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Recurrent Failures After 2-Stage Exchanges are Secondary to New Organisms Not Previously Covered by Antibiotics

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ABSTRACT

Background: Prior studies have shown that the majority of re-infections following two-stage revisions are due to organisms different from the initial organisms identified. It remains unknown whether these new organisms were susceptible to the antibiotics given (indicating the patient likely developed another infection following successful treatment) or not susceptible (indicating these organisms may have been initially present, but were not identified, and thus, inadequately treated). The purpose of this study was to determine if bacteria identified at time of re-infection following two-stage revisions were susceptible to the antibiotics administered during treatment of the index infection, in order to understand if these are new infections or from organisms that were present but not initially identified.
Methods: Thirty failures (19 knees and 11 hips) following two-stage revisions from four institutions were identified. Cultures and antibiotic sensitivities were used to determine whether the re-infectious organisms were new and if they were susceptible to the antibiotics initially given.
Results: Twenty-five (83.3%) re-infections were due to new organisms. Of these re-infections from new organisms, 16 (64.0%) were susceptible to the antibiotics previously administered, suggesting they were new infections rather than persistent infections from organisms that were not detected during initial treatment. No statistically significant differences in demographics or time to revision were observed when comparing by organism type (new vs. repeat) or by antibiotic susceptibility.
Conclusions: Failures following two-stage revisions are frequently due to organisms different than those identified prior to two-stage revision and are likely new infections rather than persistent infections from undetected organisms.

Introduction

Periprosthetic joint infection (PJI) remains one of the most devastating complications following total hip and total knee arthroplasty. PJI has been associated with substantial morbidity and mortality and shown to impart considerable costs on the health-care system [1–7]. Both the incidence and prevalence of PJI are expected to grow due to an increasingly obese and sicker patient population and with the projected increase in arthroplasties being performed in the coming decades [5,8–11].

Two-stage revisions remain the standard of care for treating chronic PJI in North America [12–14]. A 2-stage revision involves the removal of all implants, irrigation and debridement of all infected tissues, implantation of an antibiotic-impregnated spacer, parenteral administration of microorganism-directed antibiotics for 6 weeks, and reimplantation when the initial infection is deemed to have been adequately treated [15–18]. Despite this extensive process, failure rates as high as 34% have been reported, and the etiologies of failures secondary to infection remain unknown [19,20].

Failure following 2-stage revisions are thought to be due to either a recurrent reinfection due to failed treatment of the initial organism or a new infection due to a different pathogen [21]. Recent studies have reported that the majority of failures secondary

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to infection are due to organisms different than the ones originally identified, suggesting that most failures are due to a new infection [3]. However, these studies failed to evaluate the antibiotic sensitivities of the organisms associated with these failures. As a result, a third etiology, that the "new" organism was present during the initial infection but not detected (and thus not treated by the antibiotics given), cannot be ruled out [21]. The purpose of this study was to determine if reinfections following 2-stage revisions for PJI were due to the same or a new organism, and if the latter, whether these organisms were susceptible to the antibiotics originally administered.

We hypothesized that the majority of failures secondary to infection would be due to a new infection (organisms recovered at the time of failure susceptible to the antibiotics previously administered).

Material and methods

This was a retrospective study that included patients who underwent a 2-stage revision and failed due to recurrent PJI from a previously published study [22], as well as those treated by the senior author outside of the aforementioned study. All patients underwent a 2-stage revision between September 2003 and September 2017. This study was approved by the institutional review boards of all 4 participating institutions and by the senior author's institution to include additional patients. For inclusion, patients must have undergone 2-stage revision for PJI and met the 2011 Musculoskeletal Infection Society criteria for PJI with positive cultures at the time of first-stage infection and reinfection [23]. Patients who underwent revision surgery prior to the publication of the Musculoskeletal Infection Society criteria in 2011 were retroactively reviewed to confirm that they met the criteria at the time of surgery. Exclusion criteria included patients with fungal infections, culture-negative infections at either the time of first-stage infection or reinfection, and those with cultures lacking antibiotic sensitivities. Patients with fungal infections were excluded as they are fundamentally different from bacterial infections and feature less established diagnostic and therapeutic guidelines [24–27].

