Europace (2012) **14**, 1334–1339
doi:10.1093/europace/eus044

Microbiology of cardiac implantable electronic device infections

Maria Grazia Bongiorni[1], Carlo Tascini[2], Enrico Tagliaferri[2]*, Andrea Di Cori[1], Ezio Soldati[1], Alessandro Leonildi[2], Giulio Zucchelli[1], Ilaria Ciullo[2], and Francesco Menichetti[2]

[1]Second Division of Cardiovascular Diseases, Cardiac and Thoracic Department, New Santa Chiara Hospital, University Hospital of Pisa, Via paradisa 2, 56124 Pisa, Italy; and [2]Infectious Diseases Unit, New Santa Chiara Hospital, University Hospital of Pisa, Via paradisa 2, 56124 Pisa, Italy

Received 16 September 2011; accepted after revision 11 February 2012; online publish-ahead-of-print 7 March 2012

Aims The aim of the study was to describe the microbiological findings of cardiac implantable electronic devices (CIEDs) infection in the 2000–2011 period at the Cardiology Unit of New Santa Chiara Hospital in Pisa (Italy).

Methods and results Removed CIED leads and pocket material were seeded on solid media and isolates tested for antimicrobial susceptibility with the Kirby Bauer method. Electrodes from 1204 patients were analysed and 854 (70.9%) tested positive. In 663 (77.6%) cases only one species was isolated, in 175 (20.5%) two species, and in 14 (1.8%) >2 species. In 116 cases material from the pocket was also cultured. The result was consistent with that from the electrodes in 69 (59%) cases. In 359 cases a blood sample was also obtained for culture. The result was consistent with that from the leads in 124 (35%) cases. A total of 1068 strains were isolated from electrodes. Gram-positive organisms were most frequently isolated (92.5% of isolates); particularly, coagulase-negative staphylococci (CoNS), mainly *Staphylococcus epidermidis*, in 69% of cases and *Staphylococcus aureus* in 13.8%, Gram-negative rods in 6.1%, yeasts in 1% and molds in 0.4%. Overall, Oxacillin resistance was 30%, in particular 33% among CoNS and 13% among *S. aureus*. Oxacillin resistance and quinolones resistance have increased in the period 2006–2011 with respect to the 5 years before. Seventeen percent of *Enterobacteriaceae* strains had a phenotype compatible with extended spectrum beta-lactamase expression.

Conclusions Culture of the leads offers the possibility of an aetiological diagnosis in the majority of cases. When material from the pocket can be obtained, the microbiological result is often consistent with that from the electrodes, while species isolated from blood cultures are often different and more likely to be the result of contamination. Cardiac implantable electronic device infection is more often monomicrobial, CoNS are most frequently isolated and *S. epidermidis* is largely the main single agent. Very early infections were associated with *S. aureus* infection. The pattern of susceptibility to antimicrobials is in general that of community-acquired infections, although oxacillin resistance and quinolones resistance has increased in the last 5 years.

Keywords Microbiology • Cardiovascular implantable electronic devices

Introduction

The field of cardiac pacing has grown rapidly since the first insertion of a pacemaker (PM) in the late 1950s: the rate of new implantation ranges from 200 per million population in the UK to 420 per million population in the USA.[1] A worldwide cardiac pacing and implantable cardioverter defibrillator (ICD) survey was conducted in 2009 and compared with a similar survey conducted in 2005.[2] Virtually all countries showed increases in implant numbers over the 4 years between surveys. High-degree atrioventricular block and sick sinus syndrome remain the major indications for implantation of a cardiac PM. Since their introduction early in the 1980s, ICDs have become a life-saving therapeutic tool for patients with ventricular arrhythmia. Virtually all countries surveyed showed a

* Corresponding author. Tel: +39050996735; fax: +3905095471, Email: taglaferrienrico@alice.it

significant rise in the use of ICDs with the largest implanter being the USA with 434 new implants per million population.

