QUESTION 5: Do bacteria form biofilm on the surface of cement spacer in a similar fashion to a metallic implant?

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Response:

Yes. While the vast majority of studies have been *in vitro*, there is clinical evidence that majority of bacteria are able to form biofilm on the surface of cement spacer.

Level of Evidence: Strong

Delegate Vote: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

Post Meeting Rationale:

The authors performed PubMed and Google Scholar literature search from1975 to present, using combination of these words: Biofilms, polymer, mature, metal, orthopedics, growth, presence, clinical, in vitro, in vivo, monomicrobial, polymicrobial, stain, surface, bone cement, antibiotic cement, polymethylmethacrylate, phenotype, isolate names, roughness, smooth, clinic, patient and joint. Papers that involved short-term attachment strategies versus biofilm growth and presence were excluded as biofilm was the primary outcome desired. Papers that discussed biofilm on polymer- or metal-based medical devices that were not cement-related were excluded to keep the search focused. Inclusion criteria were similar to point

The majority of data assessing biofilm growth on polymeric materials and smooth surfaces has been collected from *in vitro* experiments [1]. As a general outline, microbial adherence to materials occurs in the following order: latex > silicone > PVC > Teflon > polyurethane > stainless steel > titanium [1,2]. Verran et al. showed that *Candida albicans* adhered to a greater degree on roughened surfaces compared to smooth [3]. In their experiment, polymeric samples were incubated for 1 hr, and then assessed for adhesion profiles. Similar work was performed by Taylor et al. on cobalt-chrome materials with the same conclusion [4]. While surface roughness may play a role [5], Wolcott et al. have shown that time may play an important role in biofilm maturation and antibiotic tolerance [6]. Biofilms are well-known to condition surfaces and make them conducive to their growth requirements [5]. Perhaps one of the most well-known examples of this is *Streptococcus mutans*, which conditions the enamel surface that allows adherence for hundreds of other bacterial species [7]. Given enough time, biofilms may flourish on surfaces in many environments and on surfaces that may otherwise be considered less culturable [5,8,9]. In-house experiments that are in process of publication have shown that even amongst the same species, varying strains can differ in rates of biofilm formation on titanium surfaces, but over time degree of biofilm formation is similar in bench-top conditions.

The principles of biofilm formation apply to bone cement and metallic surfaces used in orthopaedic applications. Stoodley et al. directly observed biofilms on antibiotic-loaded bone cement associated with an infected total elbow arthroplasty [10]. McConoughey et al. have also identified bacterial biofilms on implanted components [11]. Shaw et al. observed biofilm, via methylene blue staining, that had developed on a tibial tray and other total joint components

during revision surgery [12]. Minelli et al. showed the ability of multiple staphylococcal bacterial strains to form biofilm on bone cement samples in all cases [13]. Neut et al. observed that slime-producing *Pseudomonas aeruginosa* can readily form biofilm on cement material, and in the biofilm phenotype it may be more tolerant to antibiotics loaded in cement than planktonic bacteria [14]. Ensing et al. assessed biofilm growth on cement material and the potential of ultrasound to remove its presence [15]. More recently in a study by Ma et al, polymethylmacrylate spacers that were removed at the time of reimplantation following treatment of infected total knee arthroplasty were shown to have high levels of bacterial DNA despite extended exposure to antibiotics [16].

In summary, indications that biofilm forms on metallic surfaces and bone cement [with the latter either the original pathogen(s), or a secondary pathogen(s) not present in the initial infection] in a similar fashion are present from clinical samples as well as *in vitro* and *in vivo* animal studies. There are indications that bacterial cells may adhere to and form biofilms more quickly on rough/porous materials, but over time bacteria may condition material surfaces that are smoother in nature such as metal and allow biofilm to form to a similar degree.

References:

1. Schinabeck M, Ghannoum M. 2006. Pathogenesis of IMD Related Infections. In: Pace JL, Rupp ME, Finch RG, editors. Biofilms, Infection, and Antimicrobial Therapy. CRC Taylor & Francis. p 42–45.
2. Darouiche RO. 2001. Device-associated infections: a macroproblem that starts with microadherence. Clin. Infect. Dis. An Off. Publ. Infect. Dis. Soc. Am. 33(9):1567–1572.
3. Verran J, Maryan CJ. 1997. Retention of Candida albicans on acrylic resin and silicone of different surface topography. J. Prosthet. Dent. 77(5):535–539.
4. Taylor R, Maryan C, Verran J. 1998. Retention of oral microorganisms on cobalt-chromium alloy and dental acrylic resin with different surface finishes. J. Prosthet. Dent. 80(5):592–597.
5. van de Belt H, Neut D, Schenk W, et al. 2001. Infection of orthopedic implants and the use of antibiotic-loaded bone cements. A review. Acta Orthop. Scand. 72(6):557–571.
6. Wolcott RD, Rumbaugh KP, James G, et al. 2010. Biofilm maturity studies indicate sharp debridement opens a time- dependent therapeutic window. J. Wound Care 19(8):320–328.
7. Gibbons RJ, Houte J V. 1975. Bacterial adherence in oral microbial ecology. Annu. Rev. Microbiol. 29:19–44.
8. Garrett TR, Bhakoo M, Zhang Z. 2008. Bacterial adhesion and biofilms on surfaces. Prog. Nat. Sci. 18(9):1049–1056.
9. Donlan RM. 2002. Biofilms: microbial life on surfaces. Emerg. Infect. Dis. 8(9):881–890.
10. Stoodley P, Ehrlich GD, Sedghizadeh PP, et al. 2011. Orthopaedic biofilm infections. Curr. Orthop. Pract. 22(6):558–563.
11. McConoughey SJ, Howlin R, Granger JF, et al. 2014. Biofilms in periprosthetic orthopedic infections. Future Microbiol. 9(8):987–1007.
12. Shaw JD, Miller S, Plourde A, et al. 2017. Methylene Blue-Guided Debridement as an Intraoperative Adjunct for the Surgical Treatment of Periprosthetic Joint Infection. J. Arthroplasty 32(12):3718–3723.
13. Bertazzoni Minelli E, Della Bora T, Benini A. 2011. Different microbial biofilm formation on polymethylmethacrylate (PMMA) bone cement loaded with gentamicin and vancomycin. Anaerobe 17(6):380–383.
14. Neut D, Hendriks JGE, van Horn JR, et al. 2005. Pseudomonas aeruginosa biofilm formation and slime excretion on antibiotic-loaded bone cement. Acta Orthop. 76(1):109–114 Available from: http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&DbFrom=pubmed&Cmd=Link&LinkName=pubmed_pubmed&LinkReadableName=Related Articles&IdsFromResult=15788318&ordinalpos=3&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum.
15. Ensing GT, Neut D, van Horn JR, et al. 2006. The combination of ultrasound with antibiotics released from bone cement decreases the viability of planktonic and biofilm bacteria: an in vitro study with clinical strains. J. Antimicrob. Chemother. 58(6):1287–1290.
16. Ma D, Shanks RMQ, Davis CM, et al. 2018. Viable bacteria persist on antibiotic spacers following two-stage revision for periprosthetic joint infection. J. Orthop. Res. Off. Publ. Orthop. Res. Soc. 36(1):452–458.