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Biofilm formation and the "race to the surface": Is biofilm addressed in DAIR, double DAIR, and DAPRI procedures?

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Surgical site infections (SSIs) and Periprosthetic joint infections (PJIs) are a significant problem in orthopaedics. Once a site becomes infected, treatment requires tremendous healthcare resources, and outcomes have variable success rates. Over the past 5-10 years, studies have reported implant retention for PJIs including DAIR, double DAIR, and DAPRI procedures (1-13). The DAIR-infected joint procedure is an acronym for debridement, antibiotics, and implant retention. This method has a reported success rate of 50-80% (2). This relatively limited success rate encouraged Calanna et al. to modify the DAIR procedure by adding antibiotic eluting pearls before wound closure to potentially improve infection eradication rates (2). Thus, DAIR became DAPRI or debridement, antibiotic pearls, and retention of the implant (2). The authors reporting the DAPRI surgical technique in early 2021 also published two other DAPRI studies (3,4). Each study had an average follow-up of 3.5 years. In these two reports, the DAPRI technique resulted in overall infection-control rates of 87% and 90% (3,4). The double DAIR procedure is a 2-stage debridement protocol that includes the use of high-dose antibiotic beads between stages (1).The DAPRI infection control rates (87-90%) are better than the infection eradication rate reported (60-84%) for a traditional 2-stage salvage of an infected total knee arthroplasty (TKA) (5-13). The 2-stage salvage

technique was first reported by Insall et al. in JBJS in 1983 (13). In a busy elective arthroplasty practice, an 90% infection control rate for infected totals may not be acceptable. The 2-stage salvage protocol has an important limitation to consider which significant bone damage during explantation (1-4). Could we do better with current implant retention infection treatment techniques? For example, since Insall's seminal 2-stage PJI paper nearly 40 years ago, staphylococcus Aureus infection pathways are better known. Are we applying everything we have learned about bacteria and infections to implant retention techniques? The purpose of this editorial is to highlight basic science advances as they pertain to bacteria and infections. The inclusion of these relatively recent findings may lead to further modifications of the DAIR, double DAIR, and DAPRI techniques. Two years ago, Alamanda and Springer published a brief article on 12 modifiable patient factors for infection prevention (15). There may be potentially modifiable bacteria pathways to exploit in treating infections. An appreciation for these potential opportunities begins with revisiting the landmark paper by A., Gristina in Science in 1987, when he coined the phrase "The race to the surface" (16). The race to the surface concept was the culmination of several other concurrent biofilm studies at that time (17-20). These studies reported that bacteria often adhere to implants via a biofilm they form on implants (16-20). The other participant in the race to the implant surface is the human body. The body encapsulates all foreign bodies (16). Orthopaedic trauma surgeons take advantage of this phenomenon with bony defect reconstruction using the Masqulet technique (21). The body responds to a cement spacer and wins the "race" by forming a pseudomembrane around the cement spacer (21) Another noteworthy aspect of treating infections is that a bacteria's biofilm have several protective properties which contribute to infection recurrences. First, the biofilm blocks antibiotic access to bacteria. Secondly, beneath the biofilm lay planktonic bacteria. These "dormant" bacteria can re-emerge when their quorum sensing deems the milieu to be permissible. Also, within the biofilm is a reserve of nutrients essential for replication (22,23). Three additional and very important recent concepts about osteomyelitis and PJIs include the following. One, bacteria reside in the medullary canal (17). Two, Staph Aureus have been identified within osteocytes (24). Third, Staph Aureus has also been identified within skin keratinocytes (25). Collectively, bacteria dormant within the medullar canal, osteocytes, and skin keratinocytes may be the mechanism for the indolence seen in osteomyelitis, PJIs, and other SSIs. (17,22-25) These are key concepts to consider in all infection cases. For example, an infected total knee may require femoral and tibial canal sequential reaming for adequate bone debridement for bacteria and biofilm removal. The surgeon treating an infection must identify all biofilm and thoroughly remove all biofilm at the time of an infection debridement. None of the DAIR or DAPRI methods completely address biofilm removal (18-23). For example, a retained implant theoretically has biofilm somewhere on its surface. Previously, in biofilm studies, Ruthenium red was used to stain the polysaccharide portion of biofilms for visualization (18, 26). Unfortunately, Ruthenium red is approved only for histology and research purposes. It cannot be used to stain an infected joint to help identify biofilm loci. The development of biofilm staining solutions for intra-operative application to aid in biofilm identification and removal is a noteworthy project for