Despite improvements in cardiac device design, application of timely infection control practices, and administration of antibiotic prophylaxis at the time of device placement, infections continue to be observed. The infection rate is highly variable, ranging from 0.5 to 12%.[3–5]

Cardiac implantable electronic device (CIED) infection may be local, limited to the pulse generator pocket and/or the subcutaneous portion of the leads, or systemic, involving the transvenous intravascular electrode component, with or without endocarditis,[6] which accounts for ~10% of PM infections.[7,8]

The pocket may become infected at the time of implantation, during subsequent surgical manipulation of the pocket, or if the generator or subcutaneous electrodes erode through the skin. Pocket infection may track along the intravascular portion of the electrode to involve the intracardiac portion of the PM or ICD. Alternatively, the pocket or intracardiac portion of the electrode may become infected as a result of haematogenous seeding during a bout of bacteraemia or fungaemia secondary to a distant infected focus.

Several factors have been reported to be associated with a greater risk of CIED infection: (i) immunosuppression (e.g. renal dysfunction and corticosteroid use); (ii) oral anticoagulation use; (iii) patient coexisting illnesses; (iv) periprocedural factors, including the failure to administer perioperative antimicrobial prophylaxis; (v) device revision/replacement; (vi) the amount of indwelling hardware; (vii) operator experience; and (viii) the microbiology of bloodstream infection in patients with indwelling CIEDs, particularly *Staphylococcus aureus* bacteraemia.[9]

In addition to antimicrobial therapy, complete removal of all hardware is mandatory for CIED infections, considering that a conservative approach is often unsuccessful and associated with a high mortality rate.[10–13] Transvenous extraction, allowing a high success rate with few complications, is considered the gold standard.[14–16]

The aim of the study was to describe the microbiological findings of the CIED infections observed during a 10-year period at the Cardiology Unit of Pisa (Italy), the national reference centre for transvenous removal of the infected CIED.[8,17]

Materials and methods

Population study

We evaluated all consecutive patients with infected PM or ICD who underwent transvenous removal at the Cardiology Unit of our centre between January 2000 and March 2011. Patient- and lead-related data were collected at baseline on each case and entered into a computerized database for retrospective analysis.

Time to infection was recorded and we divided CIED infections as very early among 1 month from the last procedure on CIED, early infections among 2 and 12 months from the last procedure, and late infection when it happened after 12 months from the last procedure.

Extraction procedure

As a general practice, cardiac leads were engaged in the following order: coronary sinus, right atrial, and right ventricular leads. The proximal of the lead end was clipped and a standard stylet introduced. Lead extraction was then attempted using gentle manual traction (MT). If MT was unsuccessful, a single-sheath mechanical dilatation (MD) technique with a superior approach was used (Cook Intravascular Inc., Leechburg, PA, USA). When the lead tip was detached from the coronary sinus by MT and/or MD but removal was impossible due to a related fibrous adherence, or when the lead was intravascular and free floating, we used a transfemoral vein approach with or without a transjugular approach, as previously described.[17]

Microbiology

The microbiology of the infection was documented culturing on solid media (Chocolate agar, McConkey agar, mannitol salt agar, and Sabouroud agar) the removed catheters leads and/or infected material from the pocket. The tip or other parts of the leads were rolled onto the solid media while the material drawn from the pocket was spread directly on the culture plate. Blood culture system used was BACTEC 9240 (Becton-Dickinson, Milano, Italy). For organism identification an automated system (API, Bio-Merieux, Mercy L'Etoile, France) was used. Antimicrobial susceptibility was tested according to the Kirby Bauer method.[18]

Resistance phenotype was categorized according to the breakpoints indicated by the Clinical and Laboratory Standard Institute (formerly National Committee for Clinical Laboratory Standards) and the British Society for Antimicrobial Chemotherapy until 2009 and later on according to those indicated by the European Committee on Antimicrobial Susceptibility Testing.

Statistical analysis

Parametric tests for continuous variables are reported as mean and standard deviation (SD). Multiple group comparison was performed using analysis of variance. Differences between groups were evaluated using an unpaired two-tailed *t*-test. Non-parametric tests for continuous variables are reported as median and range. Differences between groups were evaluated using the Mann–Whitney *U* test. Categorical factors are summarized as percentages, and differences between groups were determined using Pearson's χ^2 test. Statistical analyses were performed using SYSTAT 10.0 (Systat Software Inc., Chicago, IL, USA). Statistical significance was defined at $P < 0.05$.

