Infectious Disease Wishes for the Ortho Team

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▶ none

Objectives

- Explain proper evaluation and work-up for potentially infected joints; properly interpret synovial fluid analyses
- Explain the potential treatment approaches to prosthetic joint infections
- Outline when to use different antibiotics and when they should be started
- Describe how cultures are processed in the lab to better interpret their results

Septic Arthritis

- 27 yo M with no significant PMH presents with 1 month of R shoulder pain and swelling. PE reveals R shoulder effusion with increased warmth. No systemic s/s of infection. Aspiration reveals 53k wbcs with 98% PMNs. Gram stain with gram neg diplococci.
- What is the diagnosis and proposed treatment?
 - Neisseria gonorrhea -> antibiotics and monitor shoulder
 - Neisseria gonorrhea -> antibiotics and urgent surgery
 - Staph aureus septic joint -> urgent surgery
 - Staph aureus septic joint -> surgery next week, it's been going on for a month so no need to rush



(thespectruhttps://www.thespectrum.com/story/news/nation/2018/08/28/cdc-reports-surgegonorrhea-other-sexually-transmitted-diseases/1115411002/m.com)

Gonococcal Septic Arthritis

Answer: Neisseria gonorrhea and monitor the shoulder

- Gram stain and culture are negative in 50% cases
 - Consider triple site GC/CT testing in work-up of high risk patients
 - ▶ 80% patients with gonococcal septic arthritis have a positive mucosal test NAAT
 - Unable to get NAAT of synovial fluid performed
- > Treatment: 10 days of IV Ceftriaxone after clinical improvement is noted
 - ▶ If you cannot get an urgent ID appointment then send pt to the ER
 - Oral therapy can only be used if you have sensitivities (rare)
 - Surgery is rarely needed

(Bardin, 2003)

Nongonococcal Septic Arthritis

- If the prior question had GPCs on the gram stain what would the diagnosis and treatment be?
 - Staph aureus septic joint -> urgent surgery
 - Staph aureus septic joint -> surgery next week, it's been going on for a month so no need to rush
 - ▶ We don't know if this is a pathogen so wait for GPC identification





Septic Arthritis

- Staph aureus septic joint -> urgent surgery
 - >50k wbcs with hot/painful joint, GPCs on gram stain are most likely SA
 - Even though this is fairly chronic SA is always an urgent manner; joint destruction and risk of bacteremia (Elsissy et al., 2020)
 - ▶ SA bacteremia has a 90-day mortality of 33% (van der Vaart et al., 2022)
 - Treatment: 2-6 weeks antibiotics (traditionally IV but PO becoming more popular – more to come on this)
- If Synovial WBC was less, ~30k, depending on the story you should wait for more culture information -> this could be a CoNS and gout for example

Pre-treated Septic Arthritis

- 54 yo M with AKI on HD and recent MSSA bacteremia that seeded his spine is on cefazolin with HD and presents with a hot painful knee. Aspiration with 24k WBCs, 98% PMNs, crystal analysis neg, gram stain with no organisms but many PMNs and cx ng. Should this be treated as a septic joint?
 - > Yes, high percentage of PMNs and pre-treated with antibiotics
 - ▶ No, low wbc and cx neg

Pre-treated Septic Arthritis

- ▶ Yes this is septic arthritis, purulence noted in the OR after >4 weeks IV abx
 - If pts have been on abx you cannot trust cultures to grow an organism
 - For these patients it is proposed to use 16k as the cutoff for WBCs rather than 50k; neutrophil percentage >90% (Massey et al., 2021)

Prosthetic Joint Infections

- 65 yo M with R TKA for OA performed 1 week ago presents with purulent drainage from his surgical site and some erythema surrounding the surgical site. What would your next step be?
 - ► Arthrocentesis
 - ▶ 10 days of po TMP-SMX
 - Apply an incisional wound vac
 - Check ESR/CRP



