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Does Dual Antibiotic Prophylaxis Better Prevent Surgical Site Infections in Total Joint Arthroplasty?

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Abstract

Introduction It is unclear which antibiotic regimen provides the best prophylaxis against surgical site infection (SSI) in patients undergoing hip and knee surgery.

Questions/purposes Therefore, we determined whether dual antibiotic prophylaxis (1) reduced the rate of SSI compared to single antibiotic prophylaxis and (2) altered the microbiology of SSI.

Methods We retrospectively reviewed 1828 primary THAs and TKAs performed between September 1, 2008 and December 31, 2010. We divided patients into two groups: (1) those who received a dual prophylactic antibiotic regimen of cefazolin and vancomycin (unless allergy), or (2) received cefazolin (unless allergy) as the sole prophylactic antibiotic. There were 701 males and 1127 females with an average age of 56 years (range, 15–97 years). We limited followup to 1 year, presuming subsequent infections were not related to the initial surgery.

Results During this period, there were 22 SSIs (1.2%). The infection rates for dual antibiotic prophylaxis compared to a single antibiotic regimen were 1.1% and 1.4%, respectively. Of 1328 patients treated with dual antibiotic prophylaxis, only one (0.08%) SSI was culture positive for methicillin resistant Staphylococcus aureus (MRSA), while four of 500 patients (0.8%) receiving only cefazolin prophylaxis had culture positive MRSA infection at the time of reoperation.

Conclusion The addition of vancomycin as a prophylactic antibiotic agent apparently did not reduce the rate of SSI compared to cefazolin alone. Use of vancomycin in addition to cefazolin appeared to reduce the incidence of MRSA infections; however, the number needed to treat to prevent a single MRSA infection was very high.

Level of Evidence Level III, therapeutic study. See Guidelines for Authors for a complete description of levels of evidence.

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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Introduction

Periprosthetic infections remain a devastating complication following total joint arthroplasty that has caused considerable pain and morbidity [5, 12, 15, 25, 28, 32]. Infections have accounted for an estimated 15% of revision THAs [6] and up to 25% of revision TKAs [7] performed annually in the United States. The treatment of infected joint arthroplasties tends to be costly and poses substantial burdens to the healthcare system: A revision THA

performed for infection costs on average 2.8 times greater than that performed for aseptic loosening [5, 12, 32]. Furthermore, some authors have reported lower rates of infection control and lower functional scores in patients with infected THA and methicillin resistant organisms [22]. Thus, these numbers have clearly underscored the importance of infection prevention.

Various methods to minimize postoperative infection [11, 15, 38] have included use of antibiotic-impregnated cement [19, 27], laminar flow [2, 23], and minimizing operating room traffic [24]. However, the most effective way to prevent infection has been administering prophylactic antibiotics within 1 hour of surgical incision and continuing its use during the immediate postoperative period [4, 18, 26]. The American Academy of Orthopaedic Surgeons (AAOS) recommended the use of cefazolin or cefuroxime as preferred prophylaxis in TKA and THA, with consideration given to the local incidence of methicillin resistant Staphylococcus aureus (MRSA) [1, 8, 27, 28, 40]. Vancomycin has been recommended when MRSA incidence was greater than 20%, but the use of this antibiotic as a sole prophylactic agent has lead to incomplete skin flora coverage, systemic reactions and toxicity, and antibiotic resistance [27, 40]. Recently, there has been increased attention towards administration of these two prophylactic antibiotics as a strategy to minimize surgical site infections (SSI) [17, 28].

Therefore, the purpose of this study was to determine whether (1) dual antibiotic prophylaxis reduced the rate of SSI compared to single antibiotic prophylaxis, and (2) dual antibiotic prophylaxis altered the microbiology of SSI.

