

The Impact of Patient-Reported Penicillin Allergy on Risk for Surgical Site Infection in Total Joint Arthroplasty

Andrea H. Stone, MSN, CRNP
Grayson Kelmer
James H. MacDonald, MD
Mary R. Clance, MD, MPH
Paul J. King, MD

From the Department of Surgical Research (Ms. Stone and Ms. Kelmer), Anne Arundel Medical Center, the Center for Joint Replacement (Dr. MacDonald and Dr. King), Anne Arundel Medical Center, and Anne Arundel Medical Center (Dr. Clance), Annapolis, MD.

Correspondence to Dr. King:
pking@osmc.net

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Abstract

Background: Penicillin (PCN) allergy is reported in 10% to 20% of the population; studies show that only 1% to 3% of patients have a true allergy. Most patients reporting a PCN allergy receive second-line antibiotic prophylaxis preoperatively, which raises concerns about antimicrobial efficacy. Studies also suggest that second-line antibiotics may increase the rate of surgical site infection (SSI). In this study we aim to analyze the effect of PCN allergy on antibiotic type prescribed and SSI in our total joint arthroplasty population.

Methods: A retrospective review of 4,903 primary total hip and total knee arthroplasty performed from January 2015 to June 2017 in a single institution. A detailed chart review was performed to identify reported reactions and antibiotic prescribed.

Results: Seven hundred ninety-six patients (16.2%) reported a PCN allergy; the reactions were classified into three tiers. Six hundred fifteen patients (12.5%) reported an IgE-mediated allergy, hypersensitivity, or a possible allergy; 89 (1.8%) reported an adverse effect; and 92 (1.9%) had an unknown reaction. Patients reporting a PCN allergy were less likely to receive cefazolin (94.9 versus 6.9%; $P < 0.001$) and more likely to receive clindamycin (1.1 versus 80.7%; $P < 0.001$) or vancomycin (4.0 versus 12.4%; $P < 0.001$). There was no difference in infection rate by reported PCN allergy (0.6 versus 0.4%; $P = 0.473$) or antibiotic prescribed (0.5 versus 0.6%; $P = 0.4817$).

Conclusion: No patient with a PCN allergy and given cefazolin experienced a reaction; based on reported reactions, most patients with a PCN allergy can safely receive first-line antibiotic therapy. In this population, PCN allergy and second-line antibiotic therapy did not influence the rate of SSI.

Primary total hip arthroplasty (THA) and total knee arthroplasty (TKA) are two most common surgical procedures performed in the United States, with the number of surgeries performed yearly expected to increase substantially over the next decades.¹⁻³ Surgical Care Improve-

ment Project (SCIP) guidelines were established in 2006 to improve compliance with infection control measures during the perioperative period and include guidelines on the timing and selection of appropriate antibiotic therapy.⁴ Cefazolin is the first-line recommended antibiotic for

total joint arthroplasty (TJA), with clindamycin and vancomycin commonly used as alternatives.⁵ Vancomycin is also recommended for patients with a history of or at high risk for methicillin-resistant *Staphylococcus aureus* (MRSA) infections and is often used in combination with other antibiotics since there is evidence that cefazolin is more effective at preventing methicillin-sensitive *S aureus* infections.⁵⁻⁷

Approximately 10% to 20% of patients report an allergy or reaction to penicillin (PCN), yet these responses are rarely true immunoglobulin E (IgE)-mediated or hypersensitivity reactions and most of these patients could safely be prescribed with PCN.⁸⁻¹⁰ Studies have shown that 80% to 99% of patients with a reported PCN allergy could have that label removed after appropriate testing.¹¹⁻¹³ Avoiding cephalosporins to patients with a reported PCN allergy has been recommended in the past because of their similar chemical structure and a reported cross-reactivity between these medications, although more recent studies suggest that the cross-reactivity between these two drug classes is overstated, with only 2.55% of patients with a confirmed PCN allergy also having a confirmed cephalosporin allergy.^{14,15} With the rise of drug-resistant organisms and concerns regarding clinical efficacy, responsible antibiotic stewardship advises that we increase the use of targeted antibiotic therapy where possible.¹⁶

