five cases occured on native valves. Only the 2 patients Corynebacterium IE were children (6 and 10 years old) with underlying heart disease and had extra cardiac complications: splenic abscess and arterial aneurisms. Four patients required valvular replacement and valvuloplasty for 1 patient. All patients cured.
Despite its rarity, IE due to unusual organisms have to be suspected in particular situations. Besides, fastidious organisms have to be ruled out by serology, cellular cultures and PCR in cases of negative blood cultures.

P 118

A CASE OF HIV-RELATED ANEURYSM OF THE AORTIC ROOT

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Objective: Atherosclerosis seems to affect Human Immunodeficiency Virus (HIV) -positive patients. While HIV vasculitis has been associated with aneurysms of the abdominal aorta, no similar pathology has been reported for the ascending aorta. We present such a case of atheromatic aneurysm and discuss relation to the HIV.
Methods: Retrospective review of medical records.
Results: A 59 year-old HIV-positive male presented with NYHA II class dyspnoea and a systolic murmur. He was normolipidaemic and non-smoker. Echocardiography revealed left ventricular dilatation, aortic stenosis and aneurysm of the ascending aorta. Coronary angiogram demonstrated calcification but no significant stenosis. At elective operation, we found a significantly calcified tri-leaflet aortic valve, macroscopically normal aortic wall and a large fusiform aneurysm of the ascending aorta. The aortic root was replaced with a 29mm composite Dacron graft. The patient made a rapid recovery except for an inguinal haematoma. Histopathology revealed atheroma. He was found well on follow-up.
Conclusions: HIV may cause accelerated atherosclerosis in the absence of other predisposing factors and thus claim a share in the aetiology of aortic disease. Attempts for a pathophysiological explanation have been recently presented in the literature.

P 119

AORTIC ANEURYSM AS PRESENTING MANIFESTATION OF TERTIARY SYPHILIS: FORGOTTEN BUT NOT GONE

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Introduction: To report a case of aneuysm of the ascending and of the descending aorta as initial manifestation of tertiary syphilis in a middle-aged woman with HCV-related chronic hepatitis.
Case Report: A 53 year-old female was admitted with the complaint of epigastric and thoracic pain which appeared 1 month before admission and which had gradually become more frequent. She did not give a history of venereal disease and denied any risk factors for sexually transmitted infections. Ultrasonography and a CT sean showed an intramural hematoma and a saccular aneurysm of the thoracic and abdominal aorta. Serological tests for syphilis and HCV were all positive. Laboratory disclosed an ESR of 65 mm/h, an AST value of 50 U/L, an ALT value of 58 U/L, and a WBC count of 12.000/mm^3, with 63% neutrophils, 20% lymphocytes and 16% monocytes. Treatment with i.v. penicillin G (24 M.U. daily for 10 days). Controls with CT and ultrasonography gave evidence of a stability of the aortic aneurysm during the following 6 months.
Conclusion: With the advent of antibiotics syphilis and its complications appear to have declining as an important cause of cardiovascular disease in developed countries. We have herein reported a case in which a diffuse aortic aneurysm due to syphilitic aortitis was diagnosed in a patient with HCV –chronic hepatitis. The case is inusual as the syphilitic aortitis caused a diffuse aneurysm affecting the thoracic and abdominal tract of the aorta in a patient coinfected with HCV. This case emphasizes this interesting association of HCV-chronic hepatitis and luetic aortitis and thoracic and abdominal aortic aneurysm in a immunologically normal host.

P 120

UNUSUAL HHV6 INFECTION AFTER CARDIAC SURGERY

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Objective: To describe an unusual form of HHV-6 infection in the post-surgical period as fever of unknow origin.
Case report: We describe a 45 years old woman presenting fever and malaise in the first week after surgery for prosthetic mitral valve replacement. On examination she was found febrile with a good general situation, liver was palpable, in the next week she developed axilar a cervical painful lymphadenopathy. Laboratory findings showed severe pancytopenia, abnormal liver function and elevated lactate dehydrogenase level. All cultures, Rx films and serology were negative, a toracoabdominal-TC showed hepatoesplenomegaly and a retroesternal collection of 5 cm that was removed without signs of infection and the culture was negative. Few days later she developed coagulopathy and acute renal failure, the patient was admitted to the intensive unit care. Axilar lymph node biopsy showed histiocityc necrotising

