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Microbiological Aetiology, Epidemiology, and Clinical Profile of Prosthetic Joint Infections: Are Current Antibiotic Prophylaxis Guidelines Effective?

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Prosthetic joint infections remain a major complication of arthroplasty. At present, local and international guidelines recommend cefazolin as a surgical antibiotic prophylaxis at the time of arthroplasty. This retrospective cohort study conducted across 10 hospitals over a 3-year period (January 2006 to December 2008) investigated the epidemiology and microbiological etiology of prosthetic joint infections. There were 163 cases of prosthetic joint infection identified. From a review of the microbiological culture results, methicillin-resistant *Staphylococcus aureus* (MRSA) and coagulase-negative staphylococci were isolated in 45% of infections. In addition, polymicrobial infections, particularly those involving Gram-negative bacilli and enterococcal species, were common (36%). The majority (88%) of patients received cefazolin as an antibiotic prophylaxis at the time of arthroplasty. In 63% of patients in this cohort, the microorganisms subsequently obtained were not susceptible to the antibiotic prophylaxis administered. The results of this study highlight the importance of ongoing reviews of the local ecology of prosthetic joint infection, demonstrating that the spectrum of pathogens involved is broad. The results should inform empirical antibiotic therapy. This report also provokes discussion about infection control strategies, including changing surgical antibiotic prophylaxis to a combination of glycopeptide and cefazolin, to reduce the incidence of infections due to methicillin-resistant staphylococci.

Since the advent of prosthetic joint replacement surgery, patients suffering from arthritis have benefited from improvements in mobility and pain relief. With an aging population, it is estimated that the demand for arthroplasty will increase by more than 6-fold by 2030 (16). Infection of the prosthesis remains one of the most devastating complications of this surgery. Prosthetic joint infections are uncommon (1% to 3%); however, they are associated with significant morbidity for patients and with health care costs (5, 32). Treatment remains challenging, with patients often requiring multiple surgical procedures and long-term antibiotic therapy (32). Therefore, strategies to prevent the occurrence of prosthetic joint infection are of paramount importance. Surgical antibiotic prophylaxis is one such strategy. At present, local and international guidelines recommend a single dose of cefazolin at the time of induction based on data from randomized control trials performed in the 1970s and 1980s (1, 6, 9, 14, 26). The guidelines stipulate, however, that the antibiotics chosen as prophylaxis should be selected to cover the most frequently encountered pathogens (6).

This multicenter study was undertaken to examine the epidemiology of prosthetic knee and hip joint replacement infections in a cohort of patients managed in Australian hospitals. The particular focus of this study was to review the causative pathogens encountered and assess the appropriateness of current antibiotic prophylaxis recommendations.

MATERIALS AND METHODS

The study was conducted in Victoria, the second most populous state in Australia. Cases of prosthetic joint infection involving the hip or knee were identified using the database of the Victorian Healthcare Associated Infection Surveillance System (VICNISS). VICNISS is a government-funded independent organization that collates data on health care-associated infections across the state. It is modeled on the U.S. Centers for Disease Control and Prevention (CDC) National Health Safety Network (NHSN) program (15, 31).

The definition of prosthetic joint infection for the purpose of VICNISS surveillance, and for this study, was based on the CDC/NHSN definition of organ or space surgical site infection (SSI). Prosthetic joint infections included in this study met the following criteria. (i) The infection occurred within 365 days of implantation and the infection was related to the operative procedure and (ii) the infection involved any part of the body, excluding the skin incision, fascia, or muscle layers, that was opened or manipulated during the operative procedure and (iii) the patient showed at least one of the following conditions: (a) purulent drainage from a drain that was inserted through a stab wound into the organ or space; (b) the presence of organisms isolated from an aseptically obtained culture of fluid or tissue in the organ or space; (c) an abscess or other evidence of infection involving the organ or space that was found on direct examination, during reoperation, or by histopathological or radiological examination; or (d) diagnosis of an organ or space SSI by a surgeon or attending physician (15, 31).

Because of the need for institutional ethical review at each hospital, hospitals that treated fewer than three prosthetic joint infections per year were excluded from the analysis. The study was reviewed and approved by the Human Research Ethics Committee at each of the participating hospitals.