For patients undergoing TJA, surgical site infections (SSIs) occurred in 0.58% to 2.5% of procedures.¹⁷⁻¹⁹ Patient-reported allergies contribute to unfavorable outcomes, in part due to the administration of less effective antibiotics.²⁰⁻²² A recent study determined that reporting a PCN allergy increased the risk of SSI by 50% in an analysis of more than 9,000 procedures in four major surgical specialties.²³ Patient-reported

PCN allergy has been associated with a higher risk of adverse outcomes in TJA.^{24,25} The impact of patient-reported PCN allergy on the infection rate of TJA specifically has not been well studied; in this study, we will analyze patient-reported PCN allergies and reactions and their influence on prescribing patterns of perioperative antibiotics and the risk of acute (≤ 90 days) postoperative SSI.

Methods

We obtained institutional review board approval and performed a retrospective chart review for a consecutive series of patients who underwent primary unilateral THA or TKA in this institution between January 2015 and June 2017. The 14 board-certified orthopedic surgeons performed the surgeries. Data were collected via an administrative database for patient demographics including age, gender, race, and body mass index, procedure performed, perioperative antibiotic given, length of stay, and discharge disposition. The American Society of Anesthesiologist score and select comorbidities were used to quantify preoperative health status. A detailed chart review was performed on all patients who reported a PCN allergy to identify the nature of the reaction reported. National Healthcare Safety Network criteria were used to identify SSI.

Perioperative Protocol

All patients were subjected to the same perioperative protocols in a coordinated Joint Replacement Center Program. All patients underwent a standard decolonization protocol with the administration of intranasal mupirocin ointment twice daily and chlorhexidine body wash both for 3 days before surgery. They also received parenteral antibiotics per the SCIP guidelines. There was no routine MRSA screening as all patients

underwent preoperative decolonization. Preoperative antibiotics were prescribed using SCIP guidelines; cefazolin was the first-line antibiotic and clindamycin and vancomycin were the alternative medications. Clindamycin was prescribed for patients reporting a PCN or cefazolin allergy, and vancomycin was used primarily for patients with a history of MRSA colonization or infection. The use of cefazolin in addition to vancomycin was phased in during the study period with the publication of new recommendations regarding patients with a history of MRSA infection or colonization. SSI was defined as any patient undergoing revision surgery for deep or joint space infection with a positive tissue culture in the first 90 days postoperatively.

Study Population

The study included 4,903 consecutive TJA patients. All TKAs (3,126 patients) were performed via a standard medial patellar arthrotomy, posterior approach THA (516 patients) in the lateral decubitus position and anterior approach THA (1,261 patients) using a modern fracture table.

Study Outcomes

The primary outcome was the influence of patient-reported PCN allergy on the rate of SSI. Secondary outcomes were the influence of antibiotic prescribed on the rate of SSI and the influence of patient-reported allergy or adverse reaction on the antibiotic prescribed.

Statistical Analysis

A series of chi-squared tests, *t*-tests and analysis of variance were used to determine the differences between groups. Multiple logistic regression was used to identify the factors independently predicting the differences. A *P*-value less than or equal to 0.05 was treated as statistically

Table 1

Demographics				
	All Patients, (n = 4,903)	No PCN Allergy, n = 4,107 (83.8%)	PCN Allergy, n = 796 (16.2%)	Sig.
Age, yr, mean $\pm$ SD	66.55 $\pm$ 9.65	66.33 $\pm$ 9.67	67.68 $\pm$ 9.48	<0.001
BMI, kg/m ² , mean $\pm$ SD	31.42 $\pm$ 6.14	31.39 $\pm$ 6.13	31.58 $\pm$ 6.20	0.439
Sex, n (%)				<0.001
Female	2,888 (58.9)	2,332 (56.8)	556 (69.8)	
Male	2,015 (41.1)	1,775 (43.2)	240 (30.2)	
Race, n (%)				0.017
White	4,089 (84.1)	3,411 (83.8)	678 (85.7)	
African American	724 (14.9)	621 (15.3)	103 (13.0)	
ASA, n (%)				0.009
1	78 (1.6)	71 (1.7)	7 (0.9)	
2	2,781 (56.7)	2,363 (57.5)	418 (52.5)	
3	2,006 (40.9)	1,641 (40.0)	365 (45.9)	
4	38 (0.8)	32 (0.8)	6 (0.8)	
Procedure, n (%)				0.083
Hip	1,777 (36.2)	1,510 (36.8)	267 (33.5)	
Knee	3,126 (63.8)	2,597 (63.2)	529 (66.5)	
LOS, d, mean $\pm$ SD	1.84 $\pm$ 1.17	1.81 $\pm$ 1.14	1.99 $\pm$ 1.27	<0.001
Discharge disposition, n (%)				<0.001
Home	4,044 (82.5)	3,424 (83.4)	620 (77.9)	
Rehab	859 (17.5)	683 (16.6)	176 (22.1)	
Total comorbidities, mean $\pm$ SD	1.69 $\pm$ 1.22	1.69 $\pm$ 1.23	1.67 $\pm$ 1.20	0.688