Patients and Methods

We retrospectively reviewed 2215 patients who underwent primary THA or TKA between September 1, 2008 and December 31, 2010. We excluded 325 patients who had drug allergies precluding the use of routine antibiotic prophylaxis (ie, cefazolin or vancomycin), and another 62 patients who received a preoperative antibiotic other than cefazolin or cefazolin plus vancomycin, without a documented allergy. This left 1828 patients for analysis. Five hundred patients received cefazolin alone while 1328 patients received both cefazolin and vancomycin at least within 1 hour prior to incision. There were 1174 primary TKAs and 654 primary THAs. All surgeries were performed by one of four fellowship trained arthroplasty surgeons (GCL, JPG, CLN, CLI). Surgical site infections, defined by the Centers for Disease Control and Prevention (CDC) as an infection occurring at the site of surgery within 30 days from the operative date or up to 1 year if an implant was inserted and the infection appears related to the surgery [18], were identified through the use of the official institutional Clinical Effectiveness and Quality Improvement (CEQI) database [16] for infection control, as well as by review of the medical records for each patient who returned to the operating room for infection within this time period. This data was reported to the state as part of the pay-for-quality incentive program. A total of 22 of 1828 (0.01%) patients developed SSI and returned to the operating room with infections related to their index arthroplasty within 1 year. There were 14 hips and eight knees. The average followup was 18 months (range, 12–24 months). The minimum followup was limited to 12 months, presuming subsequent infections were not related to the initial surgery. No patients were lost to followup. We abstracted patient variables that could impact infection, including age, sex, general health (American Society of Anesthesiologist [ASA] classification), and type of procedure (hip or knee), from each medical record. No patients were recalled specifically for this study; all data was obtained from medical records.

We compared the rate of SSI between the two groups using a Pearson's Chi-square test. Additionally, we examined hips and knees separately by similar methods to determine if the rate of infection was different between the two groups. When there was less than five patients in any cell, we used the Fisher's exact test. Three of the four surgeons (CLI, JPG, CLN) employed dual antibiotic prophylaxis (n = 1328) compared to one surgeon (GCL) who chose cefazolin as the sole prophylactic agent (n = 500). There were no differences between the two groups regarding age, ASA classification, time of cefazolin infusion, and number of hip and knee procedures (Table 1). There were a greater percentage of females in the dual antibiotic group (p = 0.001).

We used Fisher's exact test to determine if the rate of MRSA was different between groups, and conducted a

Table 1. Group demographics

Variable	Cefazolin (n = 500)	Cefazolin and vancomycin (n = 1328)	p value
Average age ± SD (years)	59.6 ± 12.0	60.6 ± 12.5	0.123
Sex			
Male	222	479	0.001
Female	278	849	
ASA class			
1 or 2	275	747	0.631
3 or 4	225	581	
Surgical site			
Knee	311	863	0.268
Hip	189	465	

ASA = American Society of Anesthesiologist.

univariate analysis to determine the effect of potential confounders on the outcome of variable (infection). These variables were tested with Chi-square tests when dichotomous or categorical (ASA class and sex) and a Mann-Whitney U test if they were continuous variables (age). We used multivariate logistic regression to adjust the risk of infection by age, sex, general health (ASA class), type of surgery (hip or knee), and type of antibiotics. A criterion of 0.10 or less on univariate analysis was used as criteria for entry into the model at each step, and a backwards likelihood ratio method was used to automatically remove variables at each step until all variables were significant. Finally, we performed a post-hoc power analysis to detect subtle differences between the two groups. The statistical analysis was performed using SPSS® software version 16.0 (SPSS®, Chicago, IL, USA).

Results

Infection occurred with a similar incidence ($p = 0.636$) in patients who received only cefazolin and patients who received both cefazolin and vancomycin: seven of 500 (1.4%) versus 15 of 1328 (1.1%), respectively. This similar incidence held when looking at the rates of SSI in the THA ($p = 0.570$) and TKA ($p = 0.999$) subgroups. While in univariate analysis age and the joint operated on predicted SSI (Table 2), the multivariate binary logistic regression showed that only the joint operated on predicted SSI, with hips getting SSI more frequently ($p = 0.01$) than knees.

The microbiology of SSI in the two groups differed (Table 3). Patients receiving cefazolin alone were more likely to develop MRSA infections compared to patients receiving cefazolin and vancomycin for prophylaxis. We found a higher percentage ($p = 0.022$) of patients with MRSA positive SSI in patients who received only cefazolin compared to those who received both cefazolin and vancomycin: four of 500 (0.008%) versus one of 500 (0.002%). The number needed to treat with vancomycin additional prophylaxis to prevent one MRSA infection was 138 (CI 101.5, 2828.2). There were no known complications attributed to the use of vancomycin in addition to cefazolin for infection prophylaxis.

Table 2. Demographics of infection groups

Demographic	Non-SSI (n = 1806)	SSI (n = 22)	p value
Average age ± SD (years)	60.4 ± 12.4	55.6 ± 13.6	0.021
Sex			
Male	690	11	0.258
Female	1116	11	
ASA			
1 or 2	1012	10	0.320
3 or 4	794	12	
Surgical site			
Knee	1166	8	0.009
Hip	640	14	
Antibiotic			
Cefazolin	493	7	0.636
Cefazolin and vancomycin	1313	15	

SSI = surgical site infections; ASA = American Society of Anesthesiologist.