All patients underwent a standardized protocol for 2-stage revision, which included removal of all implants, irrigation and debridement of any infected tissue, implantation of an antibiotic-eluting cement spacer, and microorganism-directed parenteral antibiotic therapy for a minimum of 6 weeks. Antibiotic therapy was stopped for at least 2 weeks prior to attempted reimplantation, during which time patients were monitored for clinical signs of persistent infection. If patients did not demonstrate any clinical signs of persistent infection, they underwent removal of the antibiotic spacer and reimplantation of new prostheses.

Thirty patients who underwent a 2-stage revision were included (Table 1). Of these, 19 (63%) underwent a 2-stage revision following total knee arthroplasty and 11 (36%) following total hip arthroplasty. Nine (30%) patients were randomized to receive a 3-month course of prophylactic microorganism-directed oral (PO) antibiotics as subjects in a previously published study [22]. The median time to revision, defined as the time from reimplantation to repeat surgery, was 253.5 days (range: 9 days – 6.2 years, Table 1).

A microbiologist reviewed the culture results, antibiotic sensitivities, and antibiotic regimens of each patient. Failures were deemed to be due to the same organism if they were phenotypically identical and possessed identical antibiotic sensitivities. In patients for whom the failure was determined to be due to a "new" organism, the antibiotic sensitivities and antibiotic regimens were analyzed to determine whether the organism was susceptible to either the intravenous (IV) antibiotics all patients received and/or the 3-month course of oral antibiotics received by some patients.

Patients were compared by organism type (new vs persistent) and by antibiotic susceptibility (susceptible vs not susceptible). Student's t-tests and Mann-Whitney U-tests were performed for continuous patient variables, with Mann-Whitney U-tests used for nonparametric variables, such as time to repeat revision. Chi-squared and Fisher's exact tests were utilized for categorical variables, with Fisher's exact test used whenever an observation or group had 5 or fewer occurrences. Statistical significance was set to an α of 0.05, and all analyses were performed with STATA statistical software, version 12.0 (StataCorp, College Station, TX).

Results

Of the 30 failures secondary to infection, 25 (83%) were due to organisms different than those present during the initial infection (Fig. 1). Five (17%) failures were due to the same organism that matched the species and antibiotic sensitivities of those from the

Table 1
Patient characteristics.

Characteristics	All patients (n = 30)	Reinfection from new organism(s) (n = 25)	Reinfection from repeat organism(s) (n = 5)	*P* value
Age	60.0 ± 9.1	60.4 ± 9.6	58.4 ± 6.8	.67
Gender				.91
Male	18 (60%)	14 (56%)	4 (80%)	
Female	12 (40%)	11 (44%)	1 (20%)	
Body Mass Index (kg/m^2): median, range	34.0 (range: 21.6-62.4)	34.8 (range: 21.6-62.4)	35.0 (range: 33.6-35.9)	.91
Charlson Comorbidity Index				.42
0	7 (23%)	7 (42%)	0 (0%)	
1	6 (20%)	5 (20%)	1 (20%)	
2	7 (23%)	6 (24%)	1 (20%)	
3	7 (23%)	4 (16%)	3 (60%)	
4	2 (7%)	2 (8%)	0 (0%)	
5	1 (3%)	1 (4%)	0 (0%)	
Joint				1.0
Knee	19 (63%)	16 (64%)	3 (60%)	
Hip	11 (37%)	9 (36%)	2 (40%)	
Three-mo course of oral antibiotics given				.62
No	21 (70%)	18 (72%)	3 (60%)	
Yes	9 (30%)	7 (28%)	2 (40%)	
Time to revision (time from reimplantation to repeat surgery): median, range (d)	253.5 (range: 9-2254)	253.0 (range: 9-2254)	254.0 (range: 21-334)	.58

initial infection. There were no significant differences in patient demographic variables, proportion of patients who received the 3-month course of oral antibiotics following reimplantation, or time to revision between patients with new and repeat organisms (Table 1). The majority of initial infections were due to gram-positive organisms (87%) and were monomicrobial (90%) (Table 2).