Results

Epidemiology

Data from January 2000 to March 2011 were reviewed.

The device was removed from 1204 patients. Males were 939 (78%). Mean age was 64 ± 13 years (range 17–92 years). Among patients studied, 787 (65.4%) had local signs of infection, 417 (34.6%) systemic signs of infection. The time from implantation to extraction was on average 73 ± 69 months (range 4–420). Among the removed devices, PMs were 891 (74%) and ICDs were 313 (26%). In particular, single-chamber PMs were 325 (27%), dual-chamber PMs 554 (46%), three-chamber PMs 24 (2%), single-chamber ICD 96 (8%), dual-chamber ICD 120 (10%), and three-chamber ICD 84 (7%) (*Table 1*).

Microbiology

The analysis included all consecutive patients with CIED infection in the study period. They represented 79.5% of all patients who underwent extraction in the same period. The main reason for

Table 1 Patients characteristics and device features

Total number of patients with CIED infection	1204
Males/females	939 (78%)/625 (22%)
Mean age	64 ± 13 years (range 17–92)
Signs of infection	
Local	787 (65.4%)
Systemic	417 (34.6%)
Mean time from implantation to extraction	73 ± 69 months (range 4–420)
Device	
Pacemaker (PM)/implantable cardioverter defibrillators (ICDs)	891 (74%)/313 (26%)
Single-chamber PM	325 (27%)
Dual-chamber PM	554 (46%)
Three-chamber PM	24 (2%)
Single-chamber ICD	96 (8%)
Dual-chamber ICD	120 (10%)
Three-chamber ICD	84 (7%)

Table 2 Isolates from electrodes of cardiac implantable electronic devices (Pisa, 2000–2011)

	N	%
Total infected leads	1204	
Total isolates	1068	100.0
Gram positive	988	92.5
CoNS	737	69.0
Staphylococcus aureus	147	13.8
Corynebacterium spp.	53	5.0
Propionibacterium spp.	27	2.5
Gram negative	65	6.1
Enterobacteriaceae[3]	32	3.0
Pseudomonas spp.	16	1.5
Candida spp.	11	1.0
Candida albicans	4	0.4
Molds	4	0.4

Table 3 Coagulase-negative staphylococci isolated from electrodes of cardiac implantable electronic devices (Pisa, 2000–2011)

	N	%
CoNS	737	100
Staphylococcus epidermidis	494	67.0
Staphylococcus capitis	43	5.8
Staphylococcus schleiferi	39	5.3
Staphylococcus hominis	24	3.3
Staphylococcus lugdunensis	17	2.3
Staphylococcus haemolyticus	16	2.2
Staphylococcus cohnii	8	1.1
Staphylococcus xylosus	8	1.1
Staphylococcus sciuri	7	0.9
Staphylococcus warneri	5	0.7
Staphylococcus saprophyticus	4	0.5
Staphylococcus simulans	2	0.3
Other CoNS	70	9.5

extraction except for infection was malfunctioning. Out of the 1204 extracted CIEDs, 854 (70.9%) tested positive. In 663 (77.6%) cases, only one species was isolated, in 175 (20.5%) two species, and in 14 (1.8%) >2 species.

Cardiac leads

A total of 1068 strains were isolated from electrodes. Groups of microorganisms isolated are listed in *Table 2*. Gram positives were largely the most frequently isolated (92.5% of isolates); particularly, coagulase-negative staphylococci (CoNS) were isolated in 69% of cases and *S. aureus* in 13.8%. Gram-negative rods were isolated in 6.1% of cases (*Enterobacteriaceae* 3% and *Pseudomonas* spp. 1.5%), yeasts of *Candida* genus in 1%, and molds in 0.4%.

Among very early infections, we had more polymicrobial infection (30%) with respect to early and late infections (21 and 23%, respectively). In the very early period *S. aureus* infections accounted for 22% with respect to 15.3 and 14.8% in the other two periods (*P* 0.05); conversely CoNS increased from 58.7% of very early period to 68.8 and 70.6%, respectively (*P* 0.03). No differences among bacteraemic patients and those with local infections were found. There were no other significant differences for infections due to overall Gram-positive, overall Gram-negative, or fungal infections. Erosion represented 7.2% of all CIED infections and it was not associated with any other specific type of CIED infection.

