

1 **TABLE S1. Characteristics of 33 subjects classified as having prosthetic joint infection (PJI) who had negative sonicate fluid bacterial**
 2 **PCR**

Case number	Hip or Knee	Criteria for PJI classification			ESR (mm/h)	CRP (mg/L)	Synovial fluid leukocyte count/ μ L (% neutrophils)	Other antecedent and/or relevant data	Antecedent antimicrobial therapy (within 28 days prior to index surgery) ^a	Number positive tissue cultures/ number tissues cultured, organism detected in tissue culture	Sonicate fluid culture isolate (CFU/plate)
		Acute inflammation	Purulence	Sinus tract							
Fungal PJI (not detected by bacterial PCR panel)											
236	Knee	-	+	-	26	ND	5772 (86)	<i>Candida albicans</i> TKA infection, fluconazole chronic suppression	Fluconazole	3/3, <i>C. albicans</i>	<i>C. albicans</i> (20-50)
364	Knee	ND	+	-	16	4	ND	<i>Candida glabrata</i> TKA infection (synovial fluid culture - <i>C. glabrata</i>)	No	1/4, SCN	-
PJI caused by unusual bacteria (not detected by bacterial PCR panel)											
164	Knee	+	+	-	67	56	25064 (86)	Waldenström's macroglobulinemia, alcoholism	No	3/3, <i>Capnocytophaga canimorsus</i>	<i>C. canimorsus</i> (51-100)
200	Hip	+	-	-	85	47.7	ND	Diabetes mellitus	No	7/7, <i>Mycobacterium abscessus</i>	-
PJI with negative or not significant tissue cultures											
52 ^b	Hip	+	-	-	14	<3	ND	Hip dysplasia, degenerative change. No prolonged antibiotic therapy given after index surgery. Well at follow-up 5 months later.	No	0/5	-
53 ^b	Hip	+	-	-	9	5	ND	Antibiotic therapy for 2 weeks after index surgery. Well at follow-up 2 years later	No	0/3	-
142	Hip	+	-	-	4	6	ND	Prior <i>Streptococcus</i>	Cephalexin	0/4	-

										<i>agalactiae</i> THA infection		
148	Hip	+	-	-	ND	ND	ND	Rheumatoid arthritis	No	1/3, SCN	-	
155	Knee	+	-	-	10	3	100 (88)	Prior left TKA infection with cellulitis and abscess	No	0/7	-	
157	Hip	-	-	+	ND	ND	ND	Prior removal of painful cables, complicated by cellulitis	Cephalexin	0/5	-	
181	Knee	-	+	-	30	<3	52 (38)		Ciprofloxacin	0/3	-	
195	Hip	+	+	-	25	20.7	ND		No	0/5	-	
231	Knee	+	+	-	10	11.8	ND	Two prior TKA infections. Rifampin plus minocycline suppression until one month prior to index surgery.	No	0/4	-	
242	Knee	-	+	-	22	8.7	23400 (75)	Recurrent TKA infection (synovial fluid culture – SCN)	Minocycline	0/3	-	
247	Knee	-	+	-	25	3.2	ND	Two prior two-stage exchanges. Chronic minocycline until one month prior to index surgery.	No	0/3	-	
258	Knee	-	+	+	36	33.1	1404 (65)		No	0/6	-	
292	Knee	+	+	-	51	33.1	18512 (64)		No	0/3	-	
295	Knee	-	+	-	29	16.6	6916 (78)	Undifferentiated connective tissue disease	No	1/6, <i>P. acnes</i>	-	
318	Hip	ND	+	+	17	106.3	ND	Prior THA infections	No	1/3, <i>Coryne. sp</i>	-	
333	Knee	+	-	-	37	11.5	ND		No	0/7	-	
349	Knee	-	+	-	15	<3	52 (3)		No	0/4	-	
366	Knee	+	-	-	19	19.2	49608 (77)		No	1/3, VGS	-	
399	Knee	-	+	-	26	15.8	16226 (85)		No	0/3	-	
426	Knee	-	+	-	32	9.5	9115 (26)		No	0/4	-	
431	Hip	-	+	-	24	5	20517 (ND)		No	0/3	-	

435	Knee	+	+	-	110	100.8	48130 (79)		No	1/5, <i>P. acnes</i>	-
445	Hip	+	-	-	10	13.6	4872 (95)		No	0/5	-
449	Hip	ND	-	+	21	16.1	ND	Persistently draining wound after THA reimplantation 3 weeks prior to index surgery	No	0/4	-
PJI with positive tissue cultures											
211	Hip	ND	+	-	65	199.1	ND	<i>S. aureus</i> THA infection 3 months prior to index surgery	Cefazolin	4/6, <i>S. aureus</i>	<i>S. aureus</i> (>100)
259	Hip	ND	+	-	25	6.8	ND	Prior <i>S. aureus</i> THA infection. Chronic minocycline until more than 1 month prior to index surgery.	No	3/6, <i>S. aureus</i>	<i>S. aureus</i> (>100)
298	Knee	-	+	-	6	<3	ND	Prior <i>S. aureus</i> abscess	No	4/5, <i>S. aureus</i>	-
369	Knee	+	-	+	4	70	52 (52)	Prior TKA infections	Cefazolin	2/3, <i>S. aureus</i> , <i>Coryne. sp</i>	-
425	Knee	+	+	-	38	11	ND		Cephalexin	3/3, <i>S. aureus</i>	<i>S. aureus</i> (>100)

3 ^a14/43 (32.6%) subjects with PJI and negative tissue cultures had received antimicrobics. 13/39 (33.5%) subjects with PJI and negative sonicate fluid cultures had received
4 antimicrobial therapy. For 8/13, at least one PCR assay was positive (subjects 74, 110, 214, 226, 250, 286, 352 and 379). 8/33 (24.2%) with PJI and negative PCRs had
5 received antimicrobial therapy.