Discussion

Surgical site infections have caused substantial morbidity and patient dissatisfaction following joint arthroplasty [3, 10, 34, 41]. Furthermore, these infections have reportedly lead to deep prosthetic infections, requiring additional surgeries at considerable costs to the healthcare system [31, 36]. While various techniques, such as use of laminar flow, antibiotic cement, and minimizing operating room traffic, have helped minimize infections [2, 11, 15, 19, 23, 24, 27, 38], the single most effective strategy for infection reduction has been timely administration of prophylactic antibiotics during the perioperative period [8, 29, 33, 37]. The AAOS recommended use of either cefazolin or cefuroxime as preferred prophylactic agents in patients undergoing primary THA or TKA, with consideration

Table 3. Bacteria cultured in the 22 SSIs[a]

Bacteria	Cefazolin	Cefazolin and vancomycin[b]
No infection	493	1313
Infection		
MRSA[c]	4	1
MSSA	3	6
CNS	0	4
Streptococcus varieties	0	2
Others	3[d]	6[e]

SSI = surgical site infection; MRSA = methicillin resistant Staphylococcus aureus; MSSA = methicillin-sensitive Staphylococcus aureus; CNS = coagulative negative Staphylococcus

[a] There were seven SSI in the cefazolin group. Multiple organisms grew in multiple sites.

[b] There were 15 SSI in the cefazolin and vancomycin group. Multiple organisms grew in multiple sites.

[c] Odds ratio 95% CI, 29.0 (4.0, 593.3); numbers needed to treat 95% CI, 138.0 (101.5, 2828.2).

[d] One each of E coli, Klebsiella, B fragilis.

[e] One each of Diptheria, E aerogenes, Enterococcus, Pseudomonas, Acinectobacer, Proteus.

given to the incidence of MRSA and patient allergies [1, 29, 33, 37]. However, due to changing skin flora and increasing prevalence of MRSA in the community, these cephalosporins may not provide adequate prophylaxis. Therefore, we determined whether dual antibiotic prophylaxis (1) reduced the rate of SSI compared to single antibiotic prophylaxis and (2) altered the microbiology of SSI.

There were several limitations to our study. First, this was a retrospective study with data obtained from medical records and the institutional CEQI data submitted to the state for quality improvement assurance. We did not recall any patients specifically for this study; therefore, it was possible that some patients with SSI were treated at outside hospitals and did not factor into our calculations. Second, most patients receiving cefazolin as the sole prophylactic agent underwent THA and TKA by a single surgeon (GCL), which may have introduced a selection bias. However, because the infection rates varied minimally amongst the four surgeons and the ASA classification of the patients in these two groups were similar, we believed these comparisons to be valid. Third, we did not monitor the effect of increasing vancomycin use on the emergence of resistant organisms. These data were not available to us, but we recognized the importance of these data in order to truly comment on the benefits and/or detriments of single versus dual antibiotic prophylaxis. Fourth, patients in this study were not screened for MRSA or treated for MRSA colonization prior to joint arthroplasty. Patients colonized with MRSA may have been at higher risk of developing postoperative MRSA infection [13, 17, 20]. Also, other factors, in addition to antibiotic choice, could have affected the rate of infection, including host factors (colonization, recent infection) and environmental/social factors (recent hospitalization or nursing home residence). Thus, the pathogenesis of infection was multifactorial and antibiotic choice was one of many factors that could have affected its incidence. Finally, due to the relative paucity of SSI cases, power to detect small changes in infection rate (in this case between 1.4% and 1.1%) required exceptionally large numbers. A post hoc power analysis showed that in order to detect changes this small, assuming a balanced design at 80% power and a 5% Type I error rate, would have required over 8000 patients per group. These numbers, even if they provided a result, would have resulted in a number needed to treat of over 300. This represented a highly clinically inefficient treatment [21]. However, this study had strengths. It was comprised of a large number of patients undergoing primary THA or TKA. We highlighted some of the issues associated with optimizing antibiotic prophylaxis (ie, increasing coverage at the potential expense of increasing resistant organisms). We found that, even for MRSA, treating with vancomycin represented at best an inefficient treatment strategy [21]. A larger, prospective, multicenter study would certainly help answer these questions more definitively.