Of the 25 failures due to a new organism, 16 (64%) were due to organisms that were susceptible to the IV antibiotics administered during the initial treatment, suggesting that if it had been present initially, it would have been treated by the antibiotics administered (Table 2). Of the 9 patients who received 3 months of organism-directed oral antibiotics following reimplantation, 5 (56%) were due to new organisms that were susceptible to the antibiotics administered (4 susceptible to IV antibiotics, 1 susceptible to both IV and PO antibiotics), 2 (22%) due to new organisms that were not susceptible to either IV or PO antibiotics, and 2 (22%) due to the same organisms (Supplemental Table 1). The proportion of failures due to the same organisms, new organisms that were susceptible to the antibiotics given, and new organisms that were not susceptible did not differ among those who did and did not receive 3 months of oral antibiotics following reimplantation (Table 3). Patients who received oral antibiotics following reimplantation had higher Charlson Comorbidity Index (CCI) scores than those who did not (67% with CCI $\geq$ 3 vs 20% with CCI $\geq$ 3, respectively, $P = .022$); there were no other statistically significant differences in patient demographic variables or time to revision (Table 3). No statistically significant differences were found when comparing those who were reinfected by new organisms that were susceptible to the antibiotics and those who were not (Table 4).

Discussion

As the number of PJIs continues to increase, it will be crucial to increase our understanding of the etiologies regarding failures following 2-stage revisions to improve the treatment of this challenging complication. This study found that most (83%) failures following 2-stage revisions were due to organisms different from those identified from the initial infection. Of these failures due to different organisms, the majority (64%) were susceptible to the antibiotics administered as part of the initial treatment, suggesting that these were new infections from different organisms rather than recurrent infections from unidentified and untreated organisms.

Despite surgical debridement and a 6-week course of organism-directed antibiotics, questions remain regarding the ability to eradicate identified organisms with a 2-stage exchange. The literature remains limited with only 1 study evaluating greater than 24 patients. In addition, the percentage of "persistent" infections (those due to the same organism identified prior to 2-stage revision) ranges from 0 to 31.5% [3,17,28–30]. The largest series to date by Zmistowski et al. evaluated 131 failures and found that 31.5% were due to the same organism that was initially identified, which is greater than the rate observed in our study (17%) [20]. They also reported that staphylococcal infections were more likely to be persistent than other species, finding that 37.3% of all staphylococcal infections were persistent. Two other studies evaluated PJIs due to methicillin-resistant *Staphylococcus aureus* (MRSA) and classified 66.7% and 89.9% of reinfections as persistent [29,30]. These findings differ from those of our study which found 11% and 0.0% of staphylococcal and MRSA reinfections to be persistent, respectively. However, these findings are likely limited by the small sample sizes of our study (n = 20 staphylococcal infections, n = 2 MRSA infections).

Limitations and variations in culturing protocols have led some to speculate that "new" organisms identified from failures of treatment may be organisms that were initially present but were not initially detected. Infectious organisms associated with implants may reside in biofilms, osteoblasts, and bony canaliculi which may preclude their isolation [31–34]. As a result of their complex nature, the detection of these organisms remains challenging, and negative cultures have been reported in 7% – 50% of PJI cases [31]. Recent studies have evaluated the use of new technologies, such as polymerase chain reaction and next-generation sequencing (NGS), as adjuncts in the organism-identification process. However, their utilities remain unknown with several studies reporting no increase in sensitivity or specificity compared to traditional tissue cultures and NGS demonstrating a false positive rate of up to 35% and 25% in primary and revision arthroplasties, respectively, [35–38]. In addition, intrahospital and interhospital variations in protocols and incubation times may affect the accuracy and capability of cultures to identify organisms, especially lower-virulence and slower-replicating organisms [39–42]. Our study found that of the 25 failures due to "new" organisms, the majority (64%) were susceptible to the antibiotics administered and, thus, should have hypothetically been eradicated had they been organisms that were initially undetected. Further research is required to not only improve the detection of organisms from initial

