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INSIDE

Linezolid for Nosocomial MRSA Pneumonia: A Better Option?

ABSTRACT & COMMENTARY

By Brian Blackburn, MD

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Dr. Blackburn reports no financial relationships related to this field of study.

This article originally appeared in the June 2012 issue of Infectious Disease Alert. *It was edited by Stan Deresinski, MD, FACP, FIDSA, and peer reviewed by Timothy Jenkins, MD. Dr. Deresinski is Clinical Professor of Medicine, Stanford University, and Dr. Jenkins is Assistant Professor of Medicine, University of Colorado, Denver Health Medical Center. Dr. Deresinski does research for the National Institutes of Health, and is an advisory board member and consultant for Merck, and Dr. Jenkins reports no financial relationships relevant to this field of study.*

Synopsis: *Linezolid was non-inferior to vancomycin in patients with nosocomially acquired MRSA pneumonia. Although mortality was similar among linezolid- and vancomycin-treated patients, several outcomes (such as clinical cure and microbiological cure) favored linezolid.*

Source: Wunderink RG, et. al. Linezolid in Methicillin-Resistant *Staphylococcus aureus* nosocomial pneumonia: A randomized, controlled study. *Clin Infect Dis* 2012;54:621-9.

The treatment of MRSA pneumonia is often regarded as problematic, with unacceptably high morbidity and mortality rates among affected patients. Two recent prospective, randomized, double-blind trials found that linezolid was non-inferior to vancomycin for the treatment of nosocomial pneumonia.[1,2] In addition, post-hoc analysis of pooled data from these two trials found that survival (80% vs. 63%) and clinical cure (59% vs. 36%) significantly favored linezolid in the MRSA pneumonia subgroup.[3] However, the post-hoc nature of this subgroup analysis could have introduced bias, and vancomycin dosing was not optimized

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in these trials, leading to calls for a prospective, randomized, double-blind trial to verify these findings.

The authors thus undertook such a study comparing linezolid to vancomycin. Adult patients with radiographically documented nosocomial pneumonia (including those with both HAP [hospital acquired pneumonia; 84% of the cohort] and HCAP [health care associated pneumonia; 16% of the cohort]) and a respiratory culture positive for MRSA were randomized to receive either linezolid 600 mg every 12 hours or vancomycin 15 mg/kg every 12 hours. Dosing of the latter was subsequently adjusted based on serum vancomycin levels. Patients were treated for 7-14 days, although those with bacteremia were treated for 21 days. All patients received an antibiotic with Gram-negative (but without anti-MRSA) activity, which was discontinued if no Gram-negative pathogens were identified.

Although 1,225 patients were randomized to receive the study drug, only 448 (37%) were included in the modified intent-to-treat (mITT) analysis, with most patients excluded because MRSA was not identified in cultures. Only 348 patients were included in the per-protocol analysis. This population had a median age of 61 years, and 64% had ventilator-associated pneumonia. Median vancomycin serum troughs (μg/mL) were 12 at day 3, 15 at day 6, and 16 at day 9. Eleven percent of patients in the vancomycin arm had bacteremia, compared to 5% in the linezolid arm; slightly more patients in the vancomycin arm received mechanical ventilation than in the linezolid arm.

In the per-protocol population, clinical cure at the end-of-study assessment occurred in 95 (58%) of the 165 linezolid-treated patients, and in 81 (47%) of the 174 vancomycin-treated patients (P = .042). Microbiological cure occurred in nearly the same proportion of patients in both arms at the end-of-study analysis. All-cause mortality at the end-of-study analysis did not differ significantly — 28% in the linezolid arm and 26% in the vancomycin arm.

Renal failure occurred twice as frequently in the vancomycin arm (7.3%) as in the linezolid (3.7%) arm. The frequency of cytopenias did not differ between groups.

■ Commentary

This prospective, randomized, double-blind trial seems to confirm the earlier post hoc subgroup analysis which suggested that linezolid may be superior to vancomycin for the treatment of nosocomial MRSA pneumonia. Although mortality did not differ between groups in this trial, linezolid was associated with higher clinical and microbiological cure rates than vancomycin. These results were consistent in most subgroups analyzed in the study, including among patients with mixed infections, among those who received mechanical ventilation, and among those who received systemic corticosteroids.

