

Bacterial Colonization and Infection of Electrophysiological Cardiac Devices Detected With Sonication and Swab Culture

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Background—Electrophysiological cardiac devices are increasingly used. The frequency of subclinical infection is unknown. We investigated all explanted devices using sonication, a method for detection of microbial biofilms on foreign bodies.

Methods and Results—Consecutive patients in whom cardiac pacemakers and implantable cardioverter/defibrillators were removed at our institution between October 2007 and December 2008 were prospectively included. Devices (generator and/or leads) were aseptically removed and sonicated, and the resulting sonication fluid was cultured. In parallel, conventional swabs of the generator pouch were performed. A total of 121 removed devices (68 pacemakers, 53 implantable cardioverter/defibrillators) were included. The reasons for removal were insufficient battery charge (n=102), device upgrading (n=9), device dysfunction (n=4), or infection (n=6). In 115 episodes (95%) without clinical evidence of infection, 44 (38%) grew bacteria in sonication fluid, including *Propionibacterium acnes* (n=27), coagulase-negative staphylococci (n=11), Gram-positive anaerobe cocci (n=3), Gram-positive anaerobe rods (n=1), Gram-negative rods (n=1), and mixed bacteria (n=1). In 21 of 44 sonication-positive episodes, bacterial counts were significant (≥ 10 colony-forming units/mL of sonication fluid). In 26 sterilized controls, sonication cultures remained negative in 25 cases (96%). In 112 cases without clinical infection, conventional swab cultures were performed: 30 cultures (27%) were positive, and 18 (60%) were concordant with sonication fluid cultures. Six devices and leads were removed because of infection, growing *Staphylococcus aureus*, *Streptococcus mitis*, and coagulase-negative staphylococci in 6 sonication fluid cultures and 4 conventional swab cultures.

Conclusions—Bacteria can colonize cardiac electrophysiological devices without clinical signs of infection. (*Circulation*. 2010;121:1691-1697.)

Key Words: sonication ■ pacemaker, artificial ■ cardioverter-defibrillators, implantable ■ bacteria ■ infection

Implantable electrophysiological cardiac devices are increasingly used for prevention and therapy of cardiac arrhythmias and heart failure. In 2000, an estimated number of 3.4 million patients were living with a permanent electrophysiological device worldwide.¹ These devices reduce morbidity and mortality and have proved to be cost-effective.²⁻⁹ Cardiac pacemakers (PMs) are commonly used in patients with atrioventricular conduction block, sick sinus syndrome, and sinus bradycardia, whereas implantable cardioverter/defibrillators (ICDs) target primarily patients with heart failure after myocardial infarction and those having experienced a life-threatening ventricular arrhythmia. Furthermore, cardiac resynchronization therapy ameliorates cardiac function and reduces mortality in patients with heart failure,¹⁰⁻¹³ and triple-site biventricular pacing reduces the New York

Heart Association class, improves exercise capacity, and increases ejection fraction in heart failure not responding to conventional cardiac resynchronization therapy.¹⁴⁻¹⁷

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Infection of electrophysiological cardiac devices is a rare but serious and potentially life-threatening complication, ranging between 0.7% and 1.6%.^{3,18,19} The infection may involve the generator pocket, the leads (with or without the endocardium), or both components. A population-based study among permanent PM recipients described an annual incidence of 550 cases of infective endocarditis per million recipients.²⁰ The most common isolated pathogens are coagulase-negative staphylococci (CNS) and *Staphylococcus*

Received September 6, 2009; accepted February 9, 2010.

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Circulation is available at <http://circ.ahajournals.org>

DOI: 10.1161/CIRCULATIONAHA.109.906461

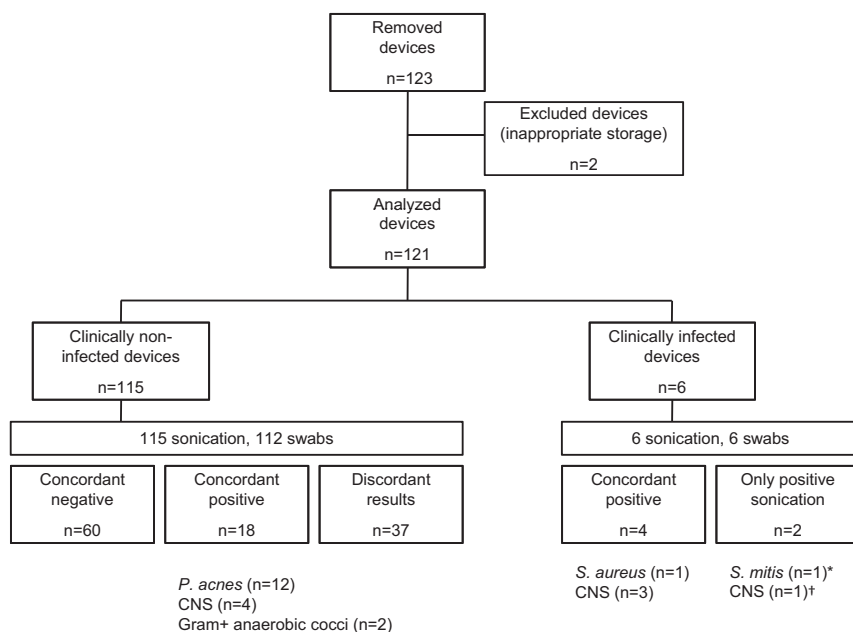


Figure 1. Analysis of devices. *Microbiology only after 2 weeks of systemic antibiotic treatment. †Disinfectant in pouch before microbiology, sonication fluid of lead only positive.