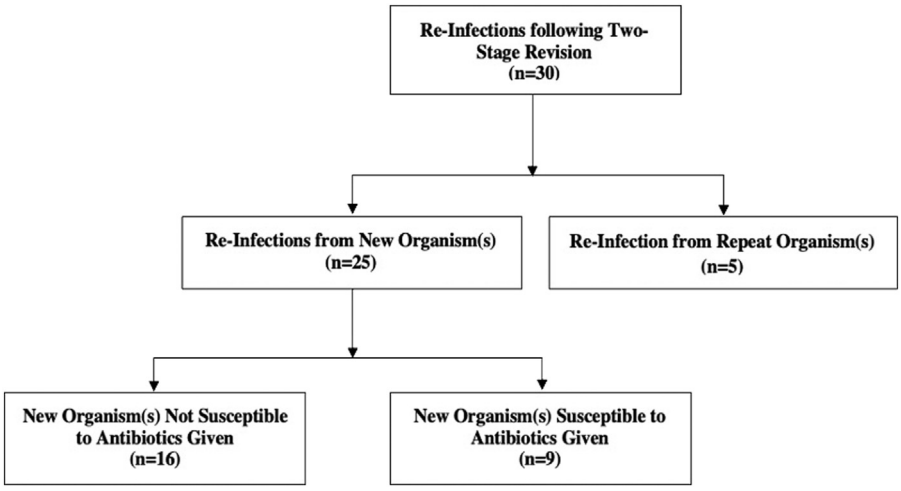

Figure 1. Flowchart of reinfectious organisms.

Table 2
Classification of reinfectious organisms.

Initial Organism (n = 30)	Reinfectious organisms, n = 30		
	New organism(s) (n = 25)		Repeat organism (n = 5)
	New organism(s) susceptible to antibiotics given (n = 16)	New organism(s) not susceptible to antibiotics given (n = 9)	
Gram positive (n = 26)	**13 (50%)**	**8 (31%)**	**5 (19%)**
Monomicrobial (n = 24)	**13 (54%)**	**8 (33%)**	**3 (13%)**
Staphylococcus, n = 18	10 (56%)	6 (33%)	2 (11%)
Staphylococcus aureus, n = 10	5 (50%)	3 (30%)	2 (20%)
MSSA, n = 8	4 (50%)	2 (25%)	2 (25%)
MRSA, n = 2	1 (50%)	1 (50%)	0 (0%)
Staphylococcus epidermidis, n = 5	3 (60%)	2 (40%)	0 (0%)
Coagulase-negative staphylococcus, n = 2	1 (50%)	1 (50%)	0 (0%)
Staphylococcus lugdunensis, n = 1	1 (100%)	0 (0%)	0 (0%)
Enterococcus faecalis, n = 2	1 (50%)	1 (50%)	0 (0%)
Corynebacterium, n = 1	1 (100%)	0 (0%)	0 (0%)
Anaerobic cocci (unspecified), n = 1	1 (100%)	0 (0%)	0 (0%)
Group C streptococcus, n = 1	0 (0%)	0 (0%)	1 (100%)
Group G streptococcus, n = 1	0 (0%)	1 (100%)	0 (0%)
Polymicrobial (n = 2)	**0 (0%)**	**0 (0%)**	**2 (100%)**
MSSA, group G streptococcus, n = 1	0 (0%)	0 (0%)	1 (100%)
MSSA, *Staphylococcus epidermidis*, n = 1	0 (0%)	0 (0%)	1 (100%)
Gram negative (n = 4)	**3 (75%)**	**1 (25%)**	**0 (0%)**
Monomicrobial (n = 3)	**2 (67%)**	**1 (33%)**	**0 (0%)**
Bacteroides fragilis, n = 1	1 (100%)	0 (0%)	0 (0%)
Escherichia coli, n = 1	0 (0%)	1 (100%)	0 (0%)
Proteus mirabilis, n = 1	1 (100%)	0 (0%)	0 (0%)
Polymicrobial (n = 1)	**1 (100%)**	**0 (0%)**	**0 (0%)**
Proteus mirabilis, *Pseudomonas aeruginosa*, n = 1	1 (100%)	0 (0%)	0 (0%)

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.
Bold font indicates grouping of organism types.

infections but to also better understand the origin of reinfectious organisms.