The apparent superiority of linezolid may have resulted from better intrinsic antimicrobial activity, better lung penetration, and more complete bacterial eradication. These findings are more robust than the previous post-hoc study, given the prospective, randomized, double-blind nature of this study, and that vancomycin dosing was optimized in this study based on serum levels. Linezolid also appeared safer than vancomycin, with less nephrotoxicity and no increase in hematologic toxicity, another compelling point in favor of linezolid (especially given that renal failure is a significant predictor of mortality in this setting).

Mortality was not lower among linezolid-treated patients, possibly in part because a lower-than-expected mortality was observed among vancomycin-treated patients. This might have been a result of the intensive dose optimization by serum drug level monitoring for vancomycin, but whether this is applicable to many real-world settings is unclear from this study.

Limitations of the study included the large number of patients excluded after randomization, which could have introduced bias. In addition, while the requirement of a positive culture for MRSA was a strength in terms of confirming the role of linezolid in patients with known MRSA pneumonia, it also introduces a limitation for real-world use, given that antibiotics are usually started empirically in patients with nosocomial pneumonia. It is common that no etiologic diagnosis is ever made in this setting, and this trial does not address the efficacy of linezolid in this situation. Another limitation was the slightly higher proportion of patients with bacteremia and mechanical ventilation in the vancomycin arm, which could have biased the results against vancomycin. Finally, even with linezolid, the clinical cure rates observed were relatively low, suggesting that we still do not have an optimal drug for this serious and difficult-to-treat condition.

Despite these limitations, this study provides compelling evi-

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Questions & Comments
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dence to bolster the notion that linezolid may be superior to vancomycin for nosocomial MRSA pneumonia. If these findings result in enthusiastic demand for linezolid in this setting, careful stewardship is of paramount importance, given that widespread use of linezolid in this setting could prove very expensive, and might promote resistance to this drug. If linezolid does become the first-line anti-Gram positive agent for nosocomial pneumonia, perhaps limiting use to clinically and microbiologically well-documented cases of nosocomial MRSA pneumonia would be prudent, with empiric use limited to a short course if MRSA is not subsequently recovered from respiratory cultures. ■

r eferences

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Should Cefazolin Be Preferred Treatment for Methicillin-susceptible *S. aureus* Bacteremia Instead of Nafcillin?

ABSTRACT & COMMENTARY

By Richard R. Watkins, MD, MS, FACP

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Dr. Watkins reports no financial relationships related to this field of study.

This article originally appeared in the June 2012 issue of Infectious Disease Alert. *It was edited by Stan Deresinski, MD, FACP, FIDSA, and peer reviewed by Timothy Jenkins, MD. Dr. Deresinski is Clinical Professor of Medicine, Stanford University, and Dr. Jenkins is Assistant Professor of Medicine, University of Colorado, Denver Health Medical Center. Dr. Deresinski does research for the National Institutes of Health, and is an advisory board member and consultant for Merck, and Dr. Jenkins reports no financial relationships relevant to this field of study.*

Synopsis: *In a retrospective, propensity-score-matched, case-control study, investigators compared clinical outcomes and drug tolerabilities between nafcillin and cefazolin in the treatment of MSSA bacteremia. The authors found that cefazolin was as efficacious as nafcillin in the treatment of MSSA bacteremia while causing fewer adverse drug events.*

Source: Lee S, et al. Is cefazolin inferior to nafcillin for treatment of methicillin-susceptible *Staphylococcus aureus* bacteremia? *Antimicrob Agents Chemother* 2011;55:5122-6.

Methicillin-susceptible *Staphylococcus aureus* (MSSA) bacteremia is a commonly encountered infection in hospitalized patients that can have serious complications if not adequately treated. In a retrospective, propensity-score-matched, case-control study, investigators compared clinical outcomes and drug tolerabilities between nafcillin and cefazolin in the treatment of MSSA bacteremia. The study was conducted between 2004 and 2009 at a tertiary care center in Seoul, South Korea. From August 2004 to August 2006 nafcillin was not available at the hospital because of supply issues. Patients with MSSA bacteremia were mainly treated with cefazolin during that period.

The authors examined the medical records of all patients with MSSA-positive blood cultures between January 2004 and June 2009 who received either nafcillin or cefazolin and placed them in two groups based on the antibiotic used. Logistic regression was used to create a propensity score based on risk factors for each patient. These risk factors included age, McCabe classification, high-burden disease, site of infection, and focus eradication. Patients in the cefazolin group were matched with patients in the nafcillin treatment group who had the closest propensity scores. The treatment failure rates were compared between the propensity-score-matched-groups 4 and 12 weeks after the start of nafcillin or cefazolin treatment.