aureus.^{1,20,21} However, the incidence of subclinical infection and the type of colonizing microorganisms are unknown. This information is crucial to understand the pathogenesis of electrophysiological device infection, implement preventive measures, and improve the outcome of infection by early detection at the time of battery or lead replacement and early antimicrobial treatment.

Therefore, we consecutively analyzed explanted devices by using conventional cultures from swabs and sonication of the device, a method for removal of microbial biofilms that has recently been validated for orthopedic devices.²²

Methods

Study Population

We performed a prospective, observational, single-center cohort study in a tertiary care hospital in Luzern, Switzerland. At the beginning of the study, in October 2007, the hospital cared for 1740 patients with implanted cardiac PMs and ICDs. All adult patients in whom the cardiac electrophysiological device was removed for any reason between October 2007 and December 2008 were considered eligible for this study. During this time period, 123 devices in 121 patients were explanted. Two patients, in whom the device was inappropriately stored, were excluded from the study, resulting in a total of 119 participating patients (Figure 1). The following baseline characteristics were assessed: age, sex, diabetes mellitus, heart failure, hypertension, renal failure, chronic liver disease, immunosuppressive therapy, history of infective endocarditis or generator pocket infection, device type (PM/ICD), device position, indwelling time, antibiotic prophylaxis before and operation time during implantation, number of previous device changes, and hematoma after implantation. Patient records were summarized with a standardized case report form to retrieve demographic, clinical, microbiological, and laboratory data. The study protocol was approved by the local ethical committee. All patients signed an informed consent.

Underlying medical conditions were defined as follows: chronic heart failure (New York Heart Association stage II to IV), chronic renal failure (creatinine level $>104 \mu\text{mol/L}$ [$>1.18 \text{ mg/dL}$]), chronic liver disease (Child classification stage B and C), diabetes mellitus (type I and II), and immunosuppressive therapy (long-term use of corticosteroids $>25 \text{ mg prednisone-equivalent/d}$ for the past month at least or methotrexate).

Infection was diagnosed as either local infection of the generator pocket (acute inflammation with redness, local warmth, pain, swelling, or purulent drainage intraoperatively or through skin erosion, but without systemic inflammatory symptoms) or PM/ICD-associated infective endocarditis, defined by the Duke criteria²³: A definitive diagnosis of endocarditis was made if 2 major criteria, 1 major and 3 minor criteria, or 5 minor criteria were fulfilled. Major criteria include (1) persistently positive blood cultures or (2) transthoracic or transesophageal echocardiographic evidence of endocardial involvement (oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets or on implanted material, dehiscence of prosthetic valve, or new valvular regurgitation). Minor criteria include (1) predisposing heart condition or intravenous drug use, (2) fever (core temperature $>38^\circ\text{C}$), (3) vascular phenomena (major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway lesions), (4) immunologic phenomena (glomerulonephritis, Osler nodes, Roth spots, and rheumatoid factor), (5) positive blood culture but not meeting the major criterion, or (6) echocardiographic findings consistent with infective endocarditis but not meeting the major criterion.

Removal of Devices

Removal of devices was performed in the electrophysiology laboratory or in the operation theater. Routine antibiotic prophylaxis was given immediately before start of operation. Skin was prepared by shaving followed by application of 50% isopropyl alcohol, 1% povidone-iodine solution (Braunoderin) 3 times and by draping with sterile cloths. Before closing, the wound was disinfected again with 7.5% povidone-iodine solution (Braunol). Generators (and leads, if removed) were aseptically removed and placed in solid air-tight containers. NaCl 0.9% was added until coverage of the device in order to prevent drying out.

In case of noninfected devices, the new generator was placed into the same pocket. In case of clinical signs of infection, the new device was placed on the other side of the chest after completion of antibiotic treatment. Patients with no signs of infection did not receive antibiotic treatment, even if bacteria were found.