lymphadenitis by Kikuchi-Fujimoto, and bone marrow biopsy revealed hemophagocytic syndrome. HHV-6 infection was demostrated by PCR analysis of the lymph node. She was treated with many transfusions and plasma and later with intravenous immunoglobulin, corticosteroides and ganciclovir. Eight weeks later the patient is completly recovered and was discharged.
Conclusion: Kikuchi's disease and hemophagocytic syndrome are two benign proliferative lesions of phagocytic histiocytes and may be diagnosed in association with malignant, genetic or autoinmune diseases, but are also strongly linked with virus infection. The herpes group, especially the Epstein-Barr virus are relationated with them. The realationship between these syndroms and HHV-6 infection has rarely been reported, and is an unusual presentation form of fever of unkown origin after cardiac surgery.

P 121

MULTIVALVULAR ENDOCARDITIS IN INTRAVENOUS DRUG ADDICTS. SURGICAL TREATMENT WITH AORTIC HOMOGRAFT AND MITRAL-TRICUSPID PROSTHESIS

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There are a lot of valvular problems in patients who are Intravenous Drug Addicts (IDA) (with VIH+ or without VIH+).
Objective: We study the results of surgical intervention with aortic homograft and mitral-triscupid prosthesis.
Methods: In the last three years, two IDA patients with polivalvular endocarditis received treatment using aortic homografts and valve prostheses; we used two SJ prostheses valves in a case with Carpentier mitral prosthesis and in the second case SJ mitral and tricuspid valves. We used ECC with anterograde-retrograde hematic cardioplegia. Due to aortic ring destruction an aortic homograph was used for left outlet reconstruction. In one case the mitral valve had ring access and it was necessary to clean and install a mitral prosthesis in an infected mitral ring as well as an SJ tricuspid valve. In the second case the left ventricle was seriously dilated and we decided to install a biological Carpentier prosthesis, and we conserved the sub-valvular apparatus.
Results: In the patient who received an aortic homograph and two SJ mitral and tricuspid valve prostheses, a re-do operation was necessary due to a valvular leak one week after the operation. In this occasion a DDD epicardial pacemaker was implanted. The patient was discharged from the hospital 43 days after the first operation. The second day after discharge the patient resumed intravenous drug use. Three years later he is still alive with moderate aortic and mitral regurgitation, postmitral prosthesis and aortic homograph endocarditis. The second patient received an aortic homograph and a mitral bioprosthesis with total sub valvular conservation. He died in the operating room of left ventricular fallure. The transesophagic echo showed an aortic regurgitation in the aortic homograph. Post-mortem showed that there was a structural defect in the aortic homograph.
Conclusion: In the literature it has been demonstrated that the homograph is effective in the treatment of aortic endocarditis. When several valves are infected and destroyed the homograph is very useful in the aortic position but the treatment of mitral and tricuspid endocarditis continues to be a challenge. In favourable cases it is possible to use both mechanical and biological prostheses.

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PULMONARY VALVE ENDOCARDITIS RECONSTRUCTION OF RIGHT VENTRICULAR OUTFLOW TRACT WITH A CRIOPRESERVED PULMONARY HOMOGRAFT