Answer = arthrocentesis (Manrique et al., 2019)

- We don't know if this is a SSTI or a PJI
- Abx may make culture results unreliable
- If a PJI then treatment becomes complicated and empiric; suppression after DAIR is a problem

Diagnostic Test	Treated $(n = 13)$		Untreated $(n = 36)$		P-Value
	Median	IQR (Q2-Q3)	Median	IQR (Q2-Q3)	
Inflammatory markers					
CRP (mg/L)	22	13-61	105	49-196	.006ª
ESR (mm/h)	45	36-63	47	30-61	.931
Synovial fluid					
Synovial WBC count (cells/µL)	4,473	1,664-15,288	57,591	15,200-101,189	.003ª
Synovial neutrophil percentage (%)	76	56-86	94	88-97	.004 ^a
Synovial ANC (cells/µL)	2,804	634-8,605	50,748	14,572-93,270	<.001ª

Median Laboratory Values of Treated and Untreated Patients.

(Dugdale et al., 2022)



- Arthrocentesis is performed and reveals 4k wbcs with 94% PMNs and culture grows MSSA. What are the options for treatment? How do you counsel your patient?
 - ► DAIR vs 2-stage
 - Antibiotics

PJI Mortality





(Stanton, 2017)

PJI Surgical Treatment Options

- DAIR/washout/poly-swap
 - ▶ success rate of 14%-100%
 - Thought better if from hematogenous spread
 - ▶ Worse outcomes with MRSA, GNR, MSSA without rif use
- ► 1 stage
 - ▶ 80-90% success, linked to extent of debridement
- 2 stage
 - ▶ 87% success



(Stanton, 2017)

(Osmon et al., 2013), (Dzaja et al., 2015)





(Osmon et al., 2013)



*Uncommonly performed in the U.S. **Relative indications see text



What's the Best Surgical Approach?

2-stage outcomes (Hartzler et al., 2020)

MSIS Success, n (%)	Overall $(n = 205)$
Tier 1: infection control, no chronic antibiotic suppression	122 (59.5%)
Tier 2: infection control, on chronic antibiotic suppression	18 (8.8%)
Tier 3: need for reoperation/revision and/or spacer retention	
Tier 3A: aseptic revision > 1 year from initiation of PJI treatment	3 (1.5%)
Tier 3B: septic revision > 1 year from initiation of PJI treatment	2 (1.0%)
Tier 3C: aseptic revision < 1 year from initiation of PJI treatment	4 (2.0%)
Tier 3D: septic revision < 1 year from initiation of PJI treatment	3 (1.5%)
Tier 3E: amputation, resection, arthrodesis, Girdlestone procedure	6 (2.9%)
Tier 3F: retained spacer	32 (15.6%)
Tier 4: death	
Tier $4A$: < 1 year from initiation of treatment	5 (2.4%)
Tier 4B: > 1 year from initiation of treatment	10 (4.9%)

Figure 2. Success Rate of DAIR Against Time Since Primary TKA



(Rahardja et al., 2023)

What's the Best Surgical Approach?



Figure 7. Kaplan-Meier survival curve. The analysis is separated in different types of surgical treatment. Vertical marks indicate censoring. IS = one-stage exchange, 2S = two-stage exchange, D = debridement, R/A = removal or arthrodesis.

PJI Treatment Options

- Washout/DAIR/Poly-swap
- 1-stage

► 2-stage



2-6 weeks IV abx with rifampin (if staph) followed by orals with rif

- ► TKA: total 6 months
- ▶ THA and others: total 3 months
- Consider indefinite suppression



4-6 weeks IV abx

(Osmon et al., 2013)

Use of Rifampin/Rifabutin



Figure 2. Treatment failure (A) and clinical failure (B) rifampin versus no-rifampin according to the type of joint.

