The administration of prophylactic antibiotics before pacemaker or internal cardioverter-defibrillator implantation has been implemented widely and routinely. The acceptance of this practice has occurred despite the absence of rigorous examination or definitive evidence. The existing data for the use of prophylactic antibiotic therapy in device implantation consist of 7 randomized, controlled trials, with all but 1 having an open design. Early trials yielded contradictory results, citing small study numbers, a low incidence of infection, and inconsistent definitions of infection as possible explanations. Four of the 7 trials found antibiotic prophylaxis effective in preventing infection; the lone double-blind, randomized, controlled study consisted of 106 patients and failed to demonstrate a difference in infection rate with antibiotic prophylaxis because there were no documented infections at 7 to 35 months of follow-up. In addition to their inconsistent results, widely varying antibiotic regimens were implemented in these trials, further confounding the ability of operators to interpret the available data and to implement evidence-based medicine into practice. Despite the equivocal findings of these individual studies, a meta-analysis of antibiotic prophylaxis for permanent pacemaker implantation by Da Costa et al in 1998 demonstrated a significant reduction in the incidence of infection. The study in this issue of Circulation: Arrhythmia and Electrophysiology by de Oliveira et al is the first large-scale, randomized, double-blind, placebo-controlled trial establishing the benefit of antibiotic prophylaxis in prevention of device implant infections.

Patients undergoing cardiac device implantation or generator replacement were randomized to treatment with a single dose of 1 g intravenous cephazolin or placebo administered immediately before the procedure. Those with penicillin allergies or active antibiotic use were excluded. The primary end point was the incidence of procedure-related infection, classified as superficial infection of the incision, pocket infection without systemic manifestations, and systemic infections. Follow-up evaluations occurred 10 days and 1, 3, and 6 months postprocedure. Additionally, patient and procedural characteristics were analyzed to establish predictors of infection.

The trial was stopped prematurely after the enrollment of 649 patients (aged 64.2±15.3 years). Ninety-one percent of the implanted devices were pacemakers, with 46.7% primary implants and 53.3% generator replacements. All device procedures were performed in an operating room (ie, not a catheterization or electrophysiology laboratory), and the pocket was not flushed with antibiotic solution. The primary end point was reached in 13 patients (2.0%). Pretreatment with cephazolin significantly reduced the incidence of post-procedural infection (0.64% cephazolin versus 3.28% placebo, \( P=0.016 \)). Univariate analysis suggested that prolonged procedure time, primary implants, pocket hematoma development, and lack of antibiotic prophylaxis were predictors of infection, and multivariate analysis identified the development of pocket hematoma and the lack of antibiotic prophylaxis as independent predictors of infection.

The time of onset of symptoms in the infected patients ranged from 11 to 33 days. Superficial infections (n=3) were managed with oral cephalexin for 10 days; patients with pocket infection with (n=4) or without (n=5) systemic manifestations were treated with intravenous antibiotics and had the entire system removed. Staphylococci species were isolated in all cases of infection; there were 4 cases of oxacillin resistance. There was no mortality caused by infection or directly related to the implant procedure. The authors conclude that their findings “firmly confirm the benefit and safety of the use of antibiotic prophylaxis during implantation of percutaneous pacing devices with a single dose of 1 g cephazolin given intravenously immediately before the surgical procedure.”

The authors highlight that the present study excluded high-risk patients, such as those with prosthetic heart valves and those requiring repeat procedure for lead revision. A prospective, observational study of 6319 patients identified early reintervention for lead dislodgement or pocket hematoma as a risk factor for infection, with an odds ratio of 15.6. Although it is difficult to extrapolate the authors’ findings to this patient population, one would suspect that prophylaxis should reduce infections in high-risk patients if it does so in those at low risk. In addition, other high-risk patients and patients with penicillin allergies were excluded. The impact of other antibiotics, especially if not bactericidal, is unknown.

The authors should be commended for this important contribution. Their findings finally provide rigorous evidence of the benefit of antibiotic prophylaxis in cardiac device implantation. The question, as always, remains, “Can we do better?” Do prophylactic antibiotics postprocedure further
reduce the incidence of infection? Six of the 7 prior randomized trials of antibiotic prophylaxis used a regimen of preprocedure and postprocedure antibiotics. Pooling these results confirmed the consistent benefit of antibiotic therapy, acknowledging the limitations of a meta-analysis.1 What is the role of intraprocedural antibiotic flush? Bluhm et al7 found no difference in the incidence of infection between systemic and local antibiotic administration at the time of generator replacement. Of the 108 patients enrolled, there were 2 cases of infection, both in the local antibiotic group, leading the readers to interpret the results with caution. What can we expect from novel adjuvant devices such as antibiotic impregnated, bioresorbable device sleeves or silver-impregnated surgical dressings? Preclinical studies of antibiotic impregnated sleeves are promising, but their benefit in patients remains to be established.8 Clinical trials of silver-impregnated surgical dressings seem to reduce the incidence of postoperative infections and methicillin-resistant *Staphylococci,* but again, rigorous data are lacking.9 The added expense of these products may only be warranted in the highest-risk patients. This study by de Oliveira et al should finally put to rest the prophylactic antibiotic debate in device implantation and compel us to systematically evaluate all aspects of the implant procedure and the management of complications that arise.

**Disclosures**

Dr. Epstein is a paid consultant to and has received honoraria from Boston Scientific, Medtronic, Inc., Spectranetics, and St. Jude Medical.

**References**


**KEY WORDS:** infection ■ pacemakers ■ ICD
Proof Positive: Efficacy of Antibiotic Prophylaxis in Device Implantation
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