Different species of CoNS isolated are listed in *Table 3*. *Staphylococcus epidermidis* was the most frequently isolated single agent (67% of CoNS isolates), followed by *Staphylococcus capitis* (5.8%) and *Staphylococcus schleiferi* (5.3%).

Corynebacterium spp. and *Propionibacterium* spp. accounted for 5 and 2.5% of all isolates, respectively.

Pocket samples

In 116 cases material from the pocket was also cultured. The result was consistent with that from the electrodes in 69 (59%) cases, including 16 cases in which culture was negative from both samples. In 17 cases, culture was positive from the pocket and negative from the electrode (*Table 4*).

Blood samples

In 359 cases a blood sample was also obtained for culture. The result was consistent with that from the electrodes in 124 (35%) cases, including 70 cases in which culture was negative from both samples. In case *S. aureus* was isolated from the blood, the same microorganism was isolated from the electrodes in 55% of cases (10/18).

Table 4 Patients with culture of pocket material compared with culture of the cardiac implantable electronic device leads

	Pocket material culture positive	Pocket material culture negative
CIED leads culture positive	62 (53%)	21 (18%)
CIED leads culture negative	17 (15%)	16 (14%)

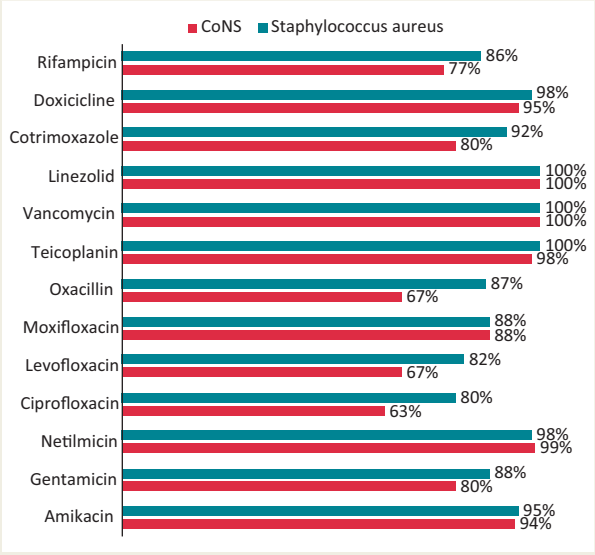

Figure 1 Antimicrobial susceptibility of staphylococci isolated from electrodes of CIEDs (Pisa, 2000–2011).

Antimicrobial susceptibility

Antimicrobial susceptibility of CoNS and *S. aureus* is reported in *Figure 1*. Netilmicin was the most active aminoglycoside against CoNS and *S. aureus* (99 and 98% of isolates susceptible) and moxifloxacin was the most active quinolone (88% in both cases); 33% of CoNS and 13% of *S. aureus* strains were resistant to oxacillin; overall, oxacillin-resistance rate among all staphylococci isolated was 30%. Between the 2000–2005 and 2006–2011 periods, resistance to oxacillin increased from 28 to 39% among CoNS (*P* 0.0016) and from 11 to 16% among *S. aureus* (*P* 0.548). Two percent of CoNS strains resulted non-susceptible to teicoplanin while all *S. aureus* strains resulted susceptible. All strains of CoNS and *S. aureus* were susceptible to vancomycin and linezolid. Cotrimoxazole was active against 80 and 92% of strains of CoNS and *S. aureus*, respectively, doxicycline against 95 and 98%, and rifampicin against 77 and 86%. For all these drugs there were no differences in susceptibility in the two periods considered (2000–2005 and 2006–2011). Instead, susceptibility to quinolones has changed in the two periods considering both CoNS and *S. aureus*. In fact, moxifloxacin susceptibility in *S. aureus* decreased from 100 to 64% ($P < 0.01$) and for CoNS from 98 to 74% ($P < 0.01$); and levofloxacin susceptibility decreased from 91 to 74% ($P < 0.01$) for *S. aureus* and from 78 to 59% for CoNS (*P* 0.01).