Out of 174 patients during the study period with MSSA bacteremia, 84 were treated with nafcillin and 90 were treated with cefazolin. Forty-one patients in the cefazolin group were matched with the 41 patients in the nafcillin group with the highest propensity scores. Times to defervescence were 4.4 ± 4.9 days in the matched cefazolin group and 5.4 ± 9.3 days in the matched nafcillin group (p=0.63). The treatment failure rates at 12 weeks were 15% (6/41) in the cefazolin group and 15% (6/41) in the nafcillin group (p >0.99). The rates of MSSA bacteremia-related mortality were 2% (1/41) in the cefazolin group and 12% (5/41) in the nafcillin group (p =0.22). There was no significant difference between the two groups in 4 week mortality (4% vs. 4%). In four patients in the cefazolin group, the antibiotic was changed due to treatment failure (3 to vancomycin, 1 to nafcillin). Pneumonia and infective endocarditis have been previously shown to be predictors of treatment failure for MSSA bacteremia. After adjusting for these risk factors, cefazolin use was found to not be a risk factor for treatment failure for MSSA bacteremia.

None of the patients in the cefazolin group had their treatment interrupted due to adverse drug events. In contrast, 7 patients discontinued nafcillin because of adverse events including fever (n=4), cytopenia (n=2), and phlebitis (n=1). The median time to the discontinuation of nafcillin was 19 days (range, 7 to 24 days).

■ **Commentary**

The authors of this study found that cefazolin was as efficacious as nafcillin in the treatment of MSSA bacteremia while causing fewer adverse drug events. One limitation is the retrospective design which could predispose to selection bias, although the authors attempted to compensate for this by using propensity scores and included patients in the cefazolin group when nafcillin was unavailable at the institution. Another limitation was that few endocarditis cases were treated with cefazolin (n =1). The number of patients in both treatment groups was small (n =41) which could limit the ability to detect differences in outcomes between nafcillin and cefazolin.

While a randomized, prospective clinical trial comparing nafcillin to cefazolin for treatment of MSSA bacteremia would be welcomed, it seems unlikely such a study will be conducted in the near future. Therefore clinicians must decide how to treat patients with MSSA bacteremia based on the best available evidence. Using cefazolin in this scenario seems to be a reasonable approach. In addition to fewer adverse drug events than nafcillin, cefazolin has a more convenient dosing schedule (every 8 hours compared to every 4 hours) and can be given at the end of a dialysis session in patients with renal failure. One caveat is that nafcillin should probably remain the first line therapy for MSSA endocarditis with brain emboli. Cefazolin poorly penetrates the blood-brain barrier, so metastatic infection of the brain from endocarditis might not be adequately treated with this drug. However, it is controversial and further studies on this are warranted. ■

Improving Patient Safety During Postoperative Handoffs

ABSTRACT & COMMENTARY

By David J. Pierson, MD

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This article originally appeared in the June 2012 issue of Critical Care Alert. *It was peer reviewed by William Thompson, MD. Dr. Thompson is Associate Professor of Medicine, University of Washington, Seattle. Drs. Pierson and Thompson report no financial relationships relevant to this field of study.*

Synopsis: *This comprehensive review on postoperative patient handoffs confirms that they are high-risk events associated with adverse patient outcomes, and permits the identification of several strategies likely to improve the process despite the incompleteness and other limitations of the existing literature.*

Source: Segall N, et al, on behalf of the Durham VA Patient Safety Center of Inquiry. Can we make postoperative patient handovers safer? A systematic review of the literature. *Anesth Analg* 2012; Apr 27. [Epub ahead of print.]

A patient handover, or handoff, in health care can be defined as the transfer of information, professional responsibility, and accountability between individuals and teams. Handoffs represent a time of particular patient vulnerability to complications and medical errors, and with the current focus on safety an increasing amount of attention has been devoted to characterizing and improving them. One context in which handoffs are especially frequent, and patients especially susceptible to adverse events, is transfer to the post-anesthesia unit or ICU after anesthesia and surgery. This study by Segall and colleagues of the Durham VA Patient Safety Center of Inquiry in North Carolina sought to better characterize current practices in patient handoffs in this setting, and to identify strategies for improving the process.