	Non-failures (n = 276)	Failures ($n = 131$)	P value	Adjusted OR (95% CI) ^a	P value
Baseline characteristics					
Male sex	40.2%(111/276)	50.4% (66/131)	.05*	2.07 (1.19 - 3.58)	.009
Age >80 years	21.1% (58/275)	28.2% (37/131)	.11		
BMI >30 kg/m ²	48.8% (122/250)	46.6% (55/118)	.70		
Medical history					
Diabetes	17.8% (49/276)	26.7% (35/131)	.04*	2.16 (1.12 - 4.15)	.022
Renal failure	6.2% (17.276)	8.4% (11/131)	.41		
COPD	17.8% (49/276)	19.8% (26/131)	.61		
Liver cirrhosis	3.6% (10/276)	3.8% (5/131)	.92		
Malignancy	13.8% (38/276)	15.3% (20/131)	.67		
Rheumatoid arthritis	6.9% (19/276)	8.4% (11/131)	.59		
Characteristics implant					
Knee	41.7% (115/276)	35.1% (46/131)	.21		
Primary	85.1% (235/276)	78.6% (103/131)	.10		
Cemented	75.4% (205/272)	81.4% (105/129)	.18		
Fracture	13.4% (37/276)	19.8% (26/131)	.09*	1.40 (0.68 - 2.91)	.36
Clinical presentation					
CRP >115 mg/L	23.3% (63/270)	47.3% (61/129)	<.001*	1.54 (0.85 - 2.79)	.16
Leucocytes >12 cells/µL	21.1% (57/270)	44.4% (56/126)	<.001*	2.79 (1.48 - 5.27)	.002
Late acute PJI	2.2% (6/276)	5.4% (7/130)	.09		
Identified micro-organism					
Staphylococcus aureus	57.2% (158/276)	71.8% (94/131)	.01*	1.63 (0.89– 2.97)	.11
Polymicrobial	37.3 (103/276)	38.9% (51/131)	.75		
Surgical treatment					
Exchange modular components	48.3% (131/271)	39.8% (51/128)	.11		
Antibiotic treatment					
Co-antibiotic other than a fluoroquinolone or clindamycin	30.4% (84/276)	78.6% (103/131)	<.001*	10.1 (5.65 - 18.2)	<.001
Rifampin dose >600 mg/24h	52.1% (139/267)	72.6% (90/124)	<.001*	1.23 (0.65 - 2.32)	.52
BMI/mg rifampin ratio >30	87.6% (242/276)	81.6% (107/131)	.12		
Start rifampin <5 days after surgical debridement	44.1% (116/263)	64.0% (80/125)	<.001*	1.96 (1.08 - 3.56)	.03

(Beldman et al., 2021)

Use of Rifampin/Rifabutin

- Don't use with doxy
- Mino okay 100 80 22% treatment failure 60 % 14% Lowers Bactrim levels so may need to 38% 40 21% 20% 21% increase Bactrim dose if on rif 18% 14% 12% 12% 20 0. Levoltozain (pas) hostozain (pr.24) cindamon (pr.29) practare (pr.24) hitocoldin (pr.19) (Beldman et al., 2021)