The use of dual antibiotics (cefazolin and vancomycin) did not decrease the incidence of SSI in patients undergoing primary THA or TKA at our institutions. During the study period, seven patients who received only cefazolin developed a SSI (as defined by the CDC) compared to 15 patients who received both cefazolin and vancomycin (1.4% versus 1.1%). Prior to 2008, patients undergoing THA and TKA at our institution received cefazolin as the sole prophylactic agent, except in cases of drug allergy, in which case vancomycin was usually given. Due to the high incidence of MRSA infections (30%) at our institution, a Committee for Infection Control recommended the addition of vancomycin to the prophylactic regimen. Miller et al. [30] developed a decision analysis model to determine what MRSA prevalence might benefit from the use of vancomycin as antibiotic prophylaxis for cardiothoracic SSIs. Their findings suggested that vancomycin should be considered in populations with MRSA prevalence greater than 3%. Furthermore, Ritter et al. [35] reported on a series of 201 consecutive patients undergoing total joint arthroplasty treated with a single dose of 1 gram of vancomycin and 80 grams of gentamicin. The trough levels of vancomycin up to 24 hours exceeded the minimum inhibitory concentration for all sensitive organisms, and they reported no postoperative infections. Finally, Finkelstein et al. [14] reported similar efficacy between vancomycin and cefazolin in preventing SSIs in 885 patients undergoing cardiac surgery. Consequently, while vancomycin should be considered in settings of high prevalence of MRSA or colonization, the addition of vancomycin to cefazolin in this study did not reduce the incidence of SSIs compared to use of cefazolin alone.

The microbiology of SSIs in patients receiving only cefazolin differed to that of patients treated with a combination of cefazolin and vancomycin. Of the seven SSIs in 500 patients who received only cefazolin, MRSA was isolated in four (0.8%) patients compared to one of 1328 (0.08%) patients who received both cefazolin and vancomycin. The most common infecting organism in patients receiving dual prophylaxis was methicillin-sensitive Staphylococcus aureus (MSSA), followed by MRSA. We found MRSA infection to be more common among patients receiving single prophylaxis. Similar changes in infecting organisms were observed by others [9, 14, 39]. Finkelstein et al. [14] reported in a series of cardiac patients that those receiving cefazolin for prophylaxis were more likely to have infections with beta lactam resistant organisms, and those who received vancomycin were more likely to have methicillin-susceptible Staphylococci. However, while there were no apparent complications of dual antibiotic

therapy in this study, the addition of vancomycin to routine prophylactic regimen should be used with caution: the AAOS has recommended against the routine use of vancomycin because it could promote the development of vancomycin resistant enterococcus (VRE) colonization and infections [1]. Furthermore, it recommended that vancomycin be reserved for the treatment of serious infection with ß-lactam-resistant organisms or for treatment of infection in patients with life-threatening allergy to ß-lactam antimicrobials [1]. So, while the addition of vancomycin to the prophylactic antibiotic regimen did appear to decrease the incidence of MRSA infections in our patient population, the number needed to prevent one single MRSA infection was very high (138). As such, this was clinically inefficient, and the risks of increasing bacterial resistance should be carefully weighed against the benefit of fewer MRSA infections.

In conclusion, dual antibiotic prophylaxis (cefazolin and vancomycin) did not appear to affect the rate of SSI in patients undergoing primary THA and TKA compared to patients receiving single agent prophylaxis (cefazolin only). The addition of vancomycin did alter the profile of the infecting organism, as patients receiving only cefazolin were more likely to get MRSA infections postoperatively compared to those receiving dual prophylaxis. These findings were consistent with those reported in the cardiac literature [14, 39]. However, because the risk of increased bacterial resistance is almost certain and the number needed to treat is so high, we concluded the use of dual antibiotic prophylaxis is not sufficiently effective to reduce infection rates for routine use. Our data support the AAOS position of applying vancomycin prophylaxis only in cases of known MRSA carrier status. Further studies to include preoperative screening and decolonization programs should be performed to ascertain the best antibiotic prophylaxis for patients undergoing elective primary THA and TKA.