The authors conducted an extensive literature search via PubMed and other databases using search terms intended to discover all studies and other publications related to postoperative handoffs. They classified candidate articles into four categories of study design and potential transferability of findings and recommendations, with Category 1 being comprehensive, intervention-based studies having strong design and potentially generalizable results, and Category 4 being published opinions and reviews, potentially useful for identifying evidence gaps, limitations, and perspectives. Segall et al thoroughly reviewed all appropriate articles and summarized them in a series of comprehensive tables included in the article and its appendices.

From more than 500 publications, 31 articles dealing with postoperative handoffs were reviewed in detail. Of these, 24 provided recommendations for structuring the handoff process, in 14 instances basing this on some sort of evidence. Only four studies were comprehensive, intervention-based investigations qualifying for Category 1 status. Five more included some level of evaluation and were classified in Category 2; 18 were cross-sectional studies (Category 3) characterizing current post-surgery handoff practices. With one exception, all the studies were published since 2000, and 14 of them in 2010 and 2011.

Despite the wide variation in study design and article quality, Segall et al report that they identified a number of common barriers to safe, effective postoperative handoffs. The latter fell into six general categories: incomplete information transfer; other communication issues such as inaccurate information, inconsistency, poor organization, and information overload; the intrusion of clinical activities and other distractions into the handoff process; inconsistency and incompleteness of the transferring and/or receiving teams; failure

of effective execution of clinical tasks; and lack of standardization. Based on their review, the authors listed a number of strategies for improving the safety and effectiveness of postoperative handoffs that were strongly supported by the existing evidence and authoritative opinion. Further, based on their findings they created an extensive list of patient information that should be included in verbal and written handoffs; the complete list is included in the article's appendix.

■ **Commentary**

This article confirms the findings of numerous previous publications about postoperative patient handoffs: they are characterized by poor teamwork and communication, processes of care are poorly structured and described, nurses and staff are often distracted by other work, and vital information is often unavailable or poorly organized. The literature review also documents a strong association between poor-quality handoffs and adverse events affecting patients, although as the authors point out it is not possible to be sure here about causation.

There are numerous potential limitations in this study, as the authors also discuss. Curiously, the four Category 1 (best designed) studies all dealt with pediatric cardiac surgery patients. Despite the limitations, however, the marked agreement about what is wrong with postoperative patient handoffs and what should ideally be done about it, gleaned from a diverse and extensive literature, represents a great deal of practical experience and collective clinical wisdom. The recommendations are not all based on best-quality evidence, but their broad implementation would surely improve both patient care and the work environment for many clinicians who participate in postoperative ICU management. ■

Hospital Cultural and Organizational Characteristics Correlate with Important Mortality Differences in Managing Acute Myocardial Infarction

ABSTRACT & COMMENTARY

By David J. Pierson, MD

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This article originally appeared in the June 2012 issue of Critical Care Alert. *It was peer reviewed by William Thompson, MD. Dr. Thompson is Associate Professor of Medicine, University of Washington, Seattle. Drs. Pierson and Thompson report no financial relationships relevant to this field of study.*

Synopsis: *This study of 537 hospitals found that those with the lowest mortality rates for acute myocardial infarction have management strategies that differ in important ways from those at hospitals with higher acute myocardial infarction mortality.*

Source: Bradley EH, et al. Hospital strategies for reducing risk-standardized mortality rates in acute myocardial infarction. *Ann Intern Med* 2012; 156:618-626.

Great strides have been made over the last couple of decades in the management of acute myocardial infarction (AMI), and widespread implementation of such interventions as aspirin, beta-blockers, and prompt reperfusion therapy has contributed to substantially reduced mortality from this leading killer. However, despite this progress, substantial differences persist with respect to AMI outcomes at different hospitals. Nationwide, the overall risk-standardized mortality rate (RSMR) within 30 days of AMI is around 15%. However, there is a 2-fold difference in RSMR between the best- and worst-performing hospitals. Bradley and colleagues at Yale sought to determine what characteristics of a hospital's organization and culture related to managing AMI might account for these differences.

In a study reported last year,[1] these authors qualitatively identified strategies pertaining to top-performing hospitals' organizational values and goals; the involvement of their senior management; the expertise, communication, and coordination of their staff; and approaches to learning and problem solving that were prominent in their AMI care but not in their poor-performing counterparts. In this study, they surveyed a sample of hospitals reporting Centers for Medicare & Medicaid Services (CMS) data in order to test their earlier results more quantitatively. They randomly selected 600 hospitals from institutions reporting CMS data for RSMRs for AMI during the fiscal years 2005-2008, eliminating 10 hospitals that had since closed. They asked the CEO of each hospital to identify the person most involved in AMI quality improvement, and asked that individual to complete a Web-based survey based on the findings of the earlier study.