Corynebacterium spp. and *Propionibacterium* spp. isolates showed generally low levels of antimicrobial resistance, except in an isolate of *Corynebacterium* spp. resistant to glycopeptides but still susceptible to beta-lactams.

Seventeen percent of *Enterobacteriaceae* strains had a phenotype compatible with extended spectrum beta-lactamase (ESBL) expression; none was resistant to carbapenems. Thirteen strains of *Pseudomonas aeruginosa* were isolated and none was resistant to carbapenems. Two *Acinetobacter baumannii* strains were isolated and one was susceptible only to polymyxins.

Discussion

In our knowledge, this is the widest case series of CIED infection. Although our data might reflect the Italian epidemiology, we believe they could be of interest for the general debate about CIED infection and provide useful information for the lab and clinical staff involved in CIED infection management.

Epidemiology

Cardiac implantable electronic device infection more often occurs with local signs of infection and this is also consistent with the fact that a bloodstream infection was contemporarily demonstrated in a small minority of patients. The fact that most of the patients had only local signs of infection but the culture of the electrode resulted positive in the majority of them confirms the indication for hardware removal in all cases of suspected CIED infection.

Demographic characteristics of patients and type of device reflect those of the general population of CIED carriers. The fact that dual-chamber and three-chamber devices were more represented in our case series might also be due to the fact that the total amount of hardware is also recognized as a risk factor for CIED infection.[9] Infections generally occurred a long time after implantation and might therefore be assumed to be community-acquired infections.

Microbiology

Culture of the removed electrodes offers the possibility of an aetiological diagnosis of the CIED infection in the great majority of cases. This means that microbiological analysis is mandatory in the case of suspected CIED infection. Sterile manipulation after removal, fast submission to the microbiology laboratory, and seeding of the removed hardware are essential to optimize the management of CIED infection. The proportion of positive samples we found is consistent with what reported in other works.[19,20]

When material from the pocket is cultured, the microbiological result is often consistent with that from the electrodes. Therefore, the possibility of obtaining a sample from the pocket, by swab in the case of skin erosion or by aspiration in the case of deep abscess, should always be pursued. The fact that in 17 cases the culture of the electrode was negative while that from the pocket was positive, might suggest that contamination does not necessarily occur when the electrode is removed through an infected pocket, as some authors have speculated.

Species isolated from blood cultures are often different and therefore more likely to be the result of contamination. In other words, one single blood culture positive for CoNS is insufficient evidence for a therapeutic strategy. Instead, a blood culture positive for *S. aureus* has a greater diagnostic value, both in our study and in the existing literature. In fact, in a cohort of 33 patients with implanted devices and subsequent *S. aureus* bacteraemia, nearly one-half (45.4%) had confirmed CIED infection, and only a minority had local signs or symptoms that suggested generator–pocket infection.[21] Similarly, in a cohort study from Olmsted County, MN, USA, 55% of 22 patients with cardiac devices and subsequent *S. aureus* bacteraemia had definite or possible CIED infection.[22]

Cardiac implantable electronic device infection is monomicrobial in the great majority of cases, consistently with the existing literature and with the pathogenesis, mainly due to contamination at the moment of implantation or subsequent bacteraemia.

The dominant role of staphylococci is in line with what has been reported previously: staphylococcal species account for 60 to 80% of cases in most reported series.[10,20,23–28] Coagulase-negative staphylococci are most frequently isolated and *S. epidermidis* is largely the main single agent in our work as in the existing literature.

Isolation of CoNS usually represents a challenge for the clinician since it might be the result of contamination, given the generally low pathogenicity of CoNS, with the exception of *S. lugdunensis* which tends to cause infections with a more severe course, resembling that of *S. aureus*.[29]