6 ^bThese two cases were reviewed by an infectious diseases physician who considered them not to represent PJI.

7 ND, not done; THA, total hip arthroplasty; TKA, total knee arthroplasty; SCN, coagulase-negative *Staphylococcus* species; *Coryne. sp.*, Gram-positive bacillus resembling
8 *Corynebacterium* species; VGS, viridans group *Streptococcus* species; +, positive; -, negative

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TABLE S2. Discordant results between sonicate fluid PCR and culture

Case number #	PJI (yes, no)	Antimicrobial treatment within 28 days prior to index surgery	Number positive tissue cultures/ number tissues cultured, organism detected in tissue culture	Synovial fluid culture isolate	Sonicate fluid culture isolate (CFU/plate)	Assay result	
<i>Staphylococcus</i> assay							11
74	Yes	Vancomycin	4/5, <i>Staphylococcus aureus</i>	<i>S. aureus</i>	-	+ (<i>S. aureus</i>)	12
110 ^a	Yes	Oxacillin	3/5, SCN	ND	-	+ (<i>S. aureus</i>)	13
226	Yes	TMP-SMX, levofloxacin	2/4, SCN	ND	-	+ (SCN) ^d	14
250 ^a	Yes	Fusidic acid	0/5	ND	-	+ (SCN) ^b	15
352	Yes	Amoxicillin-clavulanate	2/3, SCN	SCN	-	+ (SCN)	16
430	Yes	No	2/3, SCN	SCN	-	+ (SCN)	17
38	No ^c	No	1/2, <i>Coryne. sp.</i>	-	<i>S. aureus</i> (>100)	-	18
211	Yes	Cefazolin	4/6, <i>S. aureus</i>	ND	<i>S. aureus</i> (>100)	- ^d	19
259	Yes	No	3/6, <i>S. aureus</i>	SCN	<i>S. aureus</i> (>100)	-	20
342	Yes	Vancomycin, rifampin	0/3	SCN	SCN (51-100)	- ^{d, e}	21
425	Yes	Cephalexin	3/3, <i>S. aureus</i>	<i>S. aureus</i>	<i>S. aureus</i> (>100)	- ^d	22
428	Yes	No	1/4, SCN	<i>Enterococcus sp.</i>	<i>Enterococcus sp.</i> (51-100), SCN (51-100)	- ^f	23
<i>Streptococcus</i> assay							24
214	Yes	Penicillin G, ceftriaxone	0/5	<i>S. agalactiae</i>	-	+ ^g	25
280 ^a	Yes	No	1/7, SCN	-	-	+	26
299	No ^c	Vancomycin	0/3	ND	-	+	27
397 ^a	No	Penicillin, clindamycin	0/5	ND	-	+ ^g	28
Enterobacteriaceae assay							29
175*	Yes	TMP-SMX	5/5, <i>S. aureus</i> , 2/5 <i>Fingoldia magna</i> , <i>Coryne. sp.</i>	<i>S. aureus</i>	<i>S. aureus</i> (>100), <i>F. magna</i> (>100)	+ ^{e, h}	30
217	Yes	No	2/9, <i>Escherichia coli</i>	ND	-	+	31
245	Yes	TMP-SMX, rifampin	3/5, <i>S. aureus</i> , 1/5 <i>Klebsiella pneumoniae</i>	ND	<i>S. aureus</i> (>100)	+ ^h	32
321	No ^c	No	0/3	-	-	+	33
379 ^a	Yes	Cefazolin, vancomycin	0/7	-	-	+	34
<i>Pseudomonas aeruginosa</i> assay							35
286	Yes	Ceftazidime	3/3 <i>P. aeruginosa</i>	-	-	+	36
No specific assay							37
164	Yes	No	3/3, <i>Capnocytophaga canimorsus</i>	<i>C. canimorsus</i>	<i>C. canimorsus</i>	NA	38
236	Yes	Fluconazole	3/3, <i>Candida albicans</i>	<i>C. albicans</i>	<i>C. albicans</i>	NA	39

31 ^a110: *S. aureus* infection of the same total knee arthroplasty and *S. aureus* bacteremia 2 months prior; 250: SCN infection of the same total hip arthroplasty 17 months prior
32 with two prior irrigation/debridement procedures; 280: Total knee arthroplasty infection with *Streptococcus sanguis* septic native contralateral hip with psoas abscess nine
33 months prior; 397: Chronic total hip arthroplasty infection with β -hemolytic *Streptococcus* species nine months prior; 175, 379: No prior history of Enterobacteriaceae
34 infection.

35 ^bPositive with *Propionibacterium* assay.

36 ^c38: Antibiotic therapy given only 2 weeks after one-stage exchange. Well at follow-up 1 year later; 299: No antibiotic therapy given after index surgery. Well at follow-up 2
37 years later; 321: No antibiotic therapy given after index surgery. Well at follow-up 2 years later.

38 ^dPositive with repeat testing (211: *S. aureus*; 342, 425: SCN).

39 ^ePositive with Gram-positive anaerobic cocci assay.

40 ^fPositive with *Enterococcus* assay.

41 ^gTm compatible with *Streptococcus agalactiae*.

42 ^hPositive with *Staphylococcus* assay.

43 SCN, coagulase-negative *Staphylococcus* species; ND, not done; TMP-SMX, trimethoprim-sulfamethoxazole; *Coryne. sp.*, Gram-positive bacillus resembling

44 *Corynebacterium* species; -, negative; +, positive; NA: not applicable.