Data were collected regarding patients who presented with prosthetic joint infection between January 2006 and December 2008. The medical

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TABLE 1 Demographic characteristics

Variable	No. of patients ($n = 163$)
Median age (IQR)	73 (66–79)
Female	96 (59%)
Index arthroplasty site	
Hip	125 (77%)
Knee	38 (23%)
Indication for index arthroplasty	
Primary joint replacement	88 (54%)
Fractured NOF	49 (30%)
Revision arthroplasty for mechanical loosening	19 (12%)
Revision arthroplasty in patient with history of infection	7 (4%)
Median body mass index (IQR)	31.6 (26.6–39.3)
Diabetes mellitus	27 (17%)
Rheumatoid arthritis	11 (7%)
American Society of Anesthesiologists score	
1	5 (3%)
2	51 (31%)
3	92 (57%)
4	14 (9%)

records of each patient were reviewed and summarized on a standardized case report form. The causative organism(s) was determined to be a pathogen if isolated in 2 or more intraoperative specimens or from blood culture. This was cross-referenced with the infectious disease clinician's entry in the medical chart and the microbiological data recorded by VICNISS. Information pertaining to antibiotic prophylaxis was collected, and the appropriateness of the agent employed was evaluated with reference to the antimicrobial susceptibility of subsequently isolated pathogens (12).

Descriptive statistics were used to summarize and report the data. Descriptive analyses were based on percentages and frequencies for categorical variables and for continuous variables, means and standard deviations, or medians and interquartile ranges (IQR) if the data were skewed. Logistic regression analysis was used to produce odds ratios (OR) with 95% confidence intervals (CIs). Multivariate logistic regression models were used in assessment of risk factors by forward stepwise selection of factors identified as significantly associated with outcome in the univariate analysis ($P < 0.1$). All reported P values were two-tailed, and for each analysis, $P < 0.05$ was considered statistically significant. All analyses were performed using Stata 10.1 software (2009; StataCorp, College Station, TX).

RESULTS

The study involved 10 hospitals performing 9,392 prosthetic knee and hip joint replacements over the 3-year period. From a review of the VICNISS database, 188 patients with organ or space infection were identified. After review of the medical charts, 25 patients were excluded from the analysis; the medical charts for 5 patients were unavailable for review, 6 patients had no record of infection, and 14 patients had infections that did not meet the definition of organ or space infection. Therefore, 163 patients were included in the study.

The demographic characteristics of the patients are outlined in Table 1. Most patients underwent hip arthroplasty, with the predominant indication being elective primary arthroplasty (for conditions such as osteoarthritis). Emergency arthroplasty for fracture of the neck of femur (NOF), however, was the next most common indication for arthroplasty. A minority of patients had infections involving knee prostheses. The majority of patients were overweight or obese, with only 25% of patients having a normal weight (body mass index ≤ 25 kg/m^2).

TABLE 2 Clinical features of patients presenting with prosthetic joint infection

Clinical symptom	No. (%) of patients ($n = 163$)
Pain involving the index joint	68 (42)
Fever (≥37.5°C)	62 (38)
Erythema of the surgical wound	68 (42)
Swelling of the surgical wound	40 (25)
Purulent discharge from surgical wound	115 (72)
Sinus tract infection	8 (5)
Hypotension (systolic blood pressure <90 mm Hg)	10 (6)

The antibiotic chosen for surgical prophylaxis at the time of index arthroplasty was recorded for 155 patients (95%). Cefazolin was the most frequently prescribed antibiotic for surgical prophylaxis, with 70% of patients receiving this agent alone; a further 16% received a combination of cefazolin and gentamicin, and 1% received cefazolin plus vancomycin. Vancomycin was administered as a single agent for 6% of the patients and in combination with gentamicin for 1%. Of the remaining patients, 3% received gentamicin and 2% received another antibiotic or antibiotic combination (1 received clindamycin, 1 ceftriaxone, and 1 clindamycin plus gentamicin). The majority (93%) of patients received surgical antibiotic prophylaxis in accordance with local guidelines.