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Objective: We describe a case of isolated pulmonary valve endocarditis resistant to antibiotics, which necessitated pulmonary valve resection and replacement with a pulmonary homograft.
Methods: A 68 –year– old woman was transferred to our hospital from another center in a context of infective disease (pyrexia, confusing state, vomits and diarrhoea). Neither cardiovascular risks factors nor previous history of heart valve disease were present. She had leukocytosis and three preoperative positive blood cultures for *Staphylococcus aureus* methicillin – sensitive. New York Heart Association (NYHA) class was II. Transthoracic echocardiography revealed aneurysmal dilatation of pulmonary artery (5 cm), vegetations on the pulmonary valve and a calcified mitral annulus. Antibiotic treatment with vancomycin and gentamicin failed to resolve valve infection, and preoperative course complicated with the development of acute drug induced renal failure (creatinine: 5.3 mgr/dl). Computarized tomography (CT) and magnetic resonance imaging (MRI) showed the presence of a dilated pulmonary artery and signs of severe bilateral pulmonary septic embolisms. All these data confirmed the diagnosis of active infective endocarditis (IE).
Results: Surgical treatment consisted of pulmonary valve replacement with a cryopreserved 28 mm pulmonary: homograft. Blood group matching was done. At opertion we found a dilated pulmonary artery, vegetations on pulmonary valve and perforation of posterior pulmonary cusp. Cross – clamp and bypass time were 96 and 155 minutes respectively. Although histopathological examination of pulmonary valve confirmed the diagnosis of acute IE with the presence of polymorphonuclear neutrophil leukocytes and necrosis of excised tissue valve, intraoperative pulmonary valve cultures showed no growth. The patient's postoperative course was excellent, and she was transferred out of the intensive care unit on 48 hours and discharged from the hospital after 3 weeks of intravenous antibiotherapy. Postoperative echocardiography was unremarkable with a peak systolic pulmonary gradient of 1,3 mm Hg and a maximum pulmonary flow velocity of 0,57 m/s (normal 0.6-0.9 m/s), without homograft vlve regurgitation. Six months later, the patients is asymptomatic (NYHA class I) and she has not any sign of infection.
Conclusions: Homografts have a low reinfection rate for patients with active infective endocarditis. We agree with others investigators, and believe that homograft is the prosthesis of choice in this kind of patients. Although right –side infective endocarditis is an uncommon disease, we think that the use of a cryopreserved pulmonary hornograft permits adequate replacement of infected valve with satisfactory immediate and long– term results.

P 123

PROSTHETIC VASCULAR GRAFT INFECTION REVEALED BY HYPERTROPHIC OSTEOARTHROPATHY - REPORT OF FOUR CASES AND REVIEW

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We report 4 unusual cases of prosthetic vascular graft infection revealed by hypertrophic osteoarthropathy (HO) and review the literature.
Case reports: Four men aged from 54 to 75 years, with a vascular history of aortic bifurcation prosthetic graft were hospitalized with complaints of pain of lower limbs and fever. The graft had been put from 1 to 8 years before the onset of the first symptoms of HO (interval 1). The diagnosis of HO related-infected graft was suspected from 3 to 6 months after the first symptoms of HO (interval 2). A digestive bleeding was present in one case. Antibiotics were started in two patients and non steroidal anti-inflammatory drugs in one. Surgery was added for all cases and consisted of extraanatomic bypass graft and aortic graft excision. A graft-enteric fistula was demonstrated for each case on the duodenum. Two patients died. Our review of the literature disclosed 25 previous cases (22 men). Patient age ranged from 15 to 76 years with a mean age of 60 years. The arterial graft was placed on the aortic bifurcation in 19 patients. The intervals 1 and 2 ranged respectively from 4 months to 10 years, and from 1 month to 4 years. Fever was present in 23 cases and a digestive bleeding was noted in 9 cases. The location of HO was unilateral in 17 cases. A bone scintiscan allowed the diagnosis of OH for the 25 cases. Blood cultures grew Streptococcus sp. in 9 cases and E. coli in 4 cases. The culture of the infected graft grew E. coli in 7 cases. Thirteen cases had a proved aorto-enteric fistula. An extraanatomic bypass graft was performed for 20 patients, in 12 cases in association with antibiotics.The mortality rate was 36%. The diagnosis of infected vascular graft is delayed in case of HO as demonstrated in the previous cases and ours. The realization of a bone scan in these situations helps unmistakably to approach the positive diagnosis of OH. In such cases, an infection of the vascular prosthesis is likely and an aortoenteric fistula must be highly suspected. As a result, physicians should be aware of this unusual association as to reduce the timespan to the diagnosis of infected graft and graft-enteric fistula.