This study has several limitations. First, although this study was large when compared to others regarding this subject, it is likely underpowered to detect differences in many of the variables studied. Second, this study drew upon a heterogenous data set as it featured patients who were and were not a part of a previous randomized controlled trial. As a result, some patients received extended oral antibiotics while others did not. Third, patients with negative cultures and those lacking antibiotic sensitivities were excluded, and as a result, these findings may not be entirely representative of the reinfections following 2-stage revisions. Fourth, organisms that were classified as “new” may have been present but not identified via culturing techniques. Other detection methods, such as polymerase chain reaction and NGS, may have aided in identifying these potentially missed organisms. However, they were not utilized at all the participating institutions during this study period and, conversely, could have introduced bias into the study via false positives. Fifth, antibiotic sensitivities from cultures were used to determine whether an organism was

Table 3
Comparison of patients who did and did not receive 3-month course of oral antibiotics following reimplantation.

	Did not receive 3-mo course of oral antibiotics (n = 21)	Received 3-mo course of oral antibiotics (n = 9)	*P* value
Age	61.1 ± 8.1	57.6 ± 11.2	.34
Gender			.70
Male	12 (57%)	6 (67%)	
Female	9 (43%)	3 (33%)	
Body Mass Index (kg/m^2): median, range	33.1 (range: 21.6-42.6)	35.9 (range: 23.7-62.4)	.16
Charlson Comorbidity Index			*.022*
0	5 (24%)	2 (22%)	
1	6 (29%)	0 (0%)	
2	6 (29%)	1 (11%)	
3	2 (10%)	5 (56%)	
4	2 (10%)	0 (0%)	
5	0 (0.0%)	1 (11%)	
Joint			.42
Knee	12 (57%)	7 (78%)	
Hip	9 (43%)	2 (22%)	
Reinfectious organism			.077
New organism, susceptible to antibiotics administered	14 (67%)	2 (22%)	
New organism, not susceptible to antibiotics administered	4 (19%)	5 (56%)	
Repeat organism	3 (14%)	2 (22%)	
Time to revision (time from reimplantation to repeat surgery): median, range (d)	254.0 (range: 10-2082)	245.0 (range: 9-2254)	.82

Table 4
Comparison of patients reinfected by new organisms.

	New organism(s) susceptible to antibiotics given (n = 16)	New organism(s) not susceptible to antibiotics given (n = 9)	*P* value
Age	57.6 ± 10.2	65.2 ± 5.9	.054
Gender			.21
Male	7 (44%)	7 (78%)	
Female	9 (56%)	2 (22%)	
Body Mass Index (kg/m^2): median, range	35.0 (range: 23.0-35.0)	28.5 (range: 21.6-62.4)	.85
Charlson Comorbidity Index			.38
0	5 (31%)	2 (22%)	
1	4 (25%)	1 (11%)	
2	4 (25%)	2 (22%)	
3	1 (6%)	3 (33%)	
4	2 (13%)	0 (0%)	
5	0 (0%)	1 (11%)	
Joint			1.0
Knee	10 (63%)	6 (67%)	
Hip	6 (37%)	3 (33%)	
Three-mo course of oral antibiotics given			.14
No	14 (88%)	5 (56%)	
Yes	2 (12%)	4 (44%)	
Time to revision (time from reimplantation to repeat surgery): median, range (d)	320 (range: 16-2254)	47 (range: 9-807)	.13

