SH62: What are the optimal oral or IV antibiotics to be used based on the most common bacteria cultured?

Liaison: Benjamin Zmistowski
Lead delegate: Benjamin Clark
Supportive delegate: Alexander Aleem

Response/Recommendation: There is limited data on preferred antibiotics, oral or intravenous, in shoulder periprosthetic infection. The most cause of infections, *Cutibacterium acnes,* should be managed initially with IV penicillin or cephalosporin, treatment can be stepped down to oral antibiotics according to OVIVA principles, ideally a beta lactam antibiotic. The evidence for additional rifampicin is conflicting but it may be considered as an adjunctive therapy when the prosthesis is retained. Because of increasing resistance, in patients with beta-lactam antibiotic allergy other treatment options should be chosen according to susceptibility testing results (when available).

Strength of Recommendation: Limited

Delegate Vote:

Rationale:

What are the most common bacteria cultured in periprosthetic infection of the shoulder?
Cutibacterium acnes is the most common organism involved in periprosthetic joint infection of the shoulder (PJI), historically accounting for 31% to 70% of all infections. Other bacteria associated with shoulder periprosthetic infections are pathogens typically found in the normal skin flora of the axillary region, particularly *S. epidermidis* and other coagulase-negative *Staphylococcus* (CoNS) species, and *S. aureus.* Increasingly, haematogenous infections are recognised as a cause of acute PJI's, including shoulder PJI, and as such *Streptococcus* species and Gram-negative organisms may also play a role.[1]

In contemporary reviews *C. acnes* remains the most common organism causing periprosthetic joint infection of the shoulder (PJI), followed by CoNS. Belay's metanalysis of 36 retrospective studies described 652 shoulder PJI's managed with revision arthroplasty. In single stage studies *C. acnes* was reported in 48.7%, CoNS in 23.2%, and *S. aureus* in 13.8% of all identified organisms. In the two-stage revision groups, *C. acnes* was identified in 33.7% of cases, CoNS in 20.3%, and *S. aureus* in 26.5% (MRSA in 9.7%). Polymicrobial infections were reported in 10.3% of single-stage and 5.5% cases of two-stage revisions.[2] Kunutsor's review of revision arthroplasty papers described 498 shoulders revised for PJI and 69 re-infections, *C. acnes* was the most common causative organism in 6/10 of one stage studies and 11/27 two stage. Staphylococcal species were most common in 12/27 studies. [3] Xiao's metanalysis of shoulder PJI managed with permanent spacers (177 pts) and resection arthroplasty (116 infection patients) reported *C. acnes* 23.6 % and S. aureus in 27.9%. [4] Three studies describe *S. epidermidis* then *C. acnes* as the commonest infecting organism in cohorts undergoing 2- and 3-stage revision arthroplasty and all had a high rate of polymicrobial infections, 30% of patients in Sievert's study [5,6,7] In a multicentre retrospective study of shoulder PJI in patients under 60 years old, *Cutibacterium acnes* and/or *S.*

epidermidis were identified in 80% of 55 cases, and again a high number of polymicrobial infections (16%). [8] Kew's review of 65 cases of shoulder PJI managed by DAIR, 60% of cases cultured *C. acnes*, 20% Staphylococcal species, only 3% were polymicrobial. [9]

What is the optimal antibiotic regimen? The literature describes outcomes of surgical techniques in heterogenous population groups but there are few papers that describe antibiotic choice and duration. When described there are multiple regimens of different durations described. [10,11] Optimal regimens cannot be determined. It is common practice to employ broad spectrum agents immediately after surgical sampling [12,13] The British Elbow and Shoulder Society (BESS) guidelines recommends clinicians switch to targeted therapy with the narrowest spectrum agent likely to be effective once susceptibilities of the causative pathogen are known. The surgeon should discuss the patient, organism, and antibiotics with an Infectious diseases specialist as part of the multidisciplinary management.[14] An early switch from IV to oral therapy should be encouraged when applicable following the OVIVA trial results. [15] Complications have been described secondary to IV therapy for *C. acnes* shoulder infection. [16] There are no studies specific to each organism, except for *C. acnes* which is discussed below. For treatment of other organisms, national guidelines can be referenced.

C. acnes is universally susceptible to penicillin, cephalosporins, and glycopeptides, and susceptible to a broad range of other antibiotics. The Infectious Diseases Society of America recommends the use of beta-lactams as the preferred treatment for *Propionibacterium acnes* (now *C. acnes*) treatment. [17] See Table 1.

Similarly, the BESS guidelines recommend IV penicillin or vancomycin. IV ceftriaxone has advantages for outpatient or home administration given its once daily frequency and has been shown to be effective in other implant associated infections due to *C. acnes*.[18] Caution should be used when using clindamycin due to increasing resistance. Beig's recent metanalysis of global patterns of *C. acnes* antimicrobial susceptibility described the following resistance rates: clindamycin 31%, co-trimoxazole 9%, doxycycline 8%, levofloxacin 6%, ciprofloxacin 5%, and minocycline 2.5%. There were marked differences between countries, 90% of UK *C. acnes* isolates were clindamycin resistant compared to 15% in the US.[19] If available, susceptibility testing of *C. acnes* isolates should be utilised to guide ongoing IV therapy. Other parenteral options include daptomycin and other glycopeptides e.g. teicoplanin, dalbavancin.[20] The latter has the advantage of once weekly administration and has been shown to be non-inferior to the standard of care and may be a good choice for outpatient antibiotic delivery programs. Oral step-down therapy of penicillin V, amoxicillin, cephalexin, minocycline, or doxycycline is recommended. If continued as suppressive antibiotic therapy (SAT), reduced doses can be considered: amoxicillin 500mg bid, doxycycline 100mg qd, minocycyline 100mg qd, clindamycin 300mg bid, co-trimoxazole 960mg qd.[21]

The use of rifampicin as an adjunctive therapy remains controversial. It's addition in cases where the prosthesis is retained, as used for PJI due to Staphylococcal species, is recommended by the BESS guidelines. There are no RCT's to assist. A retrospective study of shoulder PJI due to *C. acnes* by Vilchez et al included 44 patients with *C. acnes*-related PJI and concluded that additional rifampicin treatment did not decrease recurrence in patients treated with β-lactams.[22] Similarly Jacobs et al did not describe any benefit. In Kusejko et al's multi-centre retrospective study of 187

patients with *C. acnes* PJI (revision 78.1%%, DAIR 18.2%), 43.3% received rifampicin as adjunctive therapy, but concluded than rifampicin combination is not markedly superior in Cutibacterium PJI. [23] Jacobs et al reported similar results. [24] Kobayashi's metanalysis on rifampicin combination therapy for orthopaedic implant-related infections showed that rifampicin combinations were effective in patients infected with *C. acnes* but commented that the certainty and quality of evidence were very low. [25]

Table 1. IDSA recommendations for *Cutibacterium acnes* (previously *P. acnes*) treatment.

Preferred	Alternative	Notes
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 IV Vancomycin 15 mg/kg IV q12 h	Vancomycin only in case of allergy

Note - doses assume normal renal function

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