Sonication of Removed Devices

Containers were transported to the microbiology laboratory within 24 hours of removal. The container was vortexed for 30 seconds, sonicated for 1 minute at a frequency $40 \pm 2 \text{ kHz}$ and power density $0.22 \pm 0.04 \text{ watts/cm}^2$, as determined by a calibrated hydrophone

(Type 8103, Brüel and Kjær, Naerum, Denmark), and vortexed again for 30 seconds. For sonication, an ultrasonic bath BactoSonic (Bandelin GmbH, Berlin, Germany) was used. A total of 0.1 mL of the resulting sonication fluid was each inoculated onto aerobic and anaerobic sheep blood agar plates and incubated at 37°C for 7 days and inspected daily for bacterial growth. Microorganisms were quantitated (ie, number of colony-forming units [CFU]/mL sonication fluid) and identified using routine microbiological techniques. Additional 1 mL was inoculated in 9 mL thioglycolate broth. Growth in broth only was defined as growth after enrichment. For negative controls for sonication, sterilized cardiac devices (dummies) were investigated with every 5th explanted device. Control devices were handled with sterile gloved hands and placed on the table in the regular operating room on ambient air for the duration of the explantation of devices from patients. The dummies were subsequently placed in sterile containers and processed identically to explanted devices from patients.

Conventional Microbiological Methods

Intraoperative swabs from the generator pocket were collected after removal of the device. Cotton-tipped swabs were placed in Amies agar, then inoculated to sheep blood agar, chocolate agar, and MacConkey agar and incubated aerobically for 48 hours. An additional sheep blood agar plate was incubated anaerobically for 5 days. Thioglycolate was used for enrichment. Organisms were identified by standard microbiological methods.

Outcomes

Microbiological outcome was defined as growth of bacteria in sonication or swab culture (sonication positive, swab positive). Concordance of the 2 microbiological methods was defined as detection of the same or no microorganism in swab and sonication of a device by standard microbiological methods irrespective of the amount of bacteria. If quantity of microorganism was considered, it is stated in the text.

After device change, patients were routinely seen every 6 to 12 months to control device function and to check for signs of infection. Follow-up lasted until November 15, 2009. Clinical outcomes (death, device infection, removal/change of device for any reason) were assessed at the end of follow-up. If a patient could not be seen, the patient or the doctor providing follow-up care was contacted by phone.

Statistical Analysis

All analyses were performed using STATA software version 9.2 for Windows. For graphic analysis, Origin software (version 8; Origin Laboratory Corp, Northampton, Mass) was used. According to the descriptive nature of the statistical analysis, no significance testing was used. To analyze the occurrence of clinical infection during follow-up in patients with sonication and/or swab positive cultures but no clinical infection at baseline, the incidence (percent) of infection was estimated and exact 95% binomial confidence limits were calculated.

Results

Study Population and Devices

In October 2007, 1740 patients with electrophysiological devices were followed up regularly. Until December 2008, 123 devices had to be removed in 121 patients because of insufficient battery charge (n=104), device upgrading (n=9), device dysfunction (n=4), or infection (n=6). During 14 months, 6 of 1740 patients developed an infection. This corresponds to an approximate incidence of clinical infection of 0.3%/yr. Two patients with insufficient battery charge of the device were excluded because of inadequate storage of the device. Baseline characteristics of the included 119 patients are summarized in Table 1. Characteristics of the 121

Table 1. Demographic and Clinical Characteristics of 119 Patients

Characteristic	Value
Patient age at device removal, y, median (limits)	69 (36–95)
Males, n (%)	90 (76)
Underlying medical condition, n (%)	
Chronic heart failure	44 (37)
Diabetes mellitus	18 (15)
Chronic renal failure	15 (13)
History of infective endocarditis	2 (2)
History of PM/ICD-associated infective endocarditis	1 (1)
History of generator pocket infection	1 (1)
Chronic liver disease	1 (1)
Immunosuppressive therapy	3 (2)
No. of previous device exchanges, n (%)	
0	94 (78)
1	19 (16)
2	4 (3)
≥3	4 (3)
Hematoma after implantation,* n (%)	8 (7)
Perioperative antibiotic prophylaxis during implantation, n (%)	
Cefuroxime	67 (55)
Cefazolin	29 (24)
Other antibiotics	8 (7)
No prophylaxis	1 (1)
No data available	16 (13)

ICD indicates implantable cardioverter/defibrillator; PM, pacemaker.

*In 2 of 8 patients who developed hematoma after implantation, a surgical revision was performed.

devices, of which 68 (56%) were cardiac PMs and 53 (44%) were ICDs, are shown in Table 2.

Episodes With Infection

Of the 6 cases with infection, generator pocket infection was diagnosed in 4 cases and PM/ICD-associated infective endocarditis in 2 cases (Table 3). All infected devices (3 PMs and 3 ICDs) were completely removed, including the corresponding leads. Antibiotic therapy was started after explantation of the device in the 4 cases of generator pocket infection and 2 weeks before explantation in the 2 cases of PM/ICD-associated infective endocarditis. In both patients with PM/ICD-associated infective endocarditis, transthoracic echocardiography showed vegetations on the lead and blood cultures were positive.

Before removal of the device, serum markers for inflammation were determined. For 4 cases with generator pocket infection, median C-reactive protein was 8.5 mg/L (95% confidence limits, <5 to 50 mg/L) and median procalcitonin was 0.07 µg/L (95% confidence limits, 0.04 to 0.11 µg/L). In cases with infective PM/ICD-associated endocarditis (n=2), C-reactive protein was 131 and 173 mg/L, respectively, and procalcitonin was 1.25 and 31 µg/L, respectively.