Co-antibiotic rifampin

IV abx recs

Microorganism	Preferred Treatment ^a	Alternative Treatment ^a	Comments
Staphylococci, oxacillin- susceptible	Nafcillin ^b sodium 1.5–2 g IV q4-6 h or Cefazolin 1–2 g IV q8 h or Ceftriaxone ^c 1–2 g IV q24 h	Vancomycin IV 15 mg/kg q12 h or Daptomycin 6 mg/kg IV q 24 h or Linezolid 600 mg PO/IV every 12 h	See recommended use of rifampin as a companion drug for rifampin-susceptible PJI treated with debridement and retention or 1-stage exchange in text
Staphylococci, oxacillin- resistant	Vancomycin ^d IV 15 mg/kg q12 h	Daptomycin 6 mg/kg IV q24 h or Linezolid 600 mg PO/IV q12 h	See recommended use of rifampin as a companion drug for rifampin-susceptible PJI treated with debridement and retention or 1-stage exchange in text
Enterococcus spp, penicillin-susceptible	Penicillin G 20–24 million units IV q24 h continuously or in 6 divided doses or Ampicillin sodium 12 g IV q24 h continuously or in 6 divided doses	Vancomycin 15 mg/kg IV q12 h or Daptomycin 6 mg/kg IV q24 h or Linezolid 600 mg PO or IV q12 h	4–6 wk. Aminoglycoside optional Vancomycin should be used only in case of penicillin allergy
Enterococcus spp, penicillin-resistant	Vancomycin 15 mg/kg IV q12 h	Linezolid 600 mg PO or IV q12 h or Daptomycin 6 mg IV g24 h	4–6 wk. Addition of aminoglycoside optional
Pseudomonas aeruginosa	Cefepime 2 g IV q12 h or Meropenem ^e 1 g IV q8 h	Ciprofloxacin 750 mg PO bid or 400 mg IV q12 h or Ceftazidime 2 g IV q8 h	 4–6 wk Addition of aminoglycoside optional Use of 2 active drugs could be considered based on clinical circumstance of patient. If aminoglycoside in spacer, and organism aminoglycoside susceptible than double coverage being provided with recommended IV or oral monotherapy
Enterobacter spp	Cefepime 2 g IV q12 h or Ertapenem 1 g IV q24 h	Ciprofloxacin 750 mg PO or 400 mg IV q12 h	4–6 wk.
Enterobacteriaceae	IV β-lactam based on in vitro susceptibilities or Ciprofloxacin 750 mg PO bid		4–6 wk
β-hemolytic streptococci	Penicillin G 20–24 million units IV q24 h continuously or in 6 divided doses or Ceftriaxone 2 g IV q24 h	Vancomycin 15 mg/kg IV q12 h	4–6 wk Vancomycin only in case of allergy
Propionibacterium acnes	Penicillin G 20 million units IV q24 h continuously or in 6 divided doses or Ceftriaxone 2 g IV q24 h	Clindamycin 600–900 mg IV q8 h or clindamycin 300–450 mg PO qid or Vancomycin 15 mg/kg IV q12 h	4–6 wk Vancomycin only in case of allergy

(Osmon et al., 2013)

Chronic Oral Suppression

Microorganism	Preferred Treatment	Alternative Treatment
Staphylococci, oxacillin-susceptible	Cephalexin 500 mg PO tid or qid or Cefadroxil 500 mg PO bid	Dicloxacillin 500 mg PO tid or qid Clindamycin 300 mg PO qid Amoxicillin-clavulanate 500 mg PO tid
Staphylococci, oxacillin-resistant	Cotrimoxazole 1 DS tab PO bid Minocycline or doxycycline100 mg PO bid	
β-hemolytic streptococci	Penicillin V 500 mg PO bid to qid or Amoxicillin 500 mg PO tid	Cephalexin 500 mg PO tid or qid
Enterococcus spp, penicillin susceptible	Penicillin V 500 mg PO bid to qid or Amoxicillin 500 mg PO tid	
Pseudomonas aeruginosa	Ciprofloxacin 250–500 mg PO bid	
Enterobacteriaceae	Cotrimoxazole 1 DS tab PO bid	β-lactam oral therapy based on in vitro susceptibilities
Propionibacterium spp	Penicillin V 500 mg PO bid to qid or Amoxicillin 500 mg PO tid	Cephalexin 500 mg PO tid or qid Minocycline or doxycycline 100 mg PO bid

n engl j med 380;5 nejm.org January 31, 2019

OVIVA

- Prospective IV vs PO x 6 weeks
 - ▶ 1054 patients
- IV lead in
- Mainly infected joints
- Lack of MRSA
- ▶ Treatment failure @ 1 year
 - ▶ 14.6% of IV
 - ▶ 13.2% PO