The majority of infections occurred within 3 months of the index arthroplasty (90%), 6% occurred between 3 and 12 months later, and 4% represented an acute hematogenous infection. The median implant age was 20 days (IQR, 14 to 31 days). The duration of symptoms before attention to medical care was short, with a median of 4 days (IQR, 1 to 11 days). Further details on the clinical features are outlined in Table 2. Blood cultures were obtained from 34% of patients and were positive for 40% of those patients. The same microorganism was isolated in blood culture and intraoperative specimens in 91% of cases, the exception being 2 patients with concurrent intra-abdominal sepsis. The most common bacterial species identified by blood culture was *Staphylococcus aureus*, which was isolated from 55% of the patients. In 27% of the patients with positive blood cultures, intraoperative tissue cultures from the joint identified additional bacterial species, particularly enteric flora.

A single causative agent was isolated from intraoperative specimens from the joint space in 57% of the cases, two or more microorganisms were isolated in 36% of the cases, and 7% of the cases were culture negative (6 prosthetic hip replacements and 5 prosthetic knee infections). The etiological agents of prosthetic joint infection and the surgical antibiotic prophylaxis administered at the index arthroplasty are outlined in Table 3. *Staphylococcus aureus* was the most common isolate for both monomicrobial and polymicrobial infections; approximately half were methicillin-resistant isolates. Enterococcus species and Gram-negative bacilli were more commonly associated with polymicrobial infections and were isolated from 37% and 67% of polymicrobial infections, respectively. The spectrum of antibiotic(s)

TABLE 3 Microbiology results for culture-positive prosthetic joint infections and antibiotic prophylaxis spectrum administered at index arthroplasty

Microorganism[a]	Total no. (%) of culture-positive infections (n = 152)	No. (%) of isolates susceptible to antibiotic prophylaxis administered	No. (%) of monomicrobial infections (n = 93)	No. (%) of polymicrobial infections (n = 59)
Gram-positive organisms				
Staphylococcus aureus	86 (57)	48 (56)	48 (52)	38 (64)
MSSA	45 (30)	44 (98)	24 (26)	22 (37)
MRSA	40 (26)	4 (10)	24 (26)	16 (27)
CNS	37 (24)	7 (19)	18 (19)	19 (32)
Methicillin sensitive	4 (3)	4 (100)	3 (3)	1 (2)
Methicillin resistant	33 (22)	3 (9)	15 (16)	18 (31)
Streptococcus species	6 (4)	6 (100)	2 (2)	4 (7)
Enterococcus species	23 (15)	0 (0)	1 (1)	22 (37)
Corynebacterium species	2 (1)	1 (50)	1 (1)	1 (2)
Propionibacterium species	1 (0.7)	.	0 (0)	1 (2)
Total Gram-positive organisms	128 (84)	62 (48)	70 (75)	58 (98)
Gram-negative organisms				
Escherichia coli	17 (11)	15 (88)	4 (4)	13 (22)
Pseudomonas aeruginosa	15 (10)	3 (20)	5 (5)	10 (17)
Enterobacter species	9 (6)	2 (22)	5 (5)	4 (7)
Serratia marcescens	4 (3)	0 (0)	3 (3)	1 (2)
Proteus species	11 (7)	11 (100)	2 (2)	9 (15)
Klebsiella species	4 (3)	4 (100)	2 (2)	2 (3)
Morganella morganii	4 (3)	0 (0)	0 (0)	4 (7)
Acinetobacter species	2 (1)	0 (0)	0 (0)	2 (3)
Anaerobic Gram-negative bacilli	2 (1)	0 (0)	0 (0)	2 (3)
Moraxella catarrhalis	1 (0.7)	1 (100)	1 (1)	0 (0)
Total Gram-negative organisms	63 (42)	36 (57)	23 (25)	40 (67)
Fungal organism				
Candida parapsilosis	1 (0.7)	0 (0)	0 (0)	1 (2)

[a] MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; CNS, coagulase-negative staphylococci.

chosen as the prophylaxis at the index arthroplasty had activity against the organisms subsequently isolated in 37% of patients.

The following factors were associated with prosthetic joint infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) on univariate analysis: nonglycopeptide antibiotic prophylaxis at the index arthroplasty, NOF fracture, nursing home residence prior to arthroplasty, and arthroplasty surgery at hospital 10. On multivariate analysis, arthroplasty infections due to MRSA were associated with fever at presentation and arthroplasty performed at hospital 10.