Of the 590 surveyed hospitals, 537 (91%) responded. One-third were teaching hospitals, slightly more than half had fewer than 300 beds, roughly half managed more than 125 AMI patients per year, and three-quarters performed percutaneous coronary intervention for ST-segment elevation AMI. Weighted mean AMI mortality in the surveyed hospitals was 15.4% (SD, 1.5%; range, 11.5% to 21.7%), with no significant differences from the non-surveyed hospitals in the CMS database.

The following hospital strategies were significantly associated with lower RSMRs in patients with AMI, with decrease in RSMR percentage points in parentheses:

- Holding monthly meetings to review AMI cases involving both hospital clinicians and the staff who transported the patients to the hospital (0.70);
- Having cardiologists onsite 24/7 (0.54);
- Fostering an organizational environment in which clinicians were encouraged to solve problems creatively (0.84); and
- Having both physician and nurse champions rather than nurse champions alone with respect to AMI care (0.88).

Another significant association was not staffing the cardiac catheterization laboratory with nurses cross-trained from the

ICU (0.44). At least four of these five strategies were present in fewer than 10% of the hospitals in the study. Additional findings included significantly lower AMI mortality in hospitals that had pharmacists rounding on all patients with AMI ($P < 0.025$).

■ **Commentary**

In an era in which practice standards and the components of managing AMI are widely accepted and implemented, this study found important differences among hospitals correlating with RSMRs. These related to the organizational environment, including effective collaboration and communication among groups, broad staff presence and expertise, and a culture of problem solving and learning. Although the absolute effect sizes (for example, 0.54 to 0.88 percentage points) seem small, in the aggregate they exceeded an absolute difference of 1% in RSMR. Most importantly, considering the large numbers of patients with AMI managed nationally, eliminating the differences could make a difference of thousands of lives each year. As pointed out by the authors, the interventions involved — organizational and cultural rather than technological — carry little risk, and their implementation would not involve large amounts of new resources.

Most of the above findings suggest that high-performing and poor-performing hospitals with respect to AMI outcomes differ in their communication, collaboration, collegiality, and teamwork. Numerous studies in other aspects of critical care have shown that these characteristics are associated with better patient outcomes, and it is likely that the present study's findings have implications beyond the care of AMI. ■

r eference

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Audit Feedback Reduced Broad-Spectrum Antibiotic Use and Incidence of *C. difficile* Infections

ABSTRACT & COMMENTARY

By Leslie A. Hoffman, RN, PhD

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Leslie A. Hoffman reports no financial relationships relevant to this field of study. This article originally appeared in the June 2012 issue of Critical Care Alert. *It was edited by David J. Pierson, MD, and peer reviewed by William Thompson, MD. Dr. Pierson is Professor Emeritus, Pulmonary and Critical Care Medicine, University of Washington, Seattle, and Dr. Thompson is Associate Professor of Medicine, University of Washington, Seattle. Drs. Pierson and Thompson report no financial relationships relevant to this field of study.*

Synopsis: *Institution of a formal audit and feedback program resulted in a decrease in use of broad-spectrum antibiotics and a 31% reduction in cases of* Clostridium difficile *infection.*

Source: Elligsen M, et al. Audit and feedback to reduce broad-spectrum antibiotic use among intensive care unit patients: A controlled interrupted time series analysis. *Infect Control Hosp Epidemiol* 2012;33:354-361.

This study was conducted to evaluate the impact of a formal audit and feedback program targeted at broad-spectrum antibiotic use in critically ill patients. The study was conducted in three intensive care units (ICUs) in a single institution in Toronto: a 20-bed general ICU, a 14-bed cardiovascular ICU, and a 14-bed burn center. Records of all patients who received 3 days of therapy with broad-spectrum antibiotics were reviewed by a designated pharmacist. If an opportunity for optimization was identified, the case was reviewed with an infectious disease staff physician. If the suggestion was approved, a computer-generated progress note was placed in the patient's chart and the pharmacist provided verbal feedback to available members of the critical care team. The process was structured to provide assessment, review, and feedback within 24 hours. A similar review was performed on the 10th day of therapy to advise clinicians regarding excessive duration of treatment. All decisions to change therapy rested with the critical care team. The control group consisted of patients admitted to non-ICU wards during the same time period.