Anatomical site of infection*			
 spinal infection^a 	37 (7.0%)	35 (6.6%)	72 (6.8%)
 upper limb infection 	43 (8.2%)	59 (11.2%)	102 (9.67%)
 lower limb infection^b 	436 (82.7%)	419 (79.5%)	855 (81.1%)
 other area of infection 	12 (2.3%)	14 (2.7%)	26 (2.5%)

Characteristic	Intravenous Group (N=527)	Oral Group (N=527)	Total (N = 1054)
Age — yr			
Median (interquartile range)	61 (49–70)	60 (49–70)	60 (49–70)
Range	18–92	18–91	18–92
Male sex — no. (%)	320 (60.7)	358 (67.9)	678 (64.3)
Baseline surgical procedure — no. (%)			
No implant or device present; débridement of chronic osteomy- elitis performed	153 (29.0)	169 (32.1)	322 (30.6)
No implant or device present; débridement of chronic osteomy- elitis not performed	25 (4.7)	29 (5.5)	54 (5.1)
Débridement and implant retention	124 (23.5)	123 (23.3)	247 (23.4)
Removal of orthopedic device for infection	89 (16.9)	78 (14.8)	167 (15.8)
Prosthetic joint implant removed	68 (12.9)	67 (12.7)	135 (12.8)
Prosthetic joint implant, one-stage revision	47 (8.9)	43 (8.2)	90 (8.5)
Surgery for diskitis, spinal osteomyelitis, or epidural abscess; débridement performed	8 (1.5)	5 (0.9)	13 (1.2)
Surgery for diskitis, spinal osteomyelitis, or epidural abscess; débridement not performed	13 (2.5)	13 (2.5)	26 (2.5)
Organisms identified — no./total no. (%)§			
Staphylococcus aureus	196/500 (39.2)	182/503 (36.2)	378/1003 (37.7)

Staphylococcus aureus	196/500 (39.2)	182/503 (36.2)	378/1003 (37.7)
Coagulase-negative staphylococcus	137/500 (27.4)	135/503 (26.8)	272/1003 (27.1)
Streptococcus species	72/500 (14.4)	73/503 (14.5)	145/1003 (14.5)
Pseudomonas species	28/500 (5.6)	23/503 (4.6)	51/1003 (5.1)
Other gram-negative organisms	84/500 (16.8)	84/503 (16.7)	168/1003 (16.7)
Culture negative	77/500 (15.4)	78/503 (15.5)	155/1003 (15.5)

Highly Bioavailable po abx

- Equivalent to IV
 - Linezolid/tedizolid
 - ► TMP-SMX
 - Metronidazole
 - Quinolones
 - Clindamycin
 - Doxycycline/minocycline

- May work at high doses in highly vascularized areas
 - Amox-clav mandible only
 - Cefadroxil
- Don't trust other beta-lactams
 - Amox, PCN, cephalexin

Long Acting Lipoglycopeptides

- Dalbavancin and Oritavancin
 - Terminal half-life >14 days
 - Dose one day 1 and day 8
 - Levels in bone/joint for at least 8 weeks
 - Shorter LOS
 - Fewer complications (PICC)



(Cain et al., 2022); (Dunne et al., 2015)



- 60 yo F with history of R TSA who comes in with many months of shoulder pain. She has some humeral loosening on xray. Arthrocentesis with 2k wbcs, 90% PMNs, and cx ng. She is taken for revision with conversion to rTSA and intraoperative cultures are positive for cutibacterium acnes in 2/6 specimens. Is this a PJI?
 - ► How to interpret micro results
 - Cuti-score