Polymicrobial prosthetic joint infections were associated with antibiotic prophylaxis spectra without activity against the subsequently isolated organisms, rheumatoid arthritis, and purulent wound discharge at presentation on univariate analysis. On multivariate analysis, rheumatoid arthritis and antibiotic prophylaxis spectra remained independent predictors of polymicrobial infections.

Rheumatoid arthritis was also associated with prosthetic joint infections due to Gram-negative bacilli on univariate and multivariate models. In addition, all patients at hospital 2 had infections with Gram-negative organisms (tables not shown).

DISCUSSION

This report provides information about local ecology and highlights that the causative pathogens of prosthetic joint infections in Victoria, Australia, differ significantly from those reported from other published studies (Table 4). In particular, there were higher rates of polymicrobial infections (36% versus 14%) and isolation of methicillin-resistant staphylococci. Furthermore, this study revealed that the spectrum of pathogens is wide.

Surgical antibiotic prophylaxis was administered in line with local recommendations in the majority of patients in this cohort (1). In two-thirds however, the antibiotic prophylaxis was not active against the pathogens subsequently isolated, particularly methicillin-resistant staphylococci, enterococcus species, and Gram-negative bacilli. This paper provokes debate about the benefit of additional measures to further reduce the incidence of arthroplasty infections, in particular, infections due to methicillin-resistant staphylococci.

In this study, methicillin-resistant staphylococci were isolated in 45% of all prosthetic joint infections. At present, local guidelines recommend cefazolin or flucloxacillin as prophylaxis. Vancomycin is recommended only for patients colonized with MRSA, patients undergoing revision arthroplasty, patients at high risk of MRSA colonization (patients residing in a health care facility for greater than 5 days), and patients with immediate hypersensitivity to beta-lactam antibiotics (1, 6).

The threshold level of MRSA surgical site infections at which a glycopeptide should be included in surgical antimicrobial prophylaxis has not been determined and remains an issue of contention (6, 18). We have documented an infection rate of 1.8%; 45% of those infections were potentially preventable with vancomycin.

TABLE 4 Microbiology results from literature review

Reference	11	20	2	3	24	30	21	29	27	Current study	Total
Publication yr	1977	1989	1991	1998	2000	2000	2007	2008	2008	2012	
Country	USA	USA	Sweden	USA	UK	USA	UK	Australia	USA	Australia	
No. of isolates	42	81	357	462	81	578	112	248	63	163	2,187
No. (%) of coagulase-negative staphylococcal isolates	8 (24)	37 (46)	59 (17)	86 (19)	39 (48)	172 (30)	15 (13)	78 (31)	13 (21)	18 (11)	525 (24)
No. (%) of *Staphylococcus aureus* isolates	10 (19)	19 (23)	149 (42)	101 (22)	11 (14)	135 (23)	26 (23)	53 (21)	23 (38)	47 (29)	574 (26
No. (%) of streptococcus species isolates	5 (12)	12 (15)	17 (6)	42 (9)	8 (10)	51 (9)	6 (5)	17 (7)	8 (13)	2 (1)	168 (8)
No. (%) of enterococcus species isolates	4 (10)	7 (9)	10 (3)	6 (1)	6 (7)	16 (3)	3 (3)	15 (6)	0 (0)	1 (0.6)	68 (3)
No. (%) of diptheroid isolates	0 (0)	6 (7)	5 (1)	3 (0.6)	3 (4)	3 (0.5)	2 (2)	11 (4)	1 (2)	1 (0.6)	35 (2)
No. (%) of Gram-negative bacillus isolates	12 (29)	18 (22)	19 (5)	38 (8)	2 (2)	33 (6)	7 (6)	58 (23)	7 (11)	23 (14)	217 (10)
No. (%) of propionibacterium species isolates	1 (2)	1 (1)	1 (0.3)	0 (0)	2 (2)	0 (0)	0 (0)	1 (0.4)	0 (0)	0 (0)	6 (0.3)
No. (%) of polymicrobial isolates	11 (26)	0 (0)	55 (15)	88 (19)	10 (12)	71 (12)	53 (33)	0 (0)	4 (6)	59 (36)	351 (16)
No. (%) of anaerobe isolates	1 (2)	7 (9)	8 (2)	6 (1)	0 (0)	23 (4)	3 (3)	4 (2)	0 (0)	0 (0)	52 (2)
No. (%) of isolates of other infectious species	19 (19)	3 (4)	1 (0.3)	7 (2)	0 (0)	10 (2)	1 (1)	8 (3)	0 (0)	1 (0.6)	50 (2)
No. (%) of culture negative isolates	2 (2)	2 (2)	29 (8)	5 (1)	0 (0)	64 (11)	7 (5)	0 (0)	6 (10)	12 (7)	127 (6)