susceptible to the antibiotics given. However, these sensitivities may reflect only those of the most dominant strain. In addition, "persistent" organisms that were not initially identified may not have been adequately treated if the antibiotics were unable to reach all the periarticular tissues, if they were in a metabolically inactive "dormant" biofilm state that render them less susceptible to antibiotics [43], or if they were sequestered within osteoblasts or canaliculi [33,34]. Lastly, patients from multiple institutions were included. Although the randomized controlled trial from which many of this study's patients were enrolled featured a uniform treatment protocol, the operating techniques, clinical decisions, and laboratory protocols and findings may have differed between institutions; however, this may make the findings more generalizable.

Conclusions

With the number of PJIs projected to increase, it will become even more critical to evaluate failures to improve treatment of this devastating complication. Our study found that the majority of failures secondary to infection following a 2-stage revision were due to organisms that were different from those identified prior to 2-stage revisions and were susceptible to the antibiotics administered, indicating that they were likely new infections from different organisms rather than persistent infections from undetected organisms. Host-related factors, unless modified, may render patients with PJI susceptible to new infections and recurrent failure.

Conflicts of interest

J. C. Segreti has stock or stock options from Pfizer. S. M. Sporer receives IP royalties from DJO Surgical, Osteoremedies, and Zimmer; is a paid consultant for DJO and Osteoremedies; receives research support from Zimmer and Stryker; receives material and financial support and publishing royalties from SLACK Incorporated; and is a board or committee member in American Joint Replacement Registry and Hip Society: American Joint Replacement Registry. A. F. Chen is a paid consultant for 3M, Avanos, bOne, Convatec, Ethicon, GLG, Guidepoint, Heraeus, Irrimax, Pfizer, PhagoMed, and Stryker; has stock or stock options in bOne, Graftworx, Hyalex, Irrimax, Joint Purification Systems, and Sonoran; receives research support from Sectra; receives financial or material support from SLACK Incorporated and UpToDate; is in the editorial or governing board of *Clinical Orthopaedics and Related Research*, *Journal of Arthroplasty*, *Journal of Bone and Joint Infection*, *Journal of Bone and Joint Surgery-American*, *Journal of Orthopedic Research*, *Knee Surgery, Sports, Traumatology, Arthroscopy*; is a board member in American Academy of Orthopaedic Surgeons, American Joint Replacement Registry, American Association of Hip and Knee Surgeons, and European Knee Association. M. S. Austin is in the speakers' bureau of or gave paid presentations for Corin U.S.A.; is a paid consultant for Corin U.S.A., DePuy, and Link Orthopaedics; has stock or stock options with Corin U.S.A.; receives research support from Zimmer Biomet; receives financial or material support from JayPee and Journal of the American Academy of Orthopaedic Surgeons; and is a board member in American Association of Orthopaedic Surgeons and American Association of Hip and Knee Surgeons. C. J. Della Valle receives royalties from Zimmer Biomet and Smith & Nephew; is a paid consultant for DePuy, Smith & Nephew, and Zimmer Biomet; has stock or stock options with Parvizi Surgical Innovations and Orthophor; receives research support from Smith & Nephew, Stryker, Zimmer Biomet, and CD Diagnostics; receives financial or material support from SLACK, Wolter Kluwer, Smith & Nephew, and Zimmer Biomet; is in the editorial or governing board of *Orthopaedics Today*; and is a board member for American Association of Hip & Knee Surgeons, Arthritis Foundation, DePuy, Hip Society, Knee Society, Mid-America Orthopaedic Association, and Orthopedics Today. All other authors declare no potential conflicts of interest.

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Supplemental Table 1
Comparison of initial and reinfectious organisms.