The 4 cases of generator pocket infection were caused by CNS in 3 patients and *S. aureus* in 1 patient. The PM-

Table 2. Characteristics of 121 Electrophysiological Cardiac Devices

Characteristic	Value
Type of removed device,* n (%)	
PM	68 (56)
ICD	53 (44)
Anatomic position of the device, n (%)	
Subcutaneous	112 (92)
Submuscular†	9 (8)
Reason for device removal, n (%)	
Insufficient generator charge	102 (84)
Upgrading of the device	9 (7)
Device dysfunction	4 (3)
Generator pocket infection	4 (3)
PM/ICD-associated infective endocarditis	2 (2)
Indwelling time of the device, y, median (limits)	
Without clinical infection (n=115)	6.4 (2.4–10.2)
With clinical infection (n=6)	0.7 (0.1–7.0)

ICD indicates implantable cardioverter/defibrillator; PM, pacemaker.

*In 11 patients (9%), PM/ICD leads were removed in addition to the generator, which were removed because of dysfunction (n=5), generator pocket infection (n=4), and PM/ICD-associated infective endocarditis (n=2).

†Including pectoral muscle (n=8) and abdominal site (n=1).

associated infective endocarditis was caused by *Streptococcus mitis* (growth in 6 of 6 blood culture bottles) in 1 patient and *S. aureus* (growth in 4 of 8 bottles) in the other.

Episodes Without Infection

In 115 episodes, no clinical infection was documented. All patients received a perioperative antibiotic prophylaxis with

cefazolin before exchange of the sonicated device. All explanted devices were sonicated, and 112 conventional swab cultures were performed. For episodes without clinical infection, median C-reactive protein at the time of explantation was 9 mg/L (95% confidence limits, <5 to 130 mg/L), and median procalcitonin was 0.08 $\mu\text{g/L}$ (95% confidence limits, <0.06 to 0.35 $\mu\text{g/L}$). Values were lacking in 23 and 22 episodes, respectively.

Of 115 episodes without clinical infection, sonication fluid grew bacteria in 44 explanted devices (38%), namely in 16 of 65 PMs (25%) and 28 of 50 ICDs (56%). In 21 devices (11 ICDs, 10 PMs), bacterial counts were ≥ 10 CFU/mL of sonication fluid. Quantitative sonication cultures are shown in Figure 2. Conventional pocket swab cultures grew bacteria in 30 (16 ICDs, 14 PMs) of 112 devices (27%). Bacterial quantity was reported as moderate in 2 cultures (ICDs), few in 20 cultures (12 ICDs, 8 PMs), and after enrichment in 7 cultures (2 ICDs, 5 PMs). In 1 result (PM), quantity was not available. The microorganisms most commonly isolated with either method were *Propionibacterium acnes* and CNS. Table 4 and Figure 1 show microorganisms and the concordance of sonication and conventional swabs. Overall, concordance of the 2 methods was found in 78 cases (68%). If cultures grown in enrichment medium only were excluded, concordance rose to 83%. In the 6 patients with more than 150 CFU/mL in sonication fluid (4 *Propionibacterium acnes*, 2 CNS), concordance with conventional swabs was 100%. In the follow-up phase, 2 patients with detection of CNS (both in sonication and swab culture) developed a clinical infection with CNS 3 weeks and 4 months later.

Two of the 56 devices with bacteria detected at the time of removal by sonication or swab developed an infection,

Table 3. Characteristics of 6 Cases With Clinical Infection

Case No.	Patient Age (y)	Site of Infection	Device	Position	Indwelling Time	CRP (mg/mL) Before Start of Treatment	Blood Cultures (Bottles)	Sonicate Fluid From Device (CFU/mL)	Sonicate Fluid From Lead (CFU/mL)	Conventional Swab From Pocket (Quantity)	Comment
1	66	Pocket	PM	Subcutaneous	8 months	50	Sterile	<i>S. aureus</i> (>1000)	Sterile	<i>S. aureus</i> (plenty)	
2	60	Pocket	ICD	Submuscular	4 months	10	Sterile	CNS (200)	CNS (>1000)	CNS (few)	Detection of CNS in sonicate fluid (690 CFU/mL) and swab culture (few) at the time of previous device change Hematoma cleared out after implantation
3	68	Pocket	ICD	Subcutaneous	3 weeks	7	Sterile	Sterile	CNS (after enrichment)	Sterile	Detection of CNS in sonicate fluid (after enrichment) and swab culture (few) at the time of previous device change Disinfectant was poured into the pouch before removal of the device and performance of the swab
4	36	Pocket	ICD	Subcutaneous	8 months	<5	Sterile	CNS (after enrichment)	CNS (after enrichment)	CNS (few)	Forgotten swab tissue during implantation
5	77	Endocarditis	PM	Subcutaneous	7 years	173	<i>S. viridans</i> (8/8)	Sterile	<i>S. viridans</i> (after enrichment)	Sterile	Explantation of device and lead after 2 weeks of systemic antibiotic therapy
6	70	Endocarditis	PM	Subcutaneous	8 months	131	<i>S. aureus</i> (4/8)	CNS (after enrichment)	Sterile	CNS (few)	Explantation of device and lead after 2 weeks of systemic antibiotic therapy

CFU indicates colony-forming units; CNS, coagulase-negative staphylococci; CRP, C-reactive protein; ICD, implantable cardioverter/defibrillator; and PM, pacemaker.