If the effectiveness of vancomycin for this group is 50%, based on reported studies in the literature, we estimate the number needed to treat at around 150 (10, 17). There are no randomized clinical trials currently investigating the use of glycopeptide for surgical antibiotic prophylaxis in arthroplasty. Vancomycin, however, has been studied as a prophylactic antibiotic for use in cardiothoracic surgery. In a study by Finkelstein et al., vancomycin was compared to cefazolin for treatment of patients undergoing sternotomy (10). Those authors concluded that the antibiotics had similar levels of efficacy; however, there was a significant increase in the levels of methicillin-susceptible staphylococci in patients receiving vancomycin. In addition, there was a trend toward an increase in the number of methicillin-resistant staphylococcal infections in patients receiving cefazolin (10). The results of the study by Finkelstein et al. suggest that surgical prophylaxis with vancomycin alone may be problematic. Whether the administration of combined vancomycin and cefazolin would be beneficial has not been established. Economic modeling of patients undergoing hip arthroplasty suggests that combination prophylaxis with vancomycin and cefazolin would be cost-effective where the MRSA infection rate is $\geq$0.25% and the rate of other infections treated with cefazolin prophylaxis is $\geq$0.2% (7, 8). Therefore, given the rate of MRSA infection in this current study, combination prophylaxis with vancomycin and cefazolin may be cost-effective. This, however, raises concerns about problems associated with the use of vancomycin, including adverse reactions, bacterial resistance, and the need for slow infusion and optimal timing (19). Studies of the efficacy and cost of alterative agents, including teicoplanin and daptomycin, are not yet available to guide us. Similarly, information regarding the value of antibiotic prophylaxis with broader coverage against Gram-negative bacilli is lacking. Importantly, this study did not focus on other preventative strategies such as hand hygiene, MRSA decolonization, and preoperative screening for other active infections, in particular, skin and soft tissue infections, or on the use of antibiotic-impregnated cement (6, 13, 19, 32).

This paper is pertinent to clinicians to assist and guide empirical antibiotic choice for management of patients with prosthetic joint infection. At present, no such guidelines exist. Empirical antibiotic therapy should be tailored to the local ecology. Given the high rate of isolation of methicillin-resistant organisms and the large number of infections involving Gram-negative organisms, this report suggests that empirical antibiotic therapy for patients who present with prosthetic joint infection should include a glycopeptide and an antipseudomonal beta-lactam antibiotic.

We found a high rate of MRSA in this current study. In studies from Europe and the Americas, MRSA strains have been shown to be the causative agent in 8% to 30% of prosthetic joint infections (21, 25, 27). It is acknowledged, however, that rates of such infections can differ between institutions, as perhaps highlighted by the association between hospital 10 and MRSA prosthetic joint infections (21). MRSA is endemic in Australian hospitals. The Australian Group for Antimicrobial Resistance (AGAR) found that MRSA accounted for 31.9% of all nosocomial *Staphylococcus aureus* isolates (23). Other single centers in Australia have reported MRSA rates in arthroplasty patients. In a study by Sharma et al., the microorganisms encountered in 147 patients undergoing revision arthroplasty at Prince Charles Hospital, Brisbane, Australia, were described (29). Only 11% of *Staphylococcus aureus* isolates were methicillin resistant. Those authors, however, examined the microbiology results of patients undergoing revision knee and hip arthroplasty. In addition, the paper did not differentiate whether included patients had suspected or proven prosthetic joint infection or whether the isolates were clinically significant or potential contaminants. This may account for some of the differences observed. From the current study, there was an association between patients presenting with fever and subsequent isolation of MRSA; therefore, caution is warranted with respect to treatment of a febrile patient postarthroplasty and consideration of antibiotics with activity against MRSA.