Joint	Time to revision (d)	Initial organism	Intravenous antibiotic	Three-mo course of oral antibiotics	Oral antibiotic	Reinfectious organism	Repeat organism	New organism susceptible to antibiotics	New organism not susceptible to antibiotics
Hip	9	*Enterococcus faecalis*	Ampicillin	No	-	*CoNS*	No	No	Yes
Knee	10	*Escherichia coli*	Cefotaxime, levofloxacin	Yes	Levofloxacin	*MRSA*	No	No	Yes
Hip	16	*Gram-positive anaerobic cocci*	Cefotaxime, vancomycin	No	-	*Staphylococcus epidermidis*	No	Yes	No
Knee	21	*MSSA*	Vancomycin	No	-	*Enterococcus faecalis*	No	Yes	No
Knee	21	*Staphylococcus epidermidis*	Vancomycin	Yes	Doxycycline	*Klebsiella pneumoniae*	No	No	Yes
Hip	21	*MSSA, Staphylococcus epidermidis*	Daptomycin	No	-	*MSSA*	Yes	-	-
Hip	21	*Proteus mirabilis*	Doxycycline, vancomycin	No	-	*MSSA*	No	Yes	No
Knee	29	*MSSA*	Vancomycin	No	-	*Serratia*	No	No	Yes
Hip	36	*MSSA*	Daptomycin	No	-	*MSSA, E. coli*	Yes	-	-
Hip	40	*MSSA*	Piperacillin/Tazobactam	No	-	*Group B Streptococcus*	No	Yes	No
Knee	47	*Staphylococcus epidermidis*	Vancomycin	Yes	Doxycycline	*Pseudomonas aeruginosa*	No	No	No
Knee	83	*Staphylococcus lugdunensis*	Cefazolin	No	-	*MSSA*	No	Yes	No
Hip	175	*Proteus mirabilis*	Levofloxacin	No	-	*Morganella morganii*	No	Yes	No
Knee	245	*Corynebacterium*	Vancomycin	No	-	*Streptococcus mitis*	No	Yes	No
Hip	253	*MSSA*	Daptomycin	Yes	Doxycycline	*Group B strep*	No	Yes, susceptible to IV antibiotics	No
Knee	254	*MSSA*	Vancomycin	Yes	Trimethoprim/ Sulfamethoxazole	*MSSA, Group G Streptococcus*	Yes	-	-
Hip	266	*MSSA*	Doxycycline	Yes	Doxycycline	*Pseudomonas aeruginosa*	No	No	Yes
Knee	287	*MSSA, Group B streptococcus*	Ciprofloxacin, vancomycin	No	-	*MSSA*	Yes	-	-
Knee	334	*Group C streptococcus*	Ampicillin	Yes	Cefadroxil	*Group C Streptococcus*	Yes	-	-
Knee	347	*CoNS*	Cefazolin	Yes	Cefadroxil	*Staphylococcus epidermidis*	No	No	Yes
Knee	387	*MSSA*	Daptomycin	No	-	*Streptococcus agalactiae*	No	Yes	No
Knee	451	*Group G Streptococcus*	Cefazolin	No	-	*MRSA*	No	No	Yes
Knee	453	*Enterococcus faecalis*	Linezolid	No	-	*MRSA*	No	Yes	Yes
Knee	468	*Bacteroides fragilis*	Ertapenem	No	-	*Staphylococcus lugdunensis*	No	Yes	No
Hip	807	*MRSA*	Cefazolin	No	-	*CoNS*	No	No	Yes
Knee	828	*Staphylococcus epidermidis*	Daptomycin	No	-	*Staphylococcus epidermidis*	No	Yes	No
Knee	935	*Staphylococcus epidermidis*	Vancomycin	No	-	*Streptococcus mitis*	No	Yes	No
Hip	1600	*MRSA*	Vancomycin	No	-	*Staphylococcus epidermidis*	No	Yes	No
Knee	2082	*Staphylococcus epidermidis*	Levofloxacin, vancomycin	Yes	Doxycycline	*MSSA*	No	Yes, susceptible to IV and PO antibiotics	No
Knee	2254	*CoNS*	Vancomycin	No	-	*Streptococcus mutans*	No	Yes	No

CoNS, coagulase negative staphylococcus; MRSA, methicillin-resistant staphylococcus; MSSA, methicillin-sensitive staphylococcus.