P 124

LATE INFECTIVE ENDOCARDITIS TO LEAD PACEMAKER

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Infective endocarditis related to lead pacemaker is a rare (0.13 to 12.3% of all infective endocarditis) but severe complication (mortality from 10 up to 30%). We present 2 patients with infective endocarditis over pacemaker lead the were treated with antibiotics and surgery.
First case: A 50 years old male undergoing hemodialysis. A DDD pacemaker was implanted in 1993. In 1997 he was admitted in our hospital with fever, and an Staphilococcus aureus was isolated in blood cultures. Transesophageal echocardiography showed a vegetation located where the lead was implanted on the right ventricle. Antimicrobial treatment with vancomicyn and azactam was provided during 6 weeks, but low grade fever persisted. Surgical intervention with extraction of both leads was required, and 2 vegetations over the ventricular lead were observed. A new bicameral epligastric pacemaker was implanted with no further complications. The second patient was a 74 years old male with type II diabetes mellitus and monoclonal gammapathy with anaemia and leucopenia, who had a DDD pacemaker since 1990. In October of 2000 he was admitted to our hospital because of fever. A transesophageal echocardiography showed a 2.6 cm^2 vegetation on the right atrium, adhered to the lead. Separated sets of blood cultures isolated an penicillin and gentamicin susceptible Streptococcus orale, and both antimicrobial drugs were administered during 6 weks, followed by surgical removal of both leads. The presence of a vegetation adhered to the atrial lead was confirmed. There were no further complications and the patients recovered satisfactorily. In both cases the clinical signs appeared years after the pacemaker was implanted, which is very frequent. We isolated unusual bacteria (the most frequent bacteria are *S. epidermidis* in late endocarditis and *S. aureus* in acute ones). *S. oralis* is not a common agent. In both patients we treated with both therapies, initial treatment with 6 weeks antibiotics guided by antibiogram, and followed by surgery, with good results and no mayor complications.

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INFECTIVE ENDOCARDITIS, A SERIOUS COMPLICATION OF IMPLANTABLE CARDIOVERTER-DEFIBRILLATOR: CASE REPORT AND REVIEW OF THE LITERATURE

Fortes, C.Q., Atie, J., Araujo, N., Giambroni, R., Provenzano, S., Cardoso, F.L.L., Oliveira, M.P.B., Nouer, S.A., Marangoni, D.V., Moreira, R.B., Pereira, N.G.
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Objective: To report a serious complication of implantable cardioverter-defibrillator.
Methods: Case report.
Results: A 39 years old female with arrhythmogenic right ventricular dysplasia was treated with an implantable cardioverter-defibrillator (ICD). Eleven months later she presented an abscess in the pocket and ICD extrusion. The ICD was removed and 20 days after been in antibiotic the ICD was reimplanted. Fourteen months later she was admitted in another hospital with fever and general malaise. No vegetation was detected by echocardiography. After been treated with antibiotics for 27 days the fever persisted and she was refereed to our hospital. On examination she had fever. A ICD related infection was thought, blood cultures were drawn and started vancomycin plus gentamycin. Blood cultures were negative.
Echocardiography did not reveal vegetation. In the sixth hospital day transesophageal echocardiogram revealed large vegetation in the tricuspid valve and in the ICD lead. She was submitted to surgical remove of the entire system and tricuspid vegetectomy. After 6 weeks on asntibiotic a new ICD was implanted. Recovery was uneventful with 29 months follow up.
Conclusions: IE is a serious complication in patients with an ICD and should be always investigated in these patients when fever is present, chiefly if there is no other reason to justify it. Treatment should be done with the entire remove of the ICD. A new ICD can be reimplanted in other pocket after the entire infected ICD have been removed and a complete course of antibiotic was finished.