ASA = American Society of Anesthesiologist, BMI = body mass index, LOS = length of stay, PCN = penicillin.
P $\leq$ 0.05 in bold.

significant. All analyses were performed using SPSS (SPSS 24.0, IBM).

Results

Of the total population, 796 patients (16.2%) reported a PCN allergy. Table 1 compares the demographic data between groups with patients reporting a PCN allergy being older (66.3 versus 67.7 years; *P* < 0.001), more likely to be female (56.8 versus 69.8%; *P* < 0.001), and more likely to be white (83.8 versus 85.7%; *P* = 0.017). Patient-reported allergic reactions were classified into three tiers based on the severity of the reaction reported (Table 2). Tier 1 included reactions that occurred in an IgE-mediated allergic response, hypersensitivity reactions, and possible

allergic reactions. Six hundred fifteen patients (77.2%) reporting an allergy were included in this group, with 208 patients reporting hives, 199 patients reporting rash, 65 patients reporting angioedema, and 60 patients reporting anaphylaxis. Tier 2 reactions (89 patients) were primarily side effects, most commonly gastrointestinal related, and tier 3 were unknown or unspecified reactions.

Twenty-two patients (0.5%) were diagnosed with an infection in the first 90 days postoperatively (Table 3). There was no significant difference in infection rates between patients reporting a PCN allergy and those who did not (0.6 versus 0.4%; *P* = 0.408). There was also no significant difference in infection rates when looking at the preoperative antibiotic prescribed; 19 patients (0.5%) pre-

scribed cefazolin and 4 patients (0.6%) receiving clindamycin developed an infection, and no patients prescribed vancomycin developed an infection (*P* = 0.479).

Cefazolin was used as the primary antibiotic in 3,953 patients (80.6%), clindamycin was used in 686 patients (14.0%), and vancomycin was used in 264 patients (5.4%) (Figure 1). Most patients in the study received only one type of antibiotic (*n* = 4,733; 96.5%), and all patients receiving a second antibiotic received vancomycin. Vancomycin was used in isolation in 94 patients (1.9%). Most patients reporting a PCN allergy received a second-line antibiotic, with 642 patients (80.7%) receiving clindamycin and 99 patients (12.4%) receiving vancomycin. Fifty-five patients (6.9%) with a reported

Table 2**Reported Reactions by Tier**

Reaction Tiers	N	% of Reactions
Tier 1: Severe reactions and hypersensitivities	615	77.2
Hives	208	26.1
Rash	199	25.0
Swelling, angioedema	65	8.2
Anaphylaxis	60	7.5
Respiratory distress, stridor, palpitations	32	4.0
Itching	31	3.9
Syncope/hypotension	7	0.9
Blisters, boils, sores, SJS	5	0.6
Flushing, burning	5	0.6
Convulsions	2	0.3
Paralysis	1	0.1
Tier 2: Side effects and intolerances	89	11.2
Diarrhea, nausea/vomiting, GI symptoms	70	8.8
Musculoskeletal symptoms	8	1.0
Mental status change, headache	5	0.6
Oral thrush, yeast infection	3	0.4
<i>Clostridioides difficile</i>	2	0.3
Exacerbation of existing condition	1	0.1
Tier 3: Unknown or unspecified	92	11.6
Unknown	58	7.3
Childhood reaction	29	3.6
Family reaction	5	0.6

GI = gastrointestinal, SJS = Stevens-Johnson syndrome.