future research. In summary, the implant retention PJI techniques avoid the bony damage that explantation often imparts. This is a major advantage of DAIR methods which cannot be overlooked. Implant retention does, however, limit access to the medullary canal. Based upon two previous studies (17,24), bacteria are likely residing in osteocytes in the femoral and tibial canals, which are inaccessible to a debridement with retained implants. The key points of this editorial are that infection physiology is understood better. Moreover, bacteria form a protective biofilm that shields bacteria from antibiotics, and bacteria reside within joint regions potentially not addressed in DAIR methods. Again, biofilm and bacteria are omni present in infected joints. The vast distribution of bacteria in PJIs, requires broader inclusion in implant retention techniques. Therefore, all PJI treatments even implant retention methods possibly require some form of canal debridement. Improved methods of biofilm identification and removal are also needed for all implant-related infection treatments to improve outcomes. Finally, in recent years, bacterial biofilm and the “race to the surface” concepts appear to be relatively minor components of infection management protocols. Our infected patients would benefit from future protocols that targeted biofilm and implant surfaces the medullary canal and other known bacteria “hiding places”. Implant retention methods in PJI will likely evolve and improve outcomes if these recent infection concepts are applied.

References

1. McQuivey, Kade S., et al. “The Double DAIR: A 2-Stage Debridement with Prosthesis-Retention Protocol for Acute Periprosthetic Joint Infections.” JBJS Essential Surgical Techniques 11.1 (2021): e19.
2. Calanna, F, Chen, F, Positano, S, et al. Debridement, antibiotic pearls, and retention of the implant (DAPRI): a modified technique for implant retention in total knee arthroplasty PJI treatment. J Orthop Surg (Hong Kong) 2019; 27: 2309499019874413.
3. . Chung AS, Niesen MC, Graber TJ, Schwartz AJ, Beauchamp CP, Clarke HD, Spangehl MJ. Two-stage debridement with prosthesis retention for acute periprosthetic joint infections. J Arthroplasty. 2019 Jun;34(6):1207-13. Epub 2019 Feb 16.
4. 3. Estes CS, Beauchamp CP, Clarke HD, Spangehl MJ. A two-stage retention debridement protocol for acute periprosthetic joint infections. Clin Orthop Relat’ Res. 2010 Aug;468(8):2029-38.
5. Brandt CM, Sistrunk WW, Duffy MC, Hanssen AD, Steckelberg JM, Ilstrup DM, Osmon DR. Staphylococcus aureus prosthetic joint infection treated with debridement and prosthesis retention. Clin Infect Dis. 1997 May;24(5):914-9. 5.
6. Burger RR, Basch T, Hopson CN. Implant salvage in infected total knee arthroplasty. Clin Orthop Relat Res. 1991 Dec;273:105-12. 6.
7. Deirmengian C, Greenbaum J, Lotke PA, Booth RE Jr, Lonner JH. Limited success with open debridement and retention of components in treating acute Staphylococcus aureus infections after total knee arthroplasty. J Arthroplasty. 2003 Oct;18(7)(Suppl 1):22-6.
8. Deirmengian C, Greenbaum J, Stern J, Braffman M, Lotke PA, Booth RE Jr, Lonner JH. Open debridement of acute gram-positive infections after total knee arthroplasty. Clin Orthop Relat Res. 2003 Nov;416:129-34. 8.
9. Hartman MB, Fehring TK, Jordan L, Norton HJ. Periprosthetic knee sepsis. The role of irrigation and debridement. Clin Orthop Relat Res. 1991 Dec;273: 113-8. 9.
10. Marculescu CE, Berbari EF, Hanssen AD, Steckelberg JM, Harmsen SW, Mandrekar JN, Osmon DR. Outcome of prosthetic joint infections treated with debridement and retention of components. Clin Infect Dis. 2006 Feb 15;42(4):471-8. Epub 2006 Jan 5. 10.