Hardy Diagnostics A50 Columbia CNA https://www.amazon.com/Hardy-Diagnostics-A50-Nalidixic-Selective/dp/B01MQ27G8G?SubscriptionId=1F5PDSSXX6EPXZQTE9R2&tag=amazany_ 20&linkCode=xm2&camp=2025&creative=165953&creativeASIN=B01MQ27G8GAgar (Colistin and Nalidixic Acid), with 5% Sheep Blood for The Selective Isolation of Gram Positive Bacteria, 15 x 100 mm Plate (Pack of 10): Amazon.com: Industrial & Scientific; AGARES MAS USADOS EN MICROBIOLOGIA (josebactesthaphy.blogspot.com); Macconkey Agar Plate at best price in Nashik by Chetana

What happens in micro lab

- Specimen plated according to lab protocol (differs based on facility)
- Aerobic/Anaerobic



Blood

- Most stuff grows
- Staph, Strep
- E.coli, PSA, etc



Chocolate

- H. influenza
- Neisseria





MacConkey

- GNRs
- LF- pink
- NLF (PsA) clear

Thio BrothAnaerobes

Blood Agar

Semiquantitative Cx Results

 Helps us determine extent of bacterial burden

Clue to possible contamination



Streaking Microbiology Microbiological Culture Microorganism https://imgbin.com/png/1p8FKjBX/streakingmicrobiology-microbiological-culture-microorganism-bacteria-pngBacteria PNG, Clipart, Agar, Agar Plate, Area, Aseptic Technique, Bacteria Free PNG Download (imgbin.com)

Blood Agar



Strep – Normal Growth



Contamination or very low inoculum?

<u>blood agar</u>

cohttps://www.bing.com/images/search?view=detailV2&ccid=6Wc5iE92&id=441AE8CAC1C3FED30791086719E07EB3D1 78D0CC&thid=OIP.6Wc5iE9258XAdyMFdF_D-

wHaCX&mediaurl=https%3a%2f%2fwww.researchgate.net%2fprofile%2fStephen_Looney%2fpublication%2f263295442%2f figure%2fdownload%2ffig1%2fAS%3a203171868745741%401425451356768%2fBacterial-growth-is-seen-on-blood-agarplates A Listerine test arous B. Decapingl

https://www.sciencephoto.com/media/297053/viewg bacteria - Stock Image - M874/0550 - Science Photo Library

Blood Agar Difficulties



MBM



Proteus Swarming

Typical appearance of https://www.researchgate.net/figure/Typical-appearance-of-a-blood-agar-plate-resulting-fromswabbing-a-computer-keyboard fig1 241644149 a blood agar plate resulting from swabbing a... | Download Scientific Diagram (researchgate.net) Swarming Proteus

mirahttps://www.flickr.com/photos/143588891@N02/3373559 4670/bilis | Overnight culture of Proteus mi... | Flickr

Fungal Cultures

- Purpose isn't for candida although it will grow
- Trying to grow dimorphic fungi, molds, non-candida yeast

Может ли молочница пройти сама без лечения: у мужчин и женщин (omolochnice.comhttps://omolochnice.com/obshchee/mozhet-li-projti-sama-096.html); Pictured is a SABHI agar plate culture of the fungus Histoplasma... News Photo - Getty Images; Mucor fungus (Genus Mucor) (forestryimages.org); Zygomycota | Fungi, Stuffed mushrooms, Condiments

Can take weeks to grow



C.albicans

(pintere









Mucor

AFB Cx

Held for 2 months



Nocardia

World J Clin Infect Dis. Nov 25, 2013; 3(4): 86-89



TB on LJ Media https://www.bing.com/th?id=OIP.OH_FWfVIKUmDIvYrhf kf4QHaFj&w=160&h=119&rs=1&qlt=80&dpr=1.74&pid=3

.1

M. chimaera Culture



Presentation given at APIC 2017 in Oregon by Jack Rihs.