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References

1. American Academy of Orthopaedic Surgeons Advisory Statement: Recommendations for the use of intravenous antibiotic prophylaxis in primary total joint arthroplasty. Available at: http://www.aaos.org/about/papers/advistmt/1027.asp. Accessed August 27, 2011.
2. Ayliffe GA. Role of the environment of the operative suite in surgical wound infection. *Rev Infect Dis*. 1991;13(Suppl. 10): S800–S804.
3. Bauer TW, Parvizi J, Kobayashi N, Krebs V. Diagnosis of periprosthetic infection. *J Bone Joint Surg Am*. 2006;88:869–882.
4. Boxma H, Broekhuizen T, Patka P, Oosting H. Randomized control trial of a single dose antibiotic prophylaxis in surgical treatment of closed fractures: the Dutch Trauma Trial. *Lancet*. 1996;347:1133–1137.
5. Bozic KJ, Katz P, Cisternas M, Ono L, Ries MD, Showstack J. Hospital resource utilization for primary and revision total hip arthroplasty. *J Bone Joint Surg Am*. 2005;87:570–576.
6. Bozic KJ, Kurtz SM, Lau E, Ong K, Vail TP, Berry DJ. The epidemiology of revision total hip arthroplasty in the United States. *J Bone Joint Surg Am*. 2009;91:128–133.
7. Bozic KJ, Kurtz SM, Lau E, Ong K, Chiu V, Vail TP, Rubash HE, Berry DJ. The epidemiology of revision total knee arthroplasty in the United States. *Clin Orthop Relat Res*. 2010;468:45–51.
8. Bratzler DW, Houck PM; Surgical Infection Prevention Guideline Writers Workgroup. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Am J Surg*. 2005;189:395–404.
9. Dale WB, Peter MH. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Clin Infect Dis*. 2004;38:1706–1715.
10. Darouiche RO. Treatment of infections associated with surgical implants. *N Engl J Med*. 2004;350:1422–1429.
11. Douglas P, Asimus M, Swan J, Spigelman A. Prevention of orthopaedic wound infections: a quality improvement project. *J Qual Clin Pract*. 2001;21:149–153.
12. Dreghorn CR, Hamblen DL. Revision arthroplasty: a high price to pay. *BMJ*. 1989;296:648–649.
13. Fierobe L, Decré D, Mùller C, Lucet JC, Marmuse JP, Mantz J, Desmonts JM. Methicillin-resistant Staphylococcus aureus as a causative agent of postoperative intra-abdominal infection: relation to nasal colonization. *Clin Infect Dis*. 1999;29:1231–1238.
14. Finkelstein R, Rabino G, Mashiah T, Bar-El Y, Adler Z, Kertzman V, Cohen O, Milo S. Vancomycin versus cefazolin prophylaxis for cardiac surgery in the setting of a high prevalence of methicillin-resistant staphylococcal infections. *J Thorac Cardiovasc Surg*. 2002;123:326–332.
15. Gavin KL, Konigsberg BS. Infection following total knee arthroplasty: prevention and management. *J Bone Joint Surg Am*. 2011;93:1167–1175.
16. Gobran SR, Goldman S, Ferdinand F, Wertan MA, Trace C, Grunkemeier GL, Wu Y, Sutter FP. Outcomes after usage of a quality initiative program for off-pump coronary artery bypass surgery; a comparison with on-pump surgery. *Ann Thorac Surg*. 2004;78:2015–2021.
17. Gupta K, Strymish J, Abi-Haidar Y, Williams SA, Itani KM. Preoperative nasal methicillin-resistant Staphylococcus aureus status, surgical prophylaxis, and risk-adjusted postoperative outcomes in veterans. *Infect Control Hosp Epidemiol*. 2011;32:791–796.
18. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infect Control Hosp Epidemiol*. 1992;13:606–608.
19. Jiranek WA, Hanssen AD, Greenwald AS. Antibiotic-loaded bone cement for infection prophylaxis in total joint replacement. *J Bone Joint Surg Am*. 2006;88:2487–2500.
20. Kim DH, Spencer M, Davidson SM, Li L, Shaw JD, Gulczynski D, Hunter DJ, Martha JF, Miley GB, Parazin SJ, Dejoie P, Richmond JC. Institutional prescreening for detection and eradication of MRS in patients undergoing elective orthopaedic surgery. *J Bone Joint Surg Am*. 2010;92:1820–1826.
21. Laupacis A, Sackett DL, Roberts RS. An assessment of clinically useful measures of the consequences of treatment. *N Engl J Med*. 1988;318:1728–1733.
22. Leung F, Richards CJ, Garbuz DS, Masri BA, Duncan CP. Two stage total hip arthroplasty: how often does it control methicillin-resistant infection? *Clin Orthop Relat Res*. 2011;469: 1009–1015.