PCN allergy received cefazolin (Table 4); most of these patients reported a tier 2 or 3 reaction to PCN ($n = 30$; 54.5%). No patient who reported a PCN allergy and received cefazolin experienced an allergic or adverse reaction to this medication.

Multiple logistic regression (Table 5) was used to identify independent predictors of PCN allergy reporting. Female sex was the most significant predictor, with women being 1.74 times more likely to report a PCN allergy with all other factors held constant (95% confidence interval [CI], 1.67 to 2.07; $P < 0.001$). Higher American Society of Anesthesiologist score (adjusted odds ratio [aOR] 1.23; 95% CI, 1.04 to 1.46; $P = 0.015$), increasing age (aOR 1.01; 95% CI, 1.00 to 1.02; $P = 0.047$), and white race (aOR 1.26; 95% CI, 1.00 to 1.60; $P = 0.049$) were also significant predictors.

Discussion

Inappropriate prescription of antibiotics is a significant national concern, with the Centers for Disease Control and Prevention stating that 20% to 50% of all antibiotics used in hospitals were either inappropriately prescribed or not needed.²⁶ In 2017 the Joint Commission mandated that all hospitals have an antibiotic stewardship program in place to reduce inappropriate prescription of antibiotics.²⁷ Patient-reported PCN allergy frequently leads to the use of alternative antibiotics, which increases the risk of adverse medication effects and increased rates of drug-resistant infections.^{13,28} Failure to question the PCN allergy label influences the choice of antibiotics both in and outside of the OR and can have a long-standing impact on clinical outcomes. Consistent with the rates reported in the general population, one in six patients in this

Table 3**Infections**

Factor	Infections, N (%)	Sig.
Allergy		0.408
None	17 (0.4)	
PCN	5 (0.6)	
Reaction		0.431
None	17 (0.4)	
Tier 1	5 (0.8)	
Tier 2	0 (0.0)	
Tier 3	0 (0.0)	
Primary antibiotic		0.479
Cefazolin	18 (0.5)	
Clindamycin	4 (0.6)	
Vancomycin	0 (0.0)	
Total	22 (0.5)	

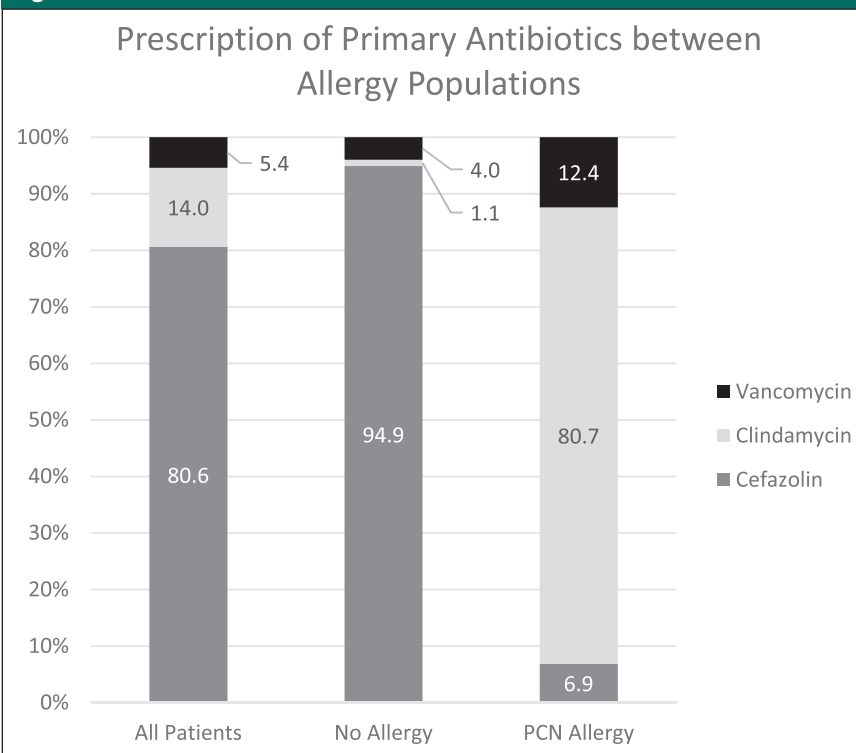
PCN = penicillin

study reported a PCN allergy, although the rate of true allergy is likely much lower.⁸⁻¹⁰ Even when isolating the most severe reaction tier, this group is almost eight times larger than the number of patients who would be expected to have a true allergy.