Cuti-score Shoulder PJI

Major PJI criteria for shoulder - meeting one is diagnostic

- Presence of a sinus tract from the skin surface to the prosthesis
- Gross intra-articular pus
- Two positive tissue cultures with phenotypically identical virulent organisms

Minor Criteria

- ▶ 6 or greater with identified organism indicates probable (PJI)
- ▶ 6 or greater without identified organism indicates possible PJI
- Fewer than 6
 - Single positive culture with virulent organism indicates possible PJI
 - ▶ 2 positive cultures with low-virulence organism indicates possible PJI
 - Negative cultures or only single positive culture with low-virulence organism indicates PJI unlikely

(Garrigues et al., 2019)

Table I Minor criteria for definition of shoulder PJI		
Minor criteria	Weight	
Unexpected wound drainage	4	
Single positive tissue culture with virulent organism	3	
Single positive tissue culture with low-virulence organism	1	
Second positive tissue culture (identical low-virulence organism)	3	
Humeral loosening	3	
Positive frozen section (5 PMNs in \geq 5 high-power fields)	3	
Positive preoperative aspirate culture (low or high virulence)	3	
Elevated synovial neutrophil percentage (>80%)*	2	
Elevated synovial WBC count (>3000 cells/µL)*	2	
Elevated ESR (>30 mm/h)*	2	
Elevated CRP level (>10 mg/L)*	2	
Elevated synovial α -defensin level	2	
Cloudy fluid	2	



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Cuti-score = 9 -> Probable F	١Ľ
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- Call micro to get sensitivities performed
- Treatment IV Ceftriaxone vs PO doxy

Minor criteria	Weight
Unexpected wound drainage	4
Single positive tissue culture with virulent organism	3
Single positive tissue culture with low-virulence organism	1
Second positive tissue culture (identical low-virulence organism)	3
Humeral loosening	3
Positive frozen section (5 PMNs in ≥5 high-power fields)	3
Positive preoperative aspirate culture (low or high virulence)	3
Elevated synovial neutrophil percentage (>80%)*	2
Elevated synovial WBC count (>3000 cells/µL)*	2
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Elevated CRP level (>10 mg/L)*	2
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Cloudy fluid	2



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OVIVA

	Participants randomized to IV Antibiotic* (N = 521)	Participants randomized to PO Antibiotic* (N = 523)	Total* (N = 1044)
Glycopeptides ^a (IV)	214 (41.1%)	22 (4.2%)	236 (22.6%)
Penicillins (IV)	38 (7.3%)	11 (2.1%)	49 (4.7%)
Cephalosporins (IV)	173 (33.2%)	8 (1.5%)	181 (17.3%)
Carbapenems (IV)	41 (7.9%)	5 (1.0%)	46 (4.4%)
Other single IV antibiotic	35 (6.7%)	2 (0.4%)	37 (3.5%)
Combination IV antibiotics	35 (6.7%)	6 (1.1%)	41 (3.9%)
Penicillins (PO)	8 (1.5%)	83 (15.9%)	91 (8.7%)
Quinolones ^b (PO)	33 (6.3%)	191 (36.5%)	224 (21.5%)
Tetracyclines ^c (PO)	4 (0.8%)	57 (10.9%)	61 (5.8%)
Macrolides / Lincosamide d (PO)	10 (1.9%)	68 (13.0%)	78 (7.5%)
Other single PO antibiotic (PO)	10 (1.9%)	54 (10.3%)	64 (6.1%)
Combination PO antibiotics (PO)	13 (2.5%)	87 (16.6%)	100 (9.6%)

rifampicin use ^a	Randomized to IV Antibiotic* (N=523)	Randomized to PO Antibiotic* (N=526)	Total* (N=1049)
No rifampicin use	310 (59.3%)	233 (44.3%)	543 (51.8%)
<2 weeks ^b	21 (4.2%)	36 (6.8%)	57 (5.4%)
2 to 6 weeks ^b	72 (13.8%)	92 (17.5%)	164 (15.6%)
>6 weeks ^b	120 (22.9%)	165 (31.4%)	285 (27.2%)