23. Lidwell OM, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, Lowe D. Effects of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacement: a randomised study. *Br Med J (Clin Res Ed)*. 1982;285:10–14.
24. Lynch RJ, Englesbe MJ, Sturm L, Bitar A, Budhiraj K, Kolla S, Polyachenko Y, Duck MG, Campbell DA Jr. Measurement of foot traffic in the operating room: implications for infection control. *Am J Med Qual.* 2009;24:45–52.
25. Malangoni MA, Cheadle WG, Dodson TF, Dohmen PM, Jones D, Katariya K, Kolvekar S, Urban JA. New opportunities for reducing risk of surgical site infection. *Surg Infect (Larchmt).* 2006;7(Suppl. 1):S23–S39.
26. Mangram AJ. A brief overview of the 1999 CDC guideline for the prevention of surgical site infection: centers for disease control and prevention. *J Chemother.* 2001;13:35–39.
27. Marculescu CE, Osmon DR. Antibiotic prophylaxis in orthopaedic prosthetic surgery. *Infect Dis Clinic N Am*. 2009;19:931–946.
28. Meehan J, Jamali AA, Nguyen, H. Prophylactic antibiotics in hip and knee arthroplasty. *J Bone Joint Surg Am*. 2009;91:2480–2489.
29. Merrer J, Desbouchages L, Serazin V, Razafimamonjy J, Pauthier F, Leneveu M. Comparison of routine prophylaxis with vancomycin or cefazolin for femoral neck fracture surgery: microbiological and clinical outcomes. *Infect Control Hosp Epidemiol*. 2006;27:1366–1371.
30. Miller LG, McKinnell JA, Vollmer ME, Spellberg B. Impact of methicillin-resistant Staphylococcus aureus prevalence among S. aureus isolates on surgical site infection risk after coronary artery bypass surgery. *Infect Control Hosp Epidemiol*. 2011;32: 342–350.
31. Peel TN, Dowsey MM, Daffy JR, Stanley PA, Choong PF, Buising KL. Risk factors for prosthetic hip and knee infections according to arthroplasty site. *J Hosp Infect*. 2011;79:129–133.
32. Perencevich EN, Sands KE, Cosgrove SE, Guadagnoli E, Meara E, Platt R. Health and economic impact of surgical site infections diagnosed after hospital discharge. *Emerg Infect Dis.* 2003;9: 196–203.
33. Prokuski L. Prophylactic antibiotics in orthopaedic surgery. *J Am Acad Orthop Surg*. 2008;16:283–293.
34. Ridgeway S, Wilson J, Charlet A, Kafatos G, Pearson A, Coello R. Infection of the surgical site after arthroplasty of the hip. *J Bone Joint Surg Br*. 2005;87:844–850.
35. Ritter MA, Barzilauskas CD, Faris PM, Keating PM. Vancomycin prophylaxis and elective total joint arthroplasty. *Orthopedics*. 1989;12:1333–1336.
36. Thomas C, Cadwallader HL, Riley TV. Surgical-site infections after orthopaedic surgery: statewide surveillance using linked administrative databases. *J Hosp Infect*. 2004;57:25–30.
37. Tyllianakis ME, Karageorgos ACh, Marangos MN, Saridis AG, Lambiris EE. Antibiotic prophylaxis in primary hip and knee arthroplasty: comparison between cefuroxime and two specific antistaphylococcal agents. *J Arthroplasty*. 2010;25:1078–1082.
38. van Kasteren ME, Mannien J, Kullberg BJ, de Boer AS, Nagelkerke NJ, Ridderhof M, Wille JC, Gyssens IC. Quality improvement of surgical prophylaxis in Dutch hospitals: evaluation of a multi-site intervention by time series analysis. *J Antimicrob Chemother*. 2005;56:1094–1102.
39. Walsh EE, Greene L, Kirshner R. Sustained reduction in methicillin-resistant Staphylococcus aureus wound infections after cardiothoracic surgery. *Arch Intern Med.* 2011;171:68–73.
40. Wiesel BB, Esterhai JJ. Chapter 4: Prophylaxis of musculoskeletal infection. In Calhoun JJ and Mader JT (eds). *Musculoskeletal Infections*. Marcel Dekker, Inc., New York, NY. 2003;115–129.
41. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med*. 2004;351:1645–1654.