The frequency of PCN allergy reporting and the finding that allergy reporting results in the use of alternative antibiotics indicate a need for allergy delabeling and possibly PCN allergy testing. In addition, patients who have had a documented IgE-mediated allergic reaction to PCN may be able to tolerate the medication in the future due to the disappearance of the IgE-mediated hypersensitivity over time.^{10,29} Improved documentation of medication allergy versus adverse reactions would enable providers to more accurately identify patients who are truly PCN allergic and improve the rate of prescribing more effective antibiotic therapy. In this study, more than 50% of patients reporting a PCN allergy had a tier 2 or 3 reaction and could have safely received cefazolin without further query; 55 patients with a documented PCN allergy did receive cefazolin with no adverse reactions. Patient and provider education on which reactions constitute a true allergy would also assist in allergy de-labeling. Secondly, PCN skin testing and oral antibiotic challenges can be performed to identify the safe antibiotics and to delabel appropriate patients.^{11,28,30}

Other studies have determined varying relationships between the prescription of alternative antibiotics and incidence of SSI. Blumenthal et al found 50% increased odds of SSI in patients who reported a PCN allergy, mediated by the prescription of alternative antibiotics. However, this study was unable to perform a fully powered analysis of infections in TJA patients, and instead analyzed patients who underwent THA, TKA, hysterectomy, colon surgery, and coronary artery bypass grafting as a

Figure 1



Prescription of antibiotics between allergy populations.

Table 4

Prescription of Antibiotics by Reaction Tier

Reaction	Primary Antibiotic, N (%)		
	Cefazolin	Clindamycin	Vancomycin
None	3,898 (94.9)	44 (1.1)	165 (4.0)
Tier 1	13 (3.4)	326 (85.8)	41 (10.8)
Tier 2	12 (5.1)	186 (79.1)	37 (15.7)
Tier 3	27 (30.3)	54 (60.7)	8 (9.0)
Tier 4	3 (3.3)	76 (82.6)	13 (14.1)
Total	3,953 (80.6)	686 (14.0)	264 (5.4)

whole.²³ More direct analyses of the impact of different antibiotics on SSI in TJA have found no difference in the risk of deep SSI between patients prescribed cefazolin or vancomycin or have attributed any differences to problems in administering the proper dosage of vancomycin.^{20,31} Factors such as inappropriate timing and dosing of antibiotics increase infection rates but are not necessarily

indicative of reduced effectiveness of the antibiotic itself.^{31,32} Our study found no difference in the rate of infection between PCN allergic or nonallergic patients, although this analysis is underpowered because of the small effect size due to the low rate of overall infection.

This study does have some limitations. Over the course of the study vancomycin use in patients changed

Table 5

Multiple Logistic Regression for Predictors of Penicillin Allergy Reporting

	Adjusted OR	95% CI	Sig.
Female	1.74	1.47-2.07	< 0.001
Age, yr	1.01	1.00-1.02	0.047
White	1.26	1.00-1.60	0.049
ASA	1.23	1.04-1.46	0.015
BMI, kg/m ²	1.00	0.99-1.02	0.670
Discharge disposition	1.10	0.87-1.39	0.421
LOS, d	1.06	0.99-1.14	0.114
Hip or knee	1.14	0.96-1.34	0.143
Hypertension	0.91	0.77-1.08	0.266
Hyperlipidemia	1.02	0.86-1.21	0.807
Diabetes	0.81	0.66-1.01	0.058
Coronary artery disease	1.07	0.78-1.47	0.677
Smoking history	0.93	0.72-1.19	0.543