The development and persistence of CoNS infections are often associated with foreign materials. The attachment is thought to be first due to non-specific physicochemical forces and then due to the specific interaction of bacterial surface adhesins with the uncoated device, directly and with host proteins that coat the device. Coagulase-negative staphylococci may adhere directly to plastic polymers of the device via fimbria-like surface protein structures or via a capsular polysaccharidic adhesin.[30] Bacteria may also adhere to host matrix proteins, such as fibrinogen, fibronectin, and collagen that coat the surface of an implanted device.[31] The layers of bacteria on the surface of an implanted device are encased in an extracellular slime made of a polysaccharide intercellular adhesin and constitute a biofilm.[32,33] Microbes in a biofilm are protected by this dense extracellular matrix and are more resistant to antibiotics and host defences.[32]

Corynebacterium spp. and *Propionibacterium* spp. are normally considered as contaminants. Nevertheless, our data suggest that they can play a significant role in CIED infection. Most likely, bacteria scarcely pathogenic in normal conditions can be responsible of invasive infections in presence of prosthetic devices and other permanent foreign bodies.

The fact that CoNS and other bacteria, usually part of the skin flora, were most frequently isolated and the generally low levels of antimicrobial resistance of the isolates in our study support the endogenous, non-healthcare-associated acquisition of the infection. Consistently, an association has been noted between the presence of preaxillary skin flora and the pathogens isolated from PM infection.[24] In particular, *S. schleiferi*, which is reported to be a member of the preaxillary skin flora,[24] accounted for 5.3% of all CoNS in our case series and it has already been described as a cause of PM infection.[34] On this basis, isolation of *S. schleiferi* from CIED infection should be evaluated cautiously rather than easily dismissed as contamination.

The pattern of susceptibility to antimicrobials, in this study, is in general that of community-acquired infections. In particular, oxacillin resistance in our case series was similar to that reported by other recent study studies, though a worrisome trend towards resistance over time was observed and was statistically significant for CoNS.[19,35] Resistance to oxacillin indicates resistance to all beta-lactams antibiotics, including cephalosporins and carbapenems. In our opinion the choice of a prophylactic drug different from a betalactam antibiotic should be probably reconsidered in the case of a resistance rate over 30% (that is our current epidemiology).

Implications for antimicrobial prevention and therapy

Given the financial and clinical burden of CIED infection, we believe that these levels of resistance already justify an initial aggressive approach in empirical treatment, for instance, with glycopeptides. For the same reason, we believe that an antimicrobial prophylaxis before implantation with an agent active against oxacillin-resistant staphylococci should be considered instead of the most commonly used cephazolin.

The fact that moxifloxacin showed an advantage compared with the other fluoroquinolones towards staphylococci is not surprising since it is in line with the existing literature.[36] In the last period we have observed a decreased activity of the two quinolone molecules with more activity against Gram-positive microorganism. This trend should be considered in the case of empiric antibiotic therapy for CIED infections. The good antistaphylococcal activity of cotrimoxazole, as well, is reported by others and this agent is included among the options for the treatment of bloodstream infections due to *S. aureus* and CoNS.[37]

The good activity of oral molecules such as doxyciclin, possibly in association with rifampicin, suggests the possibility of a shorter hospital length of stay and can be a resource for a long-term suppressive treatment in those cases where extraction is not feasible.

As far as resistance among Gram-negative organisms is concerned, at this moment ESBL production among *Enterobacteriaceae* is significant, but not yet epidemiologically relevant, given the minor role of Gram-negative bacteria in CIED infection. A phenotype consistent with carbapenemase production was revealed only for an *A. baumannii* strain.

The predominance of staphylococci as pathogens in CIED infections rather than oral, intestinal, or genitourinary flora confirms that there is no need for prophylactic antibiotics before routine invasive dental, gastrointestinal, or genitourinary procedures in patients with CIED.

We strongly believe that a close relationship between clinicians and clinical microbiologists, in the case of CIED infections as in other cases, is necessary to ensure a high-quality standard of care.

Conflict of interest: none declared.