11. Meehan AM, Osmon DR, Duffy MCT, Hanssen AD, Keating MR. The outcome of penicillin-susceptible streptococcal prosthetic joint infection treated with debridement and retention of the prosthesis. Clin Infect Dis. 2003 Apr 1;36(7):845-9. Epub 2003 Mar 20. 11.
12. Silva M, Tharani R, Schmalzried TP. Results of direct exchange or debridement of the infected total knee arthroplasty. Clin Orthop Relat Res. 2002 Nov; 404:125-31. 12.
13. Teeny SM, Dorr L, Murata G, Conaty P. Treatment of infected total knee arthroplasty. Irrigation and debridement versus two-stage reimplantation. J Arthroplasty. 1990 Mar;5(1):35-9.
14. Insall JN, Thompson FM, Brause BD. Two-stage reimplantation for the salvage of infected total knee arthroplasty. J Bone Joint Surg Am. 1983 Oct;65(8): 1087-98.
15. Alamanda VK, Springer BD. The prevention of infection: 12 modifiable risk factors. Bone Joint J. 2019 Jan;101-B(1_Supple_A):3-9. DOI: 10.1302/0301-620X.101B1.BJJ-2018-0233.R1. PMID: 30648488.
16. Gristina, Anthony G. “Biomaterial-centered infection: microbial adhesion versus tissue integration.” Science 237.4822 (1987): 1588-1595.
17. A. C. Masquelet, F. Fitoussi, T. Begue, and G. P. Muller, “Reconstruction of the long bones by the induced membrane and spongy autograft,” Annales de Chirurgie Plastique et Esthetique, vol. 45, no. 3, pp. 346–353, 2000.
18. Gristina, A. G., Oga, M., Webb, L. X., & Hobgood, C. D. (1985). Adherent bacterial colonization in the pathogenesis of osteomyelitis. Science, 228(4702), 990-993.
19. Webb, L. X., Myers, R. T., Cordell, A. R., Hobgood, C. D., Costerton, J. W., & Gristina, A. G. (1986). Inhibition of bacterial adhesion by antibacterial surface pretreatment of vascular prostheses. Journal of vascular surgery, 4(1), 16-21.
20. A. G. Gristina, L. X. Webb, E. Barth, in Infection in the Orthopaedic Patient, R. Coombs and R. Fitzgerald, Eds. (Butterworths, London, in press).
21. A. C. Masquelet, F. Fitoussi, T. Begue, and G. P. Muller, “Reconstruction of the long bones by the induced membrane and spongy autograft,” Annales de Chirurgie Plastique et Esthetique, vol. 45, no. 3, pp. 346–353, 2000.
22. Satpathy, S, Sen, SK, Pattanaik, S, et al. Review on bacterial biofilm: a universal contamination cause. Biocatal Agric Biotechnol 2016; 7: 56–66.
23. Koo, H, Allan, RN, Howlin, RP, et al.Targeting microbial biofilms: current and prospective therapeutic strategies. Nat Rev Microbiol 2017; 15: 740–755.
24. Ellington JK, Harris M, Webb L, Smith B, Smith T, Tan K, Hudson M. Intracellular Staphylococcus aureus. A mechanism for the indolence of osteomyelitis. J Bone Joint Surg Br. 2003 Aug;85(6):918-21. PMID: 12931819.
25. Al Kindi A., Alkahtani A., M., Mayimuna, N., El-Chami C., O’Neill C., Arkwright P. D., Pennock J. L. Staphylococcus aureus Internalized by Skin Keratinocytes Evade Antibiotic Killing. Frontiers in Microbiology. 2019, V10. P.2242.
26. M. Fletcher, in Bacterial Adherence, E. H. Beachey, Ed. (Chapman & Hall, London, 1980).p. 345._____

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