ASA = American Society of Anesthesiologist, BMI = body mass index, CI = confidence interval, LOS = length of stay, OR = odds ratio
P ≤ 0.05 in bold.

with a reported allergy or history of MRSA colonization or infection. More importantly, the overall infection rate was 22 of 4,903 procedures (0.5%), which left our study underpowered to detect the effect of allergy and reaction reporting and primary antibiotic prescription on infection risk. A sufficiently powered study would be difficult to perform at a single institution because of the low rate of infection associated with TJA. A multi-institution or registry analysis could potentially provide the sample size necessary to perform an adequately powered analysis on the effect of patient-reported PCN allergies in joint infection. We also acknowledge the inherent limitations of a retrospective study, although the single-institution design does limit some possible confounding variables, with all patients being subjected to the same perioperative protocols.

Conclusion

In this study 19.4% of patients received a second-line antibiotic; 52.3% of these patients reported a

history of non-IgE-mediated reactions and could have safely been prescribed cefazolin. No patient reporting a PCN allergy who received cefazolin experienced an adverse reaction. Institutions need to work toward more accurate documentation of PCN allergies and reactions and delabel patients who do not have true IgE-mediated reactions, which will also improve antibiotic stewardship. Most patients can be delabeled with a carefully constructed query alone although allergy testing may be necessary in a small number of patients who cannot be clarified based on history alone. We were unable to determine any significant effect of PCN allergy reporting and primary antibiotic prescription on the incidence of SSI.

References

References printed in **bold type** are those published within the past 5 years.

1. HCUP Fast Stats: *Healthcare Cost and Utilization Project (HCUP)*. Rockville, MD, Agency for Healthcare Research and Quality, 2017.
2. Kurtz S, Ong K, Lau E, et al: Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* 2007;89:780-785.
3. Ravi B, Croxford R, Reichmann WM, et al: The changing demographics of total joint arthroplasty recipients in the United States and Ontario from 2001 to 2007. *Best Pract Res Clin Rheumatol* 2012;26:637-647.
4. Rosenberger LH, Politano AD, Sawyer RG: The Surgical Care Improvement Project and prevention of post-operative infection, including surgical site infection. *Surg Infect (Larchmt)* 2011;12:163-168.
5. Bratzler DW, Dellinger EP, Olsen KM, et al: Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm* 2013;70:195-283.
6. Crawford T, Rodvold KA, Solomkin JS: Vancomycin for surgical prophylaxis? *Clin Infect Dis* 2012;54:1474-1479.
7. Bull AL, Worth LJ, Richards MJ: Impact of vancomycin surgical antibiotic prophylaxis on the development of methicillin-sensitive *Staphylococcus aureus* surgical site infections: Report from Australian Surveillance Data (VICNISS). *Ann Surg* 2012;256:1089-1092.
8. Inglis JM, Caughey GE, Smith W, et al: Documentation of penicillin adverse drug reactions in electronic health records: Inconsistent use of allergy and intolerance labels. *Intern Med J* 2017;47:1292-1297.
9. MacFadden DR, LaDelfa A, Leen J, et al: Impact of reported beta-lactam allergy on inpatient outcomes: A multicenter prospective cohort study. *Clin Infect Dis* 2016;63:904-910.
10. Trubiano JA, Adkinson NF, Phillips EJ: Penicillin allergy is not necessarily forever. *JAMA* 2017;318:82-83.
11. McDanel DL, Azar AE, Dowden AM, et al: Screening for beta-lactam allergy in joint arthroplasty patients to improve surgical prophylaxis practice. *J Arthroplasty* 2017; 32:S101-S108.
12. Trubiano JA, Thursky KA, Stewardson AJ, et al: Impact of an integrated antibiotic allergy testing program on antimicrobial stewardship: A multicenter evaluation. *Clin Infect Dis* 2017;65:166-174.
13. Bourke J, Pavlos R, James I, et al: Improving the effectiveness of penicillin allergy de-labeling. *J Allergy Clin Immunol Pract* 2015;3:365-434 e1.
14. Campagna JD, Bond MC, Schabelman E, et al: The use of cephalosporins in penicillin-allergic patients: A literature review. *J Emerg Med* 2012;42:612-620.
15. Buonomo A, Nucera E, Pecora V, et al: Cross-reactivity and tolerability of cephalosporins in patients with cell-mediated allergy to penicillins. *J Investig Allergol Clin Immunol* 2014;24:331-337.