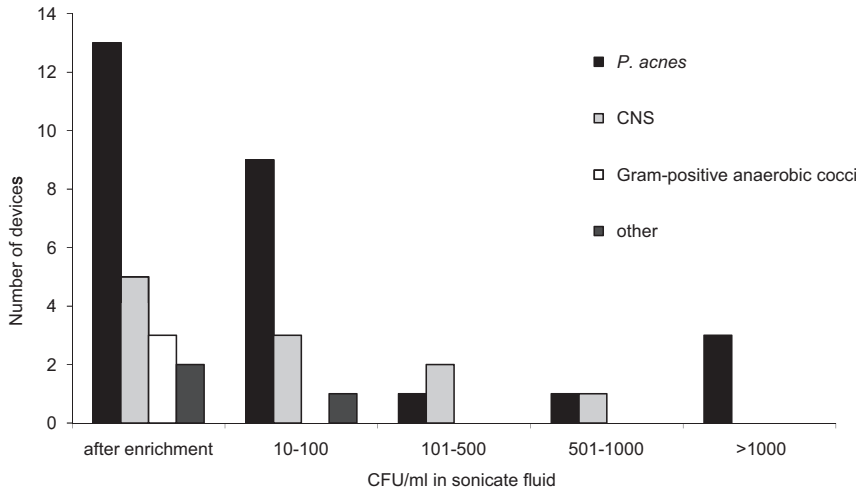


Figure 2. Quantitative sonicate cultures in episodes without clinical infection (n=44). CNS indicates coagulase-negative staphylococci; CFU, colony-forming units. Other: Gram-negative rods, Gram-positive anaerobic rods, mixed bacteria. After enrichment is defined as growth in thioglycolate broth only (ie, no growth on agar plates).

corresponding to an incidence of 3.6% (95% confidence interval [CI], 0.4% to 12.3%). Considering only the 44 devices growing microorganisms in sonication, the incidence was 4.5% (95% CI, 0.6% to 15.5%), and for sonication-positive devices with quantities >10 CFU/mL, the incidence was 9.5% (95% CI, 1.2% to 30.4%).

Table 4. Isolated Microorganisms and Concordance of Sonication and Pocket Swab Cultures From Removed Devices Without Clinical Infection (n=115)

Microorganisms	Sonication Fluid Only	Conventional Swab Only	Sonication and Conventional Swab
Episodes without clinical infection			
<i>Propionibacterium acnes</i>	15	7	12
Coagulase-negative staphylococci	7	2	4
Gram-positive anaerobic cocci*	1	2	2
Gram-positive anaerobic rods	1	0	0
Gram-negative rods	1	1	0
Mixed bacteria	1	0	0
Negative samples	11	22	60
Not done	0	3	0
Total	37	37	78
Episodes with clinical infection			
Coagulase-negative staphylococci	1†	0	3
<i>Staphylococcus aureus</i>	0	0	1
<i>Streptococcus mitis</i>	1‡	0	0
Total	2	0	4

Values represent numbers of devices.

*Include *Peptostreptococcus* spp., *Finexgoldia* spp., and *Micrococcus* spp.

†Antiseptic solution in pouch before microbiology, sonication fluid of lead only positive.

‡Microbiology after 2 weeks of systemic antibiotic treatment.

Negative Controls

As negative controls, 26 sterile devices (dummies) were sonicated, among which 25 (96%) were negative in sonication cultures; 1 grew 30 CFU/mL CNS.

Clinical Outcome

Follow-up lasted 17.9 months (median; range, 10.8 to 24.8 months). Ninety-eight of 115 patients without infection at baseline had no complication, 13 died, 2 developed an infection of the device pocket and devices were removed, and 2 were lost to follow-up. All 6 patients with infection stayed alive and had no further complications. Four of these patients received another device on the other side of the chest after completion of antibiotic treatment; 2 patients did not receive a new device.

Discussion

In cardiac devices explanted without clinical signs of infection, bacteria were detected in 38% of sonication fluid and in 27% of conventional generator pocket swab cultures, with a concordance of 68%. Accounting for higher quantities of bacteria (>150 CFU/mL) led to 100% concordance (6 devices). Sonication was more sensitive in detecting bacteria than conventional swabs.