With respect to polymicrobial prosthetic joint infections, the majority comprised mixed infections with Gram-negative and Gram-positive organisms, with a prominence of enteric bacteria. This contrasts with the common perception that the majority of prosthetic joint infections are monomicrobial infections due to *Staphylococcus aureus* (1, 32). In fact, in this cohort only 29%

(48/163) of infections fell into that group. In the current study, rheumatoid arthritis was a predictor of polymicrobial prosthetic joint infections. Rheumatoid arthritis has been previously implicated in the development of prosthetic joint infections; however, the association with polymicrobial infections had not been previously described (4). It is possible that this represents an interplay between the disease, immunosuppression, and impaired wound healing. In a study by Berbari et al. in patients with rheumatoid arthritis, polymicrobial infections were associated with a worse outcome in univariate survival analysis (4).

There are several limitations to this current report. First, as in all retrospective studies, there is a potential for variability in reports of clinical data provided by treating clinicians and infection control practitioners. We attempted to minimize bias through *a priori* definitions and data collection by a single researcher. Second, the definition for prosthetic joint infection used includes only patients with infections occurring within 1 year of implantation. It is recognized that the causative agents of prosthetic joint infections presenting after 365 days differ from the causative agents of early and hematogenous infections (32). Therefore, the results of this study cannot be extrapolated for application to delayed and late prosthetic joint infections. Third, as previously stated, this report describes the ecology of prosthetic joint infections in Victoria, Australia, and it may not be appropriate to generalize the findings to other populations. However, increasing rates of methicillin-resistant organisms in prosthetic joint infections have been reported in other countries (21, 22, 28).

Given an aging population and the increasing demand for arthroplasty, prosthetic joint infections will continue to present a challenge to clinicians. This report provides vital information about the causative agents of prosthetic joint infections, highlighting the high rate of polymicrobial and MRSA infections encountered. This information should inform management guidelines, particularly with respect to empirical antibiotic therapy for patients with prosthetic joint infection. It raises questions about whether current preventative strategies, in particular, antibiotic prophylaxis guidelines, can be optimized to further reduce the risk of prosthetic joint infections. Combination surgical antibiotic prophylaxis with cefazolin plus vancomycin may be beneficial in this population, but further studies of the efficacy, tolerability, and cost of these combinations are required. This report highlights the importance of ongoing surveillance of local ecology to inform guidelines. While this report focuses on local data, the microbiological trends observed are likely to be similar to those of other centers worldwide.