References

1. Eggiman P, Waldvogel F. Pacemaker and defibrillator infection. In Waldvogel F, Bisno A (eds). *Infections Associated with Indwelling Medical Devices*. Washington: ASM Press, 2000:247–64.
2. Mond HG, Proclemer A. The 11th World Survey of Cardiac Pacing and Implantable Cardioverter-Defibrillators: Calendar Year 2009—A World Society of Arrhythmia's Project. *Pacing Clin Electrophysiol* 2011;**34**:1013–27.
3. Bluhm G. Pacemaker infections. 2-year follow-up of antibiotic prophylaxis. *Scand J Thorac Cardiovasc Surg* 1985;**16**:65–70.
4. Lay KK, Fontecchio SA. Infections associated with implantable cardioverter defibrillators placed transvenously and via thoracotomies: epidemiology, infection control, and management. *Clin Infect Dis* 1998;**27**:265–9.
5. Kearney RA, Eisen HJ, Wolf JE. Nonvalvular infections of the cardiovascular system. *Ann Intern Med* 1994;**121**:219–30.
6. Karchmer AW. Infections of prosthetic valves and intravascular devices. In Mandell GL, Bennett JE, Dolin R (eds). *Principles and Practice of Infectious Diseases*. Philadelphia: Churchill Livingstone, 2000. p911–3.
7. Arber N, Pras E, Copperman Y, Schapiro JM, Meiner V, Lossos IS *et al.* Pacemaker endocarditis: report of 44 cases and review of the literature. *Medicine (Baltimore)* 1994;**73**:299–305.
8. Tascini C, Bongiorni MG, Gemignani G, Soldati E, Leonildi A, Arena G *et al.* Management of cardiac device infections: a retrospective survey of a non-surgical approach combining antibiotic therapy with transvenous removal. *J Chemot* 2006;**18**:157–63.
9. Baddour LM, Epstein AE, Erickson CC, Knight BP, Levison ME, Lockhart PB *et al.* Update on cardiovascular implantable electronic device infections and their management: a scientific statement from the American Heart Association. *Circulation* 2010;**121**:458–77.
10. Camus C, Leport C, Raffi F, Michelet C, Carteier F, Vilde JL. Sustained bacteraemia in 26 patients with a permanent endocardial pacemaker: assessment of wire removal. *Clin Infect Dis* 1993;**17**:46–55.
11. Choo MH, Holmes DR Jr, Gersh JB, Maloney JD, Merideth J, Pluth JR *et al.* Permanent pacemaker infections: characterization and management. *Am J Cardiol* 1981;**48**:559–64.
12. Rettig G, Doenecke P, Sen S, Volomer I, Bette L. Complications with retained transvenous pacemaker electrodes. *Am Heart J* 1979;**98**:587–94.
13. Vogt PR, Sagdic K, Lachat M, Candinas R, von Segesser LK, Turina MI. Surgical management of infected permanent transvenous pacemaker system: ten years experience. *J Card Surg* 1996;**11**:180–6.
14. Byrd CL, Schwartz SJ, Hedin NB, Goode LB, Fearnot NE, Smith HJ. Intravascular lead extraction using locking stylets and sheaths. *Pacing Clin Electrophysiol* 1990;**13**:1871–5.
15. Manolis AS, Maounis TN, Chiladakis J, Vassilikov V, Melita-Manolis H, Cokkinos DV. Successful percutaneous extraction of pacemakers leads with a novel (vascoextor) pacing lead removal system. *Am J Cardiol* 1998;**81**:935–8.
16. Wilhelm MJ, Schmid C, Hammel D, Kerber S, Loick HM, Hermann M *et al.* Cardiac pacemaker infection; surgical management with or without extracorporeal circulation. *Ann Thorac Surg* 1997;**64**:1707–12.
17. Bongiorni MG, Soldati E, Zucchelli G, Di Cori A, Segreti L, De Lucia R *et al.* Transvenous removal of pacing and implantable cardiac defibrillating leads using single sheath mechanical dilatation and multiple venous approaches: high success rate and safety in more than 2000 leads. *Eur Heart J* 2008;**29**:2886–93. Epub 23 October 2008.
18. Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing; 18th Informational Supplement*. Wayne, PA: Clinical Laboratory Standards Institute; 2008.