During the 12-month data collection period, 2339 patients were admitted to the three ICUs for a total of 15,431 patient days. Pharmacists evaluated 717 antibiotic prescriptions and made recommendations for change in 247 cases (34%); most (82%) recommendations were accepted by the critical care team. The most common recommendations were to discontinue the antibiotic (56%), change the antibiotic (26%), or change dose, frequency, or route (8%). Mean monthly broad-spectrum antibiotic use decreased from 644 days per 1000 patient days per month (preintervention) to 503 days per 1000 patient days per month (postintervention; $P < 0.0001$) with no change in non-ICU (control) units. The number of monthly *Clostridium difficile* infections decreased by 31% (n = 16 preintervention; n = 11 postintervention) compared to an increase (33%) in non-ICU units (n = 87 preintervention; n = 116 postintervention; $P = 0.04$). ICU length of stay and mortality were unchanged.

■ **Commentary**

In this study, as in studies testing use of a weaning protocol to improve patient outcomes, positive changes resulted from introduction of a structured routine daily assessment. Pharmacist review, followed by a computer-generated progress note and verbal feedback, led to a substantial (22%) reduction in broad-spectrum antimicrobial use in the ICUs that was sustained for the 12-month duration of the study. There was no change in use of broad-spectrum antibiotics in control (non-ICU) units, supporting that the reduction was a result of the intervention. Most (82%) suggestions were accepted, an outcome that authors attributed to timing of the pharmacist recommendations which

occurred on the third and tenth day of broad-spectrum antibiotic therapy. This timing allowed the pharmacist to incorporate microbiologic data and information about response to current therapy into the recommendation.

Prior studies have reported similar findings as a result of programs that incorporated a similar assessment. However, none reported a decrease in *C. difficile* infection as a result of a structured monitoring program. The authors therefore questioned whether this approach — reduction in patient susceptibility through antibiotic avoidance — may be more successful than traditional infection control measures that focus on hand hygiene, contact precautions, and isolation, all of which have known compliance issues. Systematic assessment on a specific day of antibiotic therapy, with case-by-case feedback to the critical care team, appears to be a safe, effective, and easily-introduced means to enhance patient outcomes. The recommendations had a high acceptance rate and were associated with highly positive consequences. ■

Cardiac Device-Related Infective Endocarditis

ABSTRACT & COMMENTARY

By John P. DiMarco, MD, PhD

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This article originally appeared in the June 2012 issue of Clinical Cardiology Alert. *It was edited by Michael H. Crawford, MD, and peer reviewed by Ethan Weiss, MD. Dr. Crawford is Professor of Medicine, Chief of Clinical Cardiology, University of California, San Francisco, and Dr. Weiss is Assistant Professor of Medicine, Division of Cardiology and CVRI, University of California, San Francisco. Dr. Crawford reports no financial relationships relevant to this field of study, and Dr. Weiss is a scientific advisory board member for Bionovo.*

Source: Athan E, et al, for the ICE-PCS Investigators. Clinical characteristics and outcome of infective endocarditis involving implantable cardiac devices. *JAMA* 2012;307:1727-1735.

This study reports data from the International Collaboration on Endocarditis-Prospective Cohort Study (ICE-PCS) on the clinical characteristics of infective endocarditis related to pacemakers and ICDs. ICE-PCS collected data on 3284 patients with endocarditis from 64 centers in 28 countries in a central database. Patients were enrolled if they met criteria for possible or definite infective endocarditis based on modified Duke criteria. This study includes only patients with definite infective endocarditis. The major outcomes of interest analyzed were in-hospital and 1-year mortality. Definite cardiac device infected endocarditis (CDIE) was present when valvular or lead vegetations were detected by echocardiography or the Duke criteria for infective endocarditis were met. Nosocomial infections were defined as infective endocarditis cases that developed in a patient hospitalized for more than 48 hours prior to the onset of signs or symptoms. Non-nosocomial health care associated infections were defined if endocarditis developed as a result of a health care intervention, e.g., an indwelling intravascular line. Community-acquired infective endocarditis was defined as those cases that developed before hospitalization or extensive out-of-hospital contact with health care interventions.