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REFERENCES

1. **Antibiotic Expert Group.** 2010. Therapeutic guidelines: antibiotic, 14th ed. Therapeutic Guidelines Limited, Melbourne, Australia.
2. **Bengtson S, Knutson K.** 1991. The infected knee arthroplasty. Acta Orthop. Scand. **62**:301–311.
3. **Berbari EF, et al.** 1998. Risk factors for prosthetic joint infection: case-control study. Clin. Infect. Dis. **27**:1247–1254.
4. **Berbari EF, et al.** 2006. Outcome of prosthetic joint infection in patients with rheumatoid arthritis: the impact of medical and surgical therapy in 200 episodes. Clin. Infect. Dis. **42**:216–223.
5. **Bozic KJ, Ries MD.** 2005. The impact of infection after total hip arthroplasty on hospital and surgeon resource utilization. J. Bone Joint Surg. **87**:1746–1751.
6. **Bratzler DW, Houck PM.** 2004. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. Clin. Infect. Dis. **38**:1706–1715.
7. **Cranny G, et al.** 2008. A systematic review and economic model of switching from non-glycopeptide to glycopeptide antibiotic prophylaxis for surgery. Health Technol. Assess. **12**:1–147.
8. **Elliott RA, et al.** 2010. An economic model for the prevention of MRSA infections after surgery: non-glycopeptide or glycopeptide antibiotic prophylaxis? Eur. J. Health Econ. **11**:57–66.
9. **Ericson C, Lidgren L, Lindberg L.** 1973. Cloxacillin in the prophylaxis of postoperative infections of the hip. J. Bone Joint Surg. **55**:808–843.
10. **Finkelstein R, et al.** 2002. Vancomycin versus cefazolin prophylaxis for cardiac surgery in the setting of a high prevalence of methicillin-resistant staphylococcal infections. J. Thorac. Cardiovasc. Surg. **123**:326–332.
11. **Fitzgerald RH, et al.** 1977. Deep wound sepsis following total hip arthroplasty. J. Bone Joint Surg. **59**:847–855.
12. **Giulieri SG, Graber P, Ochsner PE, Zimmerli W.** 2004. Management of infection associated with total hip arthroplasty according to a treatment algorithm. Infection **32**:222–228.
13. **Hacek DM, et al.** 2008. Staphylococcus aureus nasal decolonization in joint replacement surgery reduces infection. Clin. Orthop. Relat. Res. **466**:1349–1355.
14. **Hill C, Flamant R, Mazas F, Evrard J.** 1981. Prophylactic cefazolin versus placebo in total hip replacement. Report of a multicentre double-blind randomised trial. Lancet **i**:795–797.
15. **Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG.** 1992. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Am. J. Infect. Control **20**:271–274.
16. **Kurtz S, Ong K, Lau E, Mowat F, Halpern M.** 2007. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J. Bone Joint Surg. **89**:780–785.
17. **Maki DG, et al.** 1992. Comparative study of cefazolin, cefamandole, and vancomycin for surgical prophylaxis in cardiac and vascular operations. A double-blind randomized trial. J. Thorac. Cardiovasc. Surg. **104**:1423–1434.
18. **Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR.** 1999. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. Infect. Control Hospit. Epidemiol. **20**:250–278.
19. **Marculescu CE, Osmon DR.** 2005. Antibiotic prophylaxis in orthopedic prosthetic surgery. Infect. Dis. Clin. North Am. **19**:931–946.
20. **McDonald DJ, Fitzgerald RH, Ilstrup DM.** 1989. Two-stage reconstruction of a total hip arthroplasty because of infection. J. Bone Joint Surg. **71**:828–834.
21. **Moran E, Masters S, Berendt AR, McLardy-Smith P, Byren I, Atkins BL.** 2007. Guiding empirical antibiotic therapy in orthopaedics: the microbiology of prosthetic joint infection managed by debridement, irrigation and prosthesis retention. J. Infect. **55**:1–7.
22. **National Nosocomial Infections Surveillance (NNIS) System.** 2004. National Nosocomial Infections Surveillance (NNIS) system report, data summary from January 1992 through June 2004, issued October 2004. Am. J. Infect. Control **32**:470–485.
23. **Nimmo GR, et al.** 2007. Prevalence of MRSA among Staphylococcus aureus isolated from hospital inpatients, 2005: report from the Australian Group for Antimicrobial Resistance. Commun. Dis. Intell. **31**:288–296.
24. **Pandey R, Berendt AR, Athanasou NA.** 2000. Histological and microbiological findings in non-infected and infected revision arthroplasty tissues. Arch. Orthop. Traum. Surg. **120**:570–574.
25. **Parvizi J, et al.** 2008. Periprosthetic infection: are current treatment strategies adequate? Acta Orthop. Belg. **74**:793–800.
26. **Prokuski L.** 2008. Prophylactic antibiotics in orthopaedic surgery. J. Am. Acad. Orthop. Surg. **16**:283–293.
27. **Pulido L, et al.** 2008. Periprosthetic joint infection: the incidence, timing, and predisposing factors. Clin. Orthop. Relat. Res. **466**:1710–1715.

28. **Salgado CD, Dash S, Cantey JR, Marculescu CE.** 2007. Higher risk of failure of methicillin-resistant Staphylococcus aureus prosthetic joint infections. Clin. Orthop. Relat. Res. **461**:48–53.
29. **Sharma D, Douglas J, Coulter C, Weinrauch P, Crawford R.** 2008. Microbiology of infected arthroplasty: implications for empiric perioperative antibiotics. J. Orthop. Surg. (Hong Kong) **16**:339–342.
30. **Steckelberg JM, Osmon DR.** 2000. Prosthetic joint infections, p 173–209. *In* Waldvogel FA, Bisno AL (ed), Infections associated with indwelling medical devices, 3rd ed. ASM Press, Washington, DC.
31. **VICNISS.** December 2011, posting date. VICNISS healthcare associated infection surveillance. VICNISS Coordinating Centre, North Melbourne, Australia. http://www.vicniss.org.au/.
32. **Zimmerli W, Trampuz A, Ochsner PE.** 2004. Prosthetic-joint infections. N. Engl. J. Med. **351**:1645–1654.