19. Anselmino M, Vinci M, Comoglio C, Rinaldi M, Bongiorni MG, Trevi GP *et al.* Bacteriology of infected extracted pacemaker and ICD leads. *J Cardiovasc Med (Hagerstown)* 2009;**10**:693–8.
20. Sohail MR, Uslan DZ, Khan AH, Friedman PA, Hayes DL, Wilson WR *et al.* Management and outcome of permanent and implantable cardioverter-defibrillator infections. *J Am Coll Cardiol* 2007;**49**:1851–9.
21. Chamis AL, Peterson GE, Cabell CH, Corey GR, Sorrentino RA, Greenfield RA *et al. Staphylococcus aureus* bacteremia in patients with permanent pacemakers or implantable cardioverter-defibrillators. *Circulation* 2001;**104**:1029–33.
22. Uslan DZ, Sohail MR, St Sauver JL, Friedman PA, Hayes DL, Stoner SM *et al.* Permanent pacemaker and implantable cardioverter-defibrillator infection: a population-based study. *Arch Intern Med* 2007;**167**:669–75.
23. Klug D, Lacroix D, Savoye C, Goullard L, Grandmougin D, Hennequin JL *et al.* Systemic infection related to endocarditis on pacemaker leads: clinical presentation and management. *Circulation* 1997;**95**:2098–107.
24. Da Costa A, Lelièvre H, Kirkorian G, Célard M, Chevalier P, Vandenesch F *et al.* Role of the preaxillary flora in pacemaker infections: a prospective study. *Circulation* 1998;**97**:1791–5.
25. Fu EY, Shepard RK. Permanent pacemaker infections. *Card Electrophysiol Rev* 1999;**3**:39–41.
26. Chua JD, Wilkoff BL, Lee I, Juratli N, Longworth DL, Gordon SM. Diagnosis and management of infections involving implantable electrophysiologic cardiac devices. *Ann Intern Med* 2000;**133**:604–8.
27. Villamil Cajoto I, Rodríguez Framil M, Van den Eynde Collado A, José Villacián Vicedo M, Canedo Romero C. Permanent transvenous pacemaker infections: an analysis of 59 cases. *Eur J Intern Med* 2007;**18**:484–8.
28. Del Rio A, Anguera I, Miró JM, Mont L, Fowler VG Jr, Azqueta M *et al.* Hospital Clinic Endocarditis Study Group. Surgical treatment of pacemaker and defibrillator lead endocarditis: the impact of electrode lead extraction on outcome. *Chest* 2003;**124**:1451–9.
29. Seenivasan MH, Yu VL. *Staphylococcus lugdunensis* endocarditis—the hidden peril of coagulase-negative staphylococcus in blood cultures. *Eur J Clin Microbiol Infect Dis* 2003;**22**:489–91.
30. Veenstra GJ, Cremers FF, van Dijk H, Fleer A. Ultrastructural organization and regulation of a biomaterial adhesion of *Staphylococcus epidermidis*. *J Bacteriol* 1996;**178**:537–41.
31. Wilkinson BJ. Biology. In: Crossley KB, Archer GL (eds). *The Staphylococci in Human Disease*. New York, NY: Churchill Livingston; 1997.
32. Vuong C, Otto M. *Staphylococcus epidermidis* infections. *Microbes Infect* 2002;**4**:481–9.
33. Heilmann C, Schweitzer O, Gerke C, Vanittanakom N, Mack D, Götz F. Molecular basis of intercellular adhesion in the biofilm-forming *Staphylococcus epidermidis*. *Mol Microbiol* 1996;**20**:1083–91.
34. Celard M, Vandenesch F, Darbas H, Grando J, Jean-Pierre H, Kirkorian G *et al.* Pacemaker infections caused by *Staphylococcus schleiferi*, a member of the human pre-axillary flora. *Clin Inf Dis* 1997;**24**:1014–5.
35. Jan E, Camou F, Texier-Maugein J, Whinnett Z, Caubet O, Ploux S *et al.* Microbiological characteristics and in vitro susceptibility to antimicrobials in a large population of patients with cardiovascular implantable electronic device infection. *J Cardiovasc Electrophysiol* 2011 (Epub ahead of print).
36. Park SH, Lim JA, Choi JS, Kim KA, Joo CK. The resistance patterns of normal ocular bacterial flora to 4 fluoroquinolone antibiotics. *Cornea* 2009;**28**:68–72.
37. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP *et al.* Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America. IDSA Guidelines. *Clin Infect Dis* 2009;**49**:1–45.