CDIE was diagnosed in 177 (6.4%) of the 2760 patients with definite infective endocarditis. This group included 152 patients with permanent pacemakers, 21 with ICDs, and four patients with an unknown type device. The median age was 71.2 years; 27.1% had diabetes mellitus; 74% were male. The most common agents involved were staphylococcal species (*Staphylococcus aureus* — 35.0%; coagulase-negative staphylococci — 31.6%). Vegetations were seen on echocardiography in 159 patients (89.8%), and in 135 patients vegetations were attached to the intracardiac leads. Coexisting valve infection was found in 66 patients. As might be expected, the tricuspid valve was the valve most commonly involved. Concomitant valve infection increased the risk for in-hospital mortality with an odds ratio of 3.31. Device and lead removal was performed in 141 of 177 patients. Thirty patients also underwent valve surgery during the index hospitalization. Twenty-six of the 177 patients (14.7%) died during the index hospitalization. The death rate was 12.8% among those who underwent device removal and 23.5% among those who did not. After hospital discharge, an additional 15 patients died and 10 were lost to follow-up. For the entire group, 126 of 177 patients were alive at 1 year, 41 (22%) had died, and 10 (5.6%) were lost to follow-up. Device removal during the index hospitalization was associated with improved 1-year survival. A presence of concomitant valve infection was found to confer worse survival. The device-related infection was thought to be health care associated in 81 (45.8%) patients with 61 nosocomial and 20 non-nosocomial infections. Health-care-associated infections were more often associated by *S. aureus* and were associated with persistent bacteremia and increased in-hospital mortality.

The authors conclude that cardiac device-related infective endocarditis is frequently associated with health care interventions, has a high rate of complications — especially concomitant valve infection — and results in high in-hospital and 1-year mortality. Device removal is associated with better survival at 1 year.

■ Commentary

There are almost 2 million patients in the United States with pacemakers and ICDs. These patients often live many years with their implanted devices. As a result, the incidence of cardiac device-related infections is rising. As shown in this study, the consequences of a systemic infection involving a cardiac device are very serious with a high in-hospital and 1-year mortality.

Infections that appear within the first year after a device implant are fairly easy to manage. The device and leads can usually be removed easily and safely, and the major problem is treating the infection and supporting the patient until a new device can be implanted. When the device has been in place longer, leads become more difficult to remove and the risks of lead extraction, although low in experienced centers, increase. In current prac-

tice, more device-related infections arise after device generator changes or upgrades than with new implants, so these extraction procedures are often quite complicated.

Prevention of device infection is clearly the most important strategy. Prophylactic antibiotics around the time of device procedures have been shown to be beneficial. Whether prophylactic antibiotics should be used in all device patients undergoing any intravascular procedure or therapy is a question that will have to be addressed in future studies. Extreme caution should be exercised in any cardiac device patients with other indwelling catheters in the hospital. ■

CME / Objectives

Upon completion of this educational activity, participants should be able to:

- discuss pertinent safety, infection control and quality improvement practices;
- explain diagnosis and treatment of acute illness in the hospital setting; and
- discuss current data on diagnostic and therapeutic modalities for common inpatient problems. ■

CME Questions

1. According to the study by Athan and colleagues, what observations were made about cases cardiac device-related infective endocarditis?

a. The cases were frequently associated with healthcare interventions

b. There was a high rate of concomitant valve infections

c. There was a high in-hospital and 1-year mortality

d. All of the above

2. What conclusions can be drawn from the recent retrospective study by Lee, et al. comparing the efficacy of cefazolin and nafcillin in the treatment of methicillin-susceptible Staphylococcus aureus (MSSA) bacteremia:

a. Nafcillin was more effective and safer than cefazolin

b. Cefazolin was more effective and safer than nafcillin

c. Cefazolin should become the drug of choice for MSSA endocarditis with brain emboli because of better penetration across the blood-brain barrier

d. Cefazolin was as equally efficacious as nafcillin while causing fewer adverse drug events

3. In the controlled trial by Elligsen et al., an audit and feedback system of antibiotic use led to what outcomes?

a. Shortened ICU length of stay.

b. Decreased number of C. difficile infections.

c. Decreased mortality.

d. An increase in the number of days of antibiotic use.

CME Instructions

1. Read and study the activity, using the provided references for further research.

2. Log on to **www.cmecity.com** to take a post-test; tests can be taken after each issue or collectively at the end of the semester. *First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice, or renewal notice.*

3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.

4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.

5. Once the evaluation is received, a credit letter will be sent to you. ■