Data on microbiological analysis of electrophysiological devices are scarce. A study by Dy Chua et al²⁴ compared pocket tissue with swab culture in 36 patients without and 35 patients with clinical infection of PMs/ICDs. They found concordant positive results in only 8% of noninfected devices, whereas in infected devices, concordance was 31%; they conclude that culture in noninfected devices is nonspecific. In fact, whether the detection of bacteria on devices corresponds to true colonization/subclinical infection or contamination is difficult to determine, as is the risk for future infection. We nevertheless believe that the high proportion of bacteria found is relevant because of the following reasons:

Sonication of explanted prosthetic material has shown to be more sensitive than conventional microbiological culture in the diagnosis of foreign body infection, especially in orthopedic prosthesis and breast implants.^{22,25,26} In our study, using sonication, bacteria grew in 38% of noninfected de-

vices, whereas in conventional culture, bacteria grew in 27%. In the 6 infected devices, sonication was positive in all 6 cases; swab culture was positive in 4 cases. The higher proportion of positive sonication results in infected devices is well explained by the fact that these patients were treated with antibiotics before removal, hampering conventional culture.

Improved sensitivity of sonication compared with conventional culture in such situations is helpful in establishing the microbiological diagnosis.

In the noninfected devices, interpretation is more difficult, because no clinical correlate exists. Quantification of bacteria could help in distinguishing between colonization and contamination. In hip and knee prostheses, a cutoff of 10 CFU/mL bacteria in sonication fluid predicted infection.²² In our study, when including all results irrespective of quantity, discordance between swab and sonication was found in 32%. If cases with very small quantities of growth (after enrichment only) were excluded, discordant results were found in 17% only. Using a high cutoff of >150 CFU/mL for sonication and minimum few growth in swab culture, concordance was 100%. Thus a correlation between sonication cutoff and growth in swab culture may be postulated.

To rule out contamination of devices, we used 26 dummies undergoing a similar procedure as real devices. Only in 1 dummy was bacterial growth detected by sonication (30 CFU/mL CNS). Because all controls but 1 (dummies) were negative, contamination is not likely to have occurred during transport of the device or during sonication procedure, but if so, rather during explantation. However, a concordance up to 100% when using a high cutoff for sonication speaks for the existence of real bacterial colonization in noninfected devices.

P. acnes and CNS were by far the most frequently cultivated bacteria in sonication fluid and in conventional swabs. Both bacteria species are part of the normal skin flora and known to survive in biofilms on foreign bodies, eventually causing low-grade infections associated with different prosthetic materials, including cardiac devices.^{27–33} This fact underlines the plausibility of the relevance of these findings and exerts practical implications relative to prophylaxis during implantation of cardiac devices.

During follow-up, 2 of 115 devices explanted for battery change or dysfunction became clinically infected with CNS, which were documented also at the time of device exchange. Even if molecular studies were not performed to prove clonality, infection with the same microorganism as detected before is probable, underlining the significance of the presence of bacteria. Considering sonication-positive devices with significant numbers of bacteria (>10 CFU/mL), the incidence of infection was estimated at 9.5% (95% CI, 1.2% to 30.4%), which is clinically relevant. As follow-up was relatively short (mean, 17.9 months), the number of patients developing infection might even be higher during longer observation periods.

To our knowledge, bacterial colonization of cardiac devices is not known yet. Although the ratio of later infection in our cohort was low, we consider the issue relevant regarding the increasing number of patients with implanted devices.^{34,35} Possibly, the proportion of clinical infection is lower due to

the fact that cardiac devices are under little mechanical stress compared with prosthetic devices such as prosthetic joints.

Strengths of this study are the large number of clinically noninfected cardiac devices examined with detailed clinical and microbiological data. However, there were several important limitations in our study, including the lack of a gold standard for subclinical infections of cardiac devices. Another limitation was the nonblinded collection of controls. Also, the explanteur (cardiologist or surgeon) was another person than the collector of the controls. Another drawback is the short follow-up, when taking into account that infections in this series occurred up to 7 years after implantation. For future studies, it would be important to include histology to analyze inflammatory reaction.

In conclusion, we showed by sonication and conventional culture that microorganisms colonize electrophysiological devices. Sonication of the device before culture could represent a more sensitive technique to detect microorganisms in device-related infections. However, the role of bacteria detected in asymptomatic cardiac devices needs to be elucidated by further studies to discuss adequate preemptive antibiotic therapy.

Disclosures

None.