P 126

INFECTIONS AND ANTI-MICROBIAL RESISTANCE IN CARDIOVASCULAR SURGERY: TWO CASES (SEPTICEMIA RELATED TO *STAPHYLOCOCCUS AUREUS* WHICH IS DETECTED AS INTERMEDIATE TO VANCOMYCIN AND RESISTANT TO TEICOPLANIN AND A CASE WITH MULTIRESISTANT POLYMICROBIAL ENDOCARDITIS)

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In our study, a case with septicemia is presented. It developed following an open heart surgery and was caused by *Staphylococcus aureus* which was found intermediate to vancomycin and resistant to teicoplanin with in-vitro E-test and population analyse profile area under cure (PAP-AUC) tests. The other presented case was a polymicrobial infective endocarditis which had clinical, transesophagealecho (TEE) findings and in its culture, methicillin resistant *Staphylococcus epidermidis* and *Corynebacterium striatum* were isolated. With all these results, medical treatment was started but as the clinical situation of the patient got worse and especially, the persistance of *C. striatum* bacteriemia was observed, a valve replacement operation was performed. Our study included rare and interesting two cases since in our first case following cardiovascular surgery, we found out the decrease of vancomycin susceptibility and the presence of teicoplanin resistance in the agent causing the clinical situation and in the second case, we observed the agents causing polymicrobial endocarditis as multiresistant. We also emphasized the importance of antimicrobial resistance in both cardiac infections and infections following cardiovascular surgery.

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PROCALCITONIN AND C-REACTIVE PROTEIN IN INFECTIVE ENDOCARDITIS: THE CORRELATION WITH ETHIOLOGY AND PROGNOSIS

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Objective: To investigate the diagnostic value of serum procalcitonin (PCT) and C-reactive protein (CRP) levels in infective endocarditis (IE) and the correlation of the ethiology and prognosis of patients.
Method: Between Juli 1999-December 2000, 50 cases diagnosed as IE according to Duke criteria (major or/and minor) in Istanbul University Cardiology Institute and Florence Nightingale Hospital were included in the study. Their ages were between 18 and 66. 32 were male, 18 were female. 50 healthy blood donors consisting of 36 males and 14 females within ages 18-60 were included in the study as the control group. During the medical follow-up of the patients, plrocalcitonin and CRP levels are measured for 45 days. In the patients who had response to medical therapy according to the results of hemodynamica, transesophagealecho (TEE), culture etc. the levels were measured by obtaining 5cc. plain blood on the admission day, 24 hours later, 15th, 30th and 45th days. In the patients who were obliged to have valve replacement according to the follow-up parameters, 5cc plain blood was obtained on the admission day, 24 hours later, on the 15th day and one day before and 2, 5 days after the operation. Then procalcitonin and CRP values were measured. The PCT values were evaluated with the Immunoluminometric method (Lumitest PCT Brahma Diagnostica/Germany) and CRP with Immunturbidimetric method (Turbidimeter CRP Dade Behring / Germany). The statistical calculations were made in the STATA 5.0 program with Man-Whitney U test and Pearson correlation analyse and Fisher s chisquare test.
Results: In our study, a significant difference (P:0000) was found between the patient group and the control group in terms of serum PCT and CRP levels at the time of application. the sensitivity of PCT in comparison to CRP was found lower (100% to 84%) however its specificity was higher (72% to 88%). The PCT values of the non-operated and operated cases at the time of admission, at 24th hour, 15th day were 3.71, 5.35, 0.44; 2.45, 4.28 and 4.22 µg/ml respectively and for CRP 9.30, 10.95, 10.65; 9.5, 10.9, 10.2 µg/ml respectively. According to these, PCT value in non-operated cases decreased together with the response to therapy but in operated cases PCT value showed persistence. CRP was at the same level in both groups. The serum PCT median value was found higher in cases with IE related to Gram positive bacteria than the cases with IE related to gram negative bacteria ($p < 0.02$). This was found insignificant for CRP ($P > 0.05$).
Conclusion: As a result, our study makes us think that in addition to TEE, culture and other clinical criteria, PCT is more beneficiary with high specificity and positive predictive values than CRP. Our study also suggests that in the follow-up of the response to medical treatment, PCT is a more valuable parameter than CRP and it has a high prognostic values as a criteria for the indication of valve replacement in addition to the other clinical parameters. Furthermore, when the result of the culture is not determined yet or the agent can not be isolated, serum PCT levels may help the physicians to arrange the antimicrobial therapy combination.

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