16. Barlam TF, Cosgrove SE, Abbo LM, et al: Implementing an antibiotic stewardship program: Guidelines by the infectious diseases society of America and the society for healthcare epidemiology of America. *Clin Infect Dis* 2016;62:e51-e77.
17. Kurtz SM, Lau E, Schmier J, et al: Infection burden for hip and knee arthroplasty in the United States. *J Arthroplasty* 2008;23: 984-991.
18. Kapadia BH, Banerjee S, Cherian JJ, et al: The economic impact of periprosthetic infections after total hip arthroplasty at a specialized tertiary-care center. *J Arthroplasty* 2016;31:1422-1426.
19. Smith JO, Frampton CMA, Hooper GJ, et al: The impact of patient and surgical factors on the rate of postoperative infection after total hip arthroplasty-A New Zealand joint registry study. *J Arthroplasty*. 2018;33:1884-1890.
20. Tan TL, Springer BD, Ruder JA, et al: Is vancomycin-only prophylaxis for patients with penicillin allergy associated with increased risk of infection after arthroplasty? *Clin Orthop Relat Res* 2016; 474:1601-1606.
21. Pool C, Kass J, Spivack J, et al: Increased surgical site infection rates following clindamycin use in head and neck free tissue transfer. *Otolaryngol Head Neck Surg* 2016;154:272-278.
22. Uppal S, Harris J, Al-Niaimi A, et al: Prophylactic antibiotic choice and risk of surgical site infection after hysterectomy. *Obstet Gynecol* 2016;127:321-329.
23. Blumenthal KG, Ryan EE, Li Y, et al: The impact of a reported penicillin allergy on surgical site infection risk. *Clin Infect Dis* 2018;66:329-336.
24. Graves CM, Otero JE, Gao Y, et al: Patient reported allergies are a risk factor for poor outcomes in total hip and knee arthroplasty. *J Arthroplasty* 2014;29(9 Suppl):147-149.
25. McLawhorn AS, Bjerke-Kroll BT, Blevins JL, et al: Patient-reported allergies are associated with poorer patient satisfaction and outcomes after lower extremity arthroplasty: A retrospective cohort study. *J Arthroplasty* 2015;30:1132-1136.
26. Centers for Disease Control and Prevention: *Core Elements of Hospital Antibiotic Stewardship Programs*. <https://www.cdc.gov/antibiotic-use/healthcare/implementation/core-elements.html>. Accessed August 27, 2018.
27. Joint Commission on Hospital Accreditation. APPROVED: New antimicrobial stewardship standard. *Jt Comm Perspect* 2016;36:1.
28. Moussa Y, Shuster J, Matte G, et al: De-labeling of beta-lactam allergy reduces intraoperative time and optimizes choice in antibiotic prophylaxis. *Surgery* 2018; May 8 [Epub ahead of print].
29. Solensky R, Earl HS, Gruchalla RS: Lack of penicillin resensitization in patients with a history of penicillin allergy after receiving repeated penicillin courses. *Arch Intern Med* 2002;162:822-826.
30. Joint Task Force on Practice Parameters, American Academy of Allergy, Asthma and Immunology, American College of Allergy, Asthma and Immunology, Joint Council of Allergy, Asthma and Immunology: Drug allergy: An updated practice parameter. *Ann Allergy Asthma Immunol* 2010;105: 259-273.
31. Ponce B, Raines BT, Reed RD, et al: Surgical site infection after arthroplasty: Comparative effectiveness of prophylactic antibiotics: Do surgical care improvement project guidelines need to be updated? *J Bone Joint Surg Am* 2014;96:970-977.
32. Milstone AM, Maragakis LL, Townsend T, et al: Timing of preoperative antibiotic prophylaxis: A modifiable risk factor for deep surgical site infections after pediatric spinal fusion. *Pediatr Infect Dis J* 2008;27: 704-708.