References

1. 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;133:604–608.
2. Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, Domanski M, Troutman C, Anderson J, Johnson G, McNulty SE, Clapp-Channing N, Davidson-Ray LD, Fraulo ES, Fishbein DP, Luceri RM, Ip JH. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med*. 2005;352:225–237.
3. Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, Daubert JP, Higgins SL, Brown MW, Andrews ML. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med*. 2002;346:877–883.
4. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias: The Antiarrhythmics versus Implantable Defibrillators (AVID) investigators. *N Engl J Med*. 1997;337:1576–1583.
5. Connolly SJ, Gent M, Roberts RS, Dorian P, Roy D, Sheldon RS, Mitchell LB, Green MS, Klein GJ, O'Brien B. Canadian implantable defibrillator study (CIDS): a randomized trial of the implantable cardioverter defibrillator against amiodarone. *Circulation*. 2000;101:1297–1302.
6. Kuck KH, Cappato R, Siebels J, Ruppel R. Randomized comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest: the Cardiac Arrest Study Hamburg (CASH). *Circulation*. 2000;102:748–754.
7. Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H, Levine JH, Saksena S, Waldo AL, Wilber D, Brown MW, Heo M. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. *N Engl J Med*. 1996;335:1933–1940.
8. Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G. A randomized study of the prevention of sudden death in patients with coronary artery disease: Multicenter Unsustained Tachycardia Trial Investigators. *N Engl J Med*. 1999;341:1882–1890.
9. Hohnloser SH, Kuck KH, Dorian P, Roberts RS, Hampton JR, Hatala R, Fain E, Gent M, Connolly SJ. Prophylactic use of an implantable cardioverter-defibrillator after acute myocardial infarction. *N Engl J Med*. 2004;351:2481–2488.
10. Cazeau S, Leclercq C, Lavergne T, Walker S, Varma C, Linde C, Garrigue S, Kappenberger L, Haywood GA, Santini M, Baillet C, Daubert JC. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *N Engl J Med*. 2001;344:873–880.

11. Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, Kocovic DZ, Packer M, Clavell AL, Hayes DL, Ellestad M, Trupp RJ, Underwood J, Pickering F, Truex C, McAtee P, Messenger J. Cardiac resynchronization in chronic heart failure. *N Engl J Med*. 2002;346:1845–1853.
12. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, Tavazzi L. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med*. 2005;352:1539–1549.
13. Young JB, Abraham WT, Smith AL, Leon AR, Lieberman R, Wilkoff B, Canby RC, Schroeder JS, Liem LB, Hall S, Wheelan K. Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: the MIRACLE ICD Trial. *JAMA*. 2003;289:2685–2694.
14. Lenarczyk R, Kowalski O, Kukulski T, Szulik M, Pruszkowska-Skrzep P, Zielinska T, Kowalczyk J, Pluta S, Duszanska A, Sredniawa B, Musialik-Lydka A, Kalarus Z. Triple-site biventricular pacing in patients undergoing cardiac resynchronization therapy: a feasibility study. *Europace*. 2007;9:762–767.
15. Lenarczyk R, Kowalski O, Kukulski T, Pruszkowska-Skrzep P, Sokal A, Szulik M, Zielinska T, Kowalczyk J, Pluta S, Sredniawa B, Musialik-Lydka A, Kalarus Z. Mid-term outcomes of triple-site vs conventional cardiac resynchronization therapy: a preliminary study. *Int J Cardiol*. 2009;133:87–94.
16. Leclercq C, Gadler F, Kranig W, Ellery S, Gras D, Lazarus A, Clementy J, Boulogne E, Daubert JC. A randomized comparison of triple-site versus dual-site ventricular stimulation in patients with congestive heart failure. *J Am Coll Cardiol*. 2008;51:1455–1462.
17. Yoshida K, Seo Y, Yamasaki H, Tanoue K, Murakoshi N, Ishizu T, Sekiguchi Y, Kawano S, Otsuka S, Watanabe S, Yamaguchi I, Aonuma K. Effect of triangle ventricular pacing on haemodynamics and dyssynchrony in patients with advanced heart failure: a comparison study with conventional bi-ventricular pacing therapy. *Eur Heart J*. 2007;28:2610–2619.
18. Mela T, McGovern BA, Garan H, Vlahakes GJ, Torchiana DF, Ruskin J, Galvin JM. Long-term infection rates associated with the pectoral versus abdominal approach to cardioverter-defibrillator implants. *Am J Cardiol*. 2001;88:750–753.
19. Catanchin A, Murdock CJ, Athan E. Pacemaker infections: a 10-year experience. *Heart Lung Circ*. 2007;16:434–439.
20. Duval X, Selton-Suty C, Alla F, Salvador-Mazenq M, Bernard Y, Weber M, Lacassin F, Nazeyrolas P, Chidiac C, Hoen B, Leport C. Endocarditis in patients with a permanent pacemaker: a 1-year epidemiological survey on infective endocarditis due to valvular and/or pacemaker infection. *Clin Infect Dis*. 2004;39:68–74.
21. Baddour LM, Bettmann MA, Bolger AF, Epstein AE, Ferrieri P, Gerber MA, Gewitz MH, Jacobs AK, Levison ME, Newburger JW, Pallasch TJ, Wilson WR, Baltimore RS, Falace DA, Shulman ST, Tani LY, Taubert KA. Nonvalvular cardiovascular device-related infections. *Circulation*. 2003;108:2015–2031.
22. Trampuz A, Piper KE, Jacobson MJ, Hanssen AD, Unni KK, Osmon DR, Mandrekar JN, Cockerill FR, Steckelberg JM, Greenleaf JF, Patel R. Sonication of removed hip and knee prostheses for diagnosis of infection. *N Engl J Med*. 2007;357:654–663.
23. Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings: Duke Endocarditis Service. *Am J Med*. 1994;96:200–209.
24. Dy Chua J, Abdul-Karim A, Mawhorter S, Procop GW, Tchou P, Niebauer M, Saliba W, Schweikert R, Wilkoff BL. The role of swab and tissue culture in the diagnosis of implantable cardiac device infection. *Pacing Clin Electrophysiol*. 2005;28:1276–1281.
25. Rieger UM, Pierer G, Luscher NJ, Trampuz A. Sonication of Removed Breast Implants for Improved Detection of Subclinical Infection. *Aesthetic Plast Surg*. 2009;33:404–408.
26. Piper KE, Jacobson MJ, Cofield RH, Sperling JW, Sanchez-Sotelo J, Osmon DR, Steckelberg JM, Mandrekar JN, Fernandez Sampedro M, Patel R. Microbiologic Diagnosis of Prosthetic Shoulder Infection using Implant Sonication. *J Clin Microbiol*. 2009;47:1878–1884.
27. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med*. 2004;351:1645–1654.
28. Gunthard H, Hany A, Turina M, Wust J. Propionibacterium acnes as a cause of aggressive aortic valve endocarditis and importance of tissue grinding: case report and review. *J Clin Microbiol*. 1994;32:3043–3045.
29. Caballero Gueto J, Arana R, Calle G, Caballero Gueto FJ, Garcia del Rio E, Sancho M, Pinero C. [Acute endocarditis of the native aortic valve caused by Propionibacterium acnes]. *Rev Esp Cardiol*. 1997;50:906–908.
30. Chu VH, Woods CW, Miro JM, Hoen B, Cabell CH, Pappas PA, Federspiel J, Athan E, Stryjewski ME, Nacinovich F, Marco F, Levine DP, Elliott TS, Fortes CQ, Tornos P, Gordon DL, Utili R, Delahaye F, Corey GR, Fowler VG, Jr. Emergence of coagulase-negative staphylococci as a cause of native valve endocarditis. *Clin Infect Dis*. 2008;46:232–242.
31. Zedtwitz-Liebenstein K, Gabriel H, Graninger W. Pacemaker endocarditis due to Propionibacterium acnes. *Infection*. 2003;31:184–185.
32. Chakour M, Revel F, Godreuil C, Plotton C, Aubry A, Koeck JL. [Infectious endocarditis due to Propionibacterium acnes on a mechanical heart valve and cardiac stimulator electrode]. *Presse Med*. 2002;31:1414.
33. Chua AG, Ding J, Schoch PE, Cunha BA. Pacemaker-induced endocarditis due to Propionibacterium acnes. *Clin Infect Dis*. 1998;27:1541–1542.
34. Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, Gregoratos G, Klein G, Moss AJ, Myerburg RJ, Priori SG, Quinones MA, Roden DM, Silka MJ, Tracy C, Smith SC Jr, Jacobs AK, Adams CD, Antman EM, Anderson JL, Hunt SA, Halperin JL, Nishimura R, Ornato JP, Page RL, Riegel B, Blanc JJ, Budaj A, Dean V, Deckers JW, Despres C, Dickstein K, Lekakis J, McGregor K, Metra M, Morais J, Osterspey A, Tamargo JL, Zamorano JL. ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (writing committee to develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation*. 2006;114:e385–e484.
35. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA III, Freedman RA, Gettes LS, Gillinov AM, Gregoratos G, Hammill SC, Hayes DL, Hlatky MA, Newby LK, Page RL, Schoenfeld MH, Silka MJ, Stevenson LW, Sweeney MO, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Buller CE, Creager MA, Ettinger SM, Faxon DP, Halperin JL, Hiratzka LF, Hunt SA, Krumholz HM, Kushner FG, Lytle BW, Nishimura RA, Ornato JP, Page RL, Riegel B, Tarkington LG, Yancy CW. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices) developed in collaboration with the Am Association for Thoracic Surgery and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2008;51:e1–e62.

CLINICAL PERSPECTIVE

In this study, we showed that bacteria can colonize electrophysiological devices without signs of infection. Because only a few of the patients with bacteria detected at the time of device removal developed an infection during follow-up, antibiotic treatment is probably not indicated in these patients. However, the role of colonizing bacteria in the development in infection must be further elucidated, and perioperative antibiotic prophylaxis with additional coverage of coagulase-negative staphylococci and *Propionibacterium acnes* should be evaluated. Additionally, we showed that bacteria on electrophysiological devices can be better detected with sonication than with conventional swab culture, suggesting that sonication of removed infected devices might be more sensitive in isolating bacteria, especially when patients are already receiving antibiotic treatment.

Bacterial Colonization and Infection of Electrophysiological Cardiac Devices Detected With Sonication and Swab Culture

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Circulation. 2010;121:1691-1697; originally published online April 5, 2010;
doi: 10.1161/CIRCULATIONAHA.109.906461

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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