

Biofilm Formation

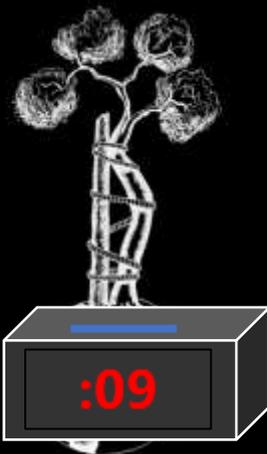
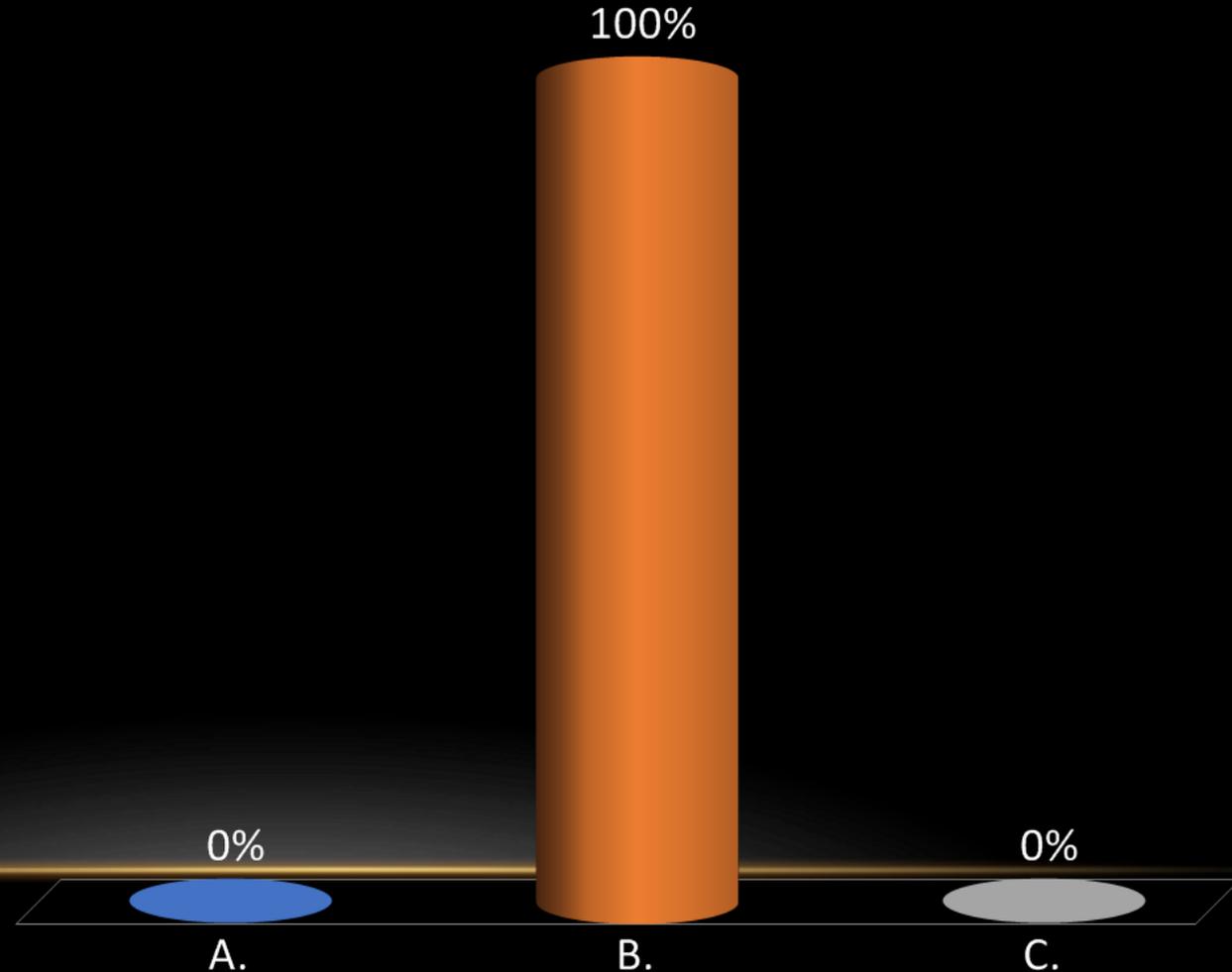


Let's test our devices

A. Yes

B. No

C. Abstain



infectionconsensus2018@gmail.com

- For any corrections, comments, edits, etc. please email the above address
- The same comments can be posted on the contact page of our website

lcmphilly.com



Biofilm-1 (Former G-135) What is the life cycle of biofilm and the mechanism of its maturation?

RESEARCHED BY:



Smeltzer, Mark MD, USA



Shirliff, Mark MD, USA

Joshi, Manjari MD, USA



Literature:

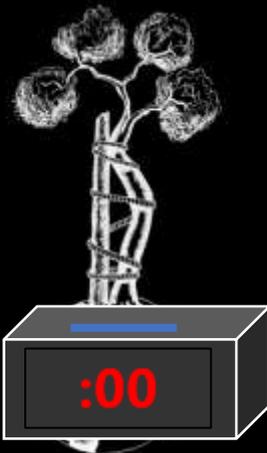
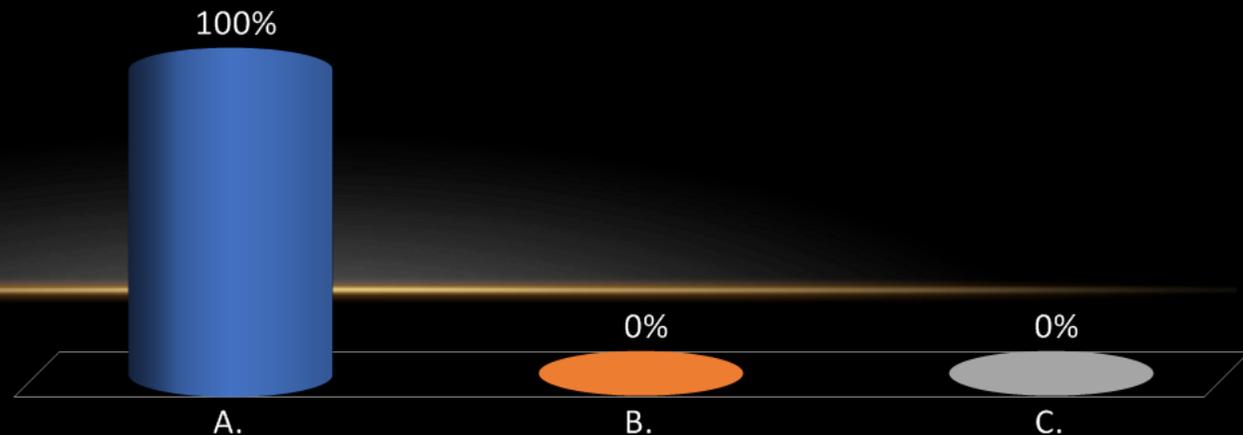
- **Understanding the progression of biofilm life cycles and the mechanisms that pathogens use to regulate this progression is essential for the development of therapeutic approaches aimed at preventing, disrupting, and eradicating biofilm-associated infections.**



Response: A biofilm may be defined as a microbe-derived sessile community characterized by organisms that are attached to a substratum, interface, or each other, are embedded in a matrix of extracellular polymeric substance, and exhibit an altered phenotype with respect to growth, gene expression, and protein production. The biofilm infection life cycle generally follows the steps of attachment (interaction between bacteria and the implant), accumulation (interactions between bacterial cells), maturation (formation of a viable 3D structure), and dispersion/detachment (release from the biofilm). The life cycle of biofilm is variable depending on the organism involved. There are characteristics in the life cycle of biofilm formation. These include, Attachment, proliferation/accumulation/maturation, and dispersal. Biofilm can either be found as adherent to a surface or as floating aggregates.

Level of Evidence: Strong (this is a scientific review)

- A. Agree
- B. Disagree
- C. Abstain



Biofilm-2 (Former G-164) What surface properties favor biofilm formation?

RESEARCHED BY:



Noble, Philip C MD, USA



Arciola, Carla Renata MD, Italy



Pidgaiska, Olga MD, Ukraine



Literature:

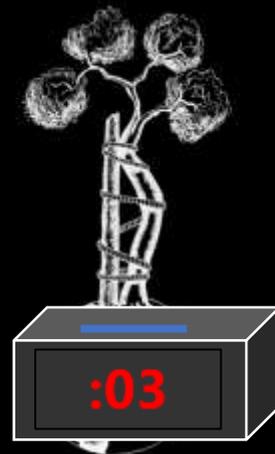
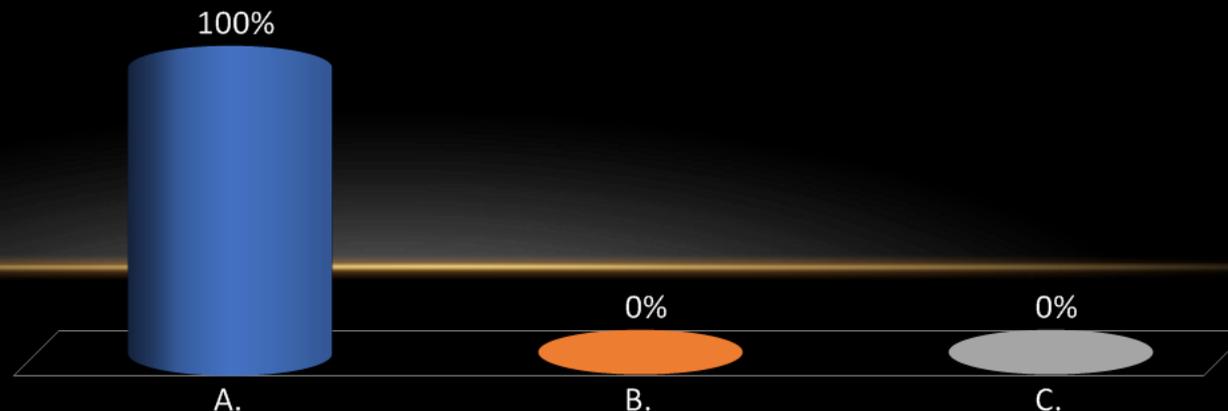
- Although there is little consensus in terms of which surface properties are most definitive in contributing to biofilm formation, there are certainly strides in examining the general impact of different properties when considered individually.



Response: The attachment of bacteria to implant and biological surfaces is a complex process, starting with the initial conditioning film. Roughness, hydrophobicity/hydrophilicity, porosity, pore topology, and other surface conditions are the key factors for microbial adhesion. Because of the huge variety of these factors, most of the studies directed at bacterial attachment to the implant surface were limited to specific surface conditions since it is difficult to examine the plethora of parameters concomitantly. There are variable conclusions among the available basic science and animal studies relevant to this topic, many of which will be described in greater detail below. Bacteria can form biofilm on almost all prosthetic surfaces and biological surfaces. To date, this consensus group knows of no surface that is inimicable to the growth of biofilm in vivo.

Level of Evidence: Strong

- A. Agree
- B. Disagree
- C. Abstain



Biofilm-3 (Former G-95) Is the biofilm on orthopedic implant surface permeable to neutrophils and macrophages in vivo? Are these innate immune cells (meaning any macrophages or neutrophils) capable of engulfing and killing bacteria?

RESEARCHED BY:



Schwarz, Edward MD, USA

Yazdi, Hamidreza MD, Iran



Esteban, Jaime MD, Spain



Literature:

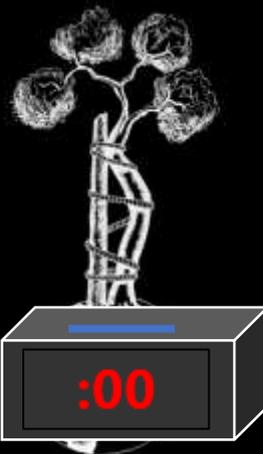
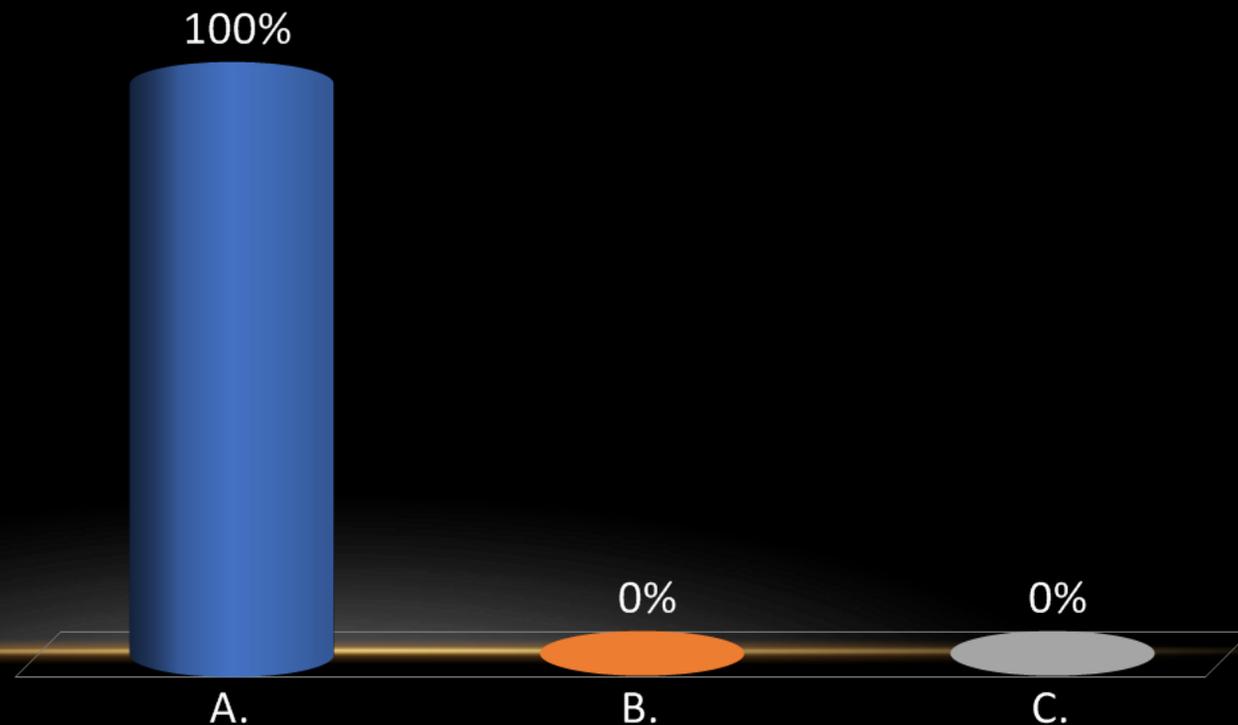
- **The most important pathogenic mechanism involved in implant-related infections is the ability of the microorganisms to form a biofilm, which leads to protection against environmental stress, host immune defense and antimicrobials. The first cells arriving at the infection site are the neutrophils and macrophages.**



Response: A mature bacterial biofilm has limited permeability to neutrophils and macrophages. Those that get through are clinically ineffective at eradicating biofilm bacteria. While neutrophils and macrophages are capable of engulfing and killing planktonic bacteria, they are not innately capable of effectively engulfing and killing sessile bacteria in biofilm.

Level of Evidence: Strong

- A. Agree
- B. Disagree
- C. Abstain



Biofilm-4 (Former G-60) Does the timescale of biofilm formation differ between bacterial species? If so, what is the timescale for common causative organisms?

RESEARCHED BY:



Moser, Claus MD, Denmark



Saeed, Kordo MD, UK



Literature:

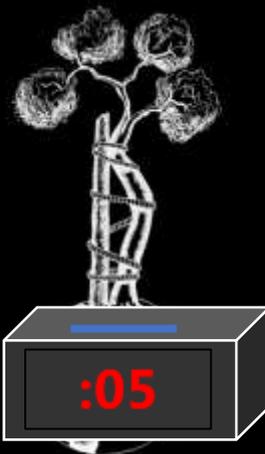
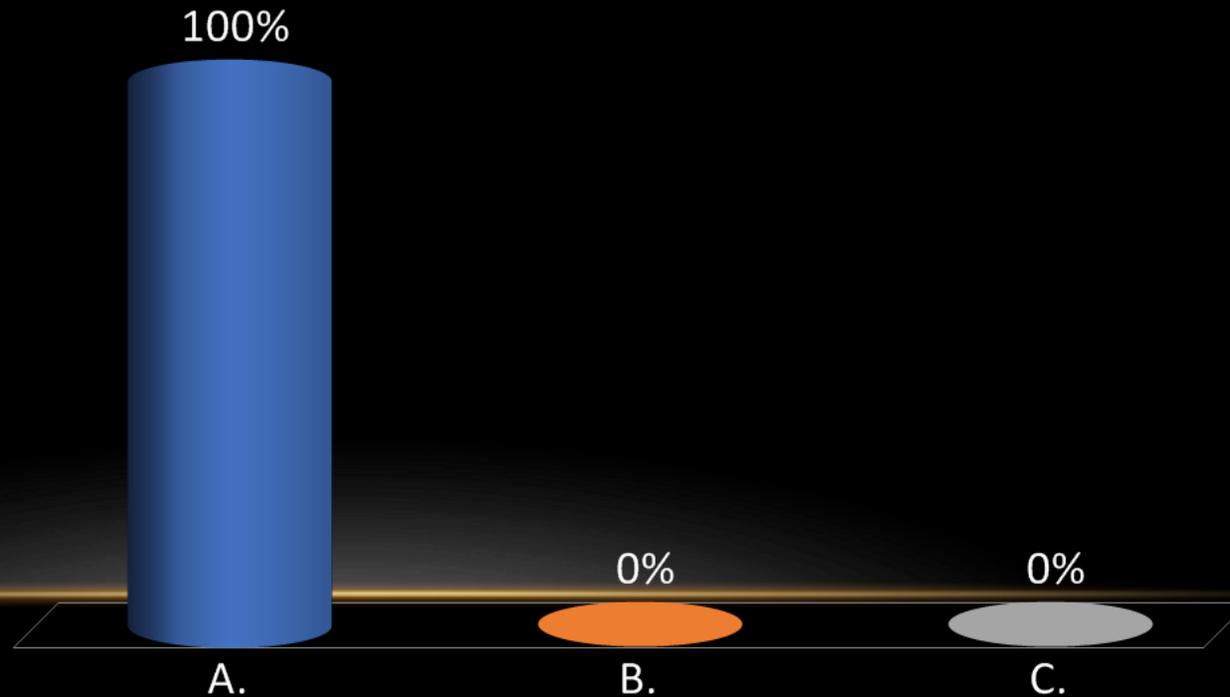
- **Some evidence suggests that bioactive substances such as hydroxyapatite may be more prone to bacterial adhesion than bioinert metals, such as titanium alloys and stainless steel.⁷ Further studies have demonstrated that polymethyl methacrylate (PMMA) is capable of hosting biofilms that can cause acute, chronic, and delayed-onset infections.**



Response: Currently, there is no clinical research available to answer whether the timescale in the development of biofilm formation differs between bacterial species. In vitro studies show high variability in biofilm formation based on bacterial strains and conditions. Animal studies have demonstrated rapid (minutes to hours) biofilm formation. The group notes that the timeline of biofilm formation may not correlate with the onset of infection symptoms.

Level of Evidence: Strong

- A. Agree
- B. Disagree
- C. Abstain



Biofilm-5 (Former G-23) Do bacteria form biofilm on the surface of cement spacer in a similar fashion to a metallic implant?

RESEARCHED BY:



Williams, Dustin MD, USA



Urish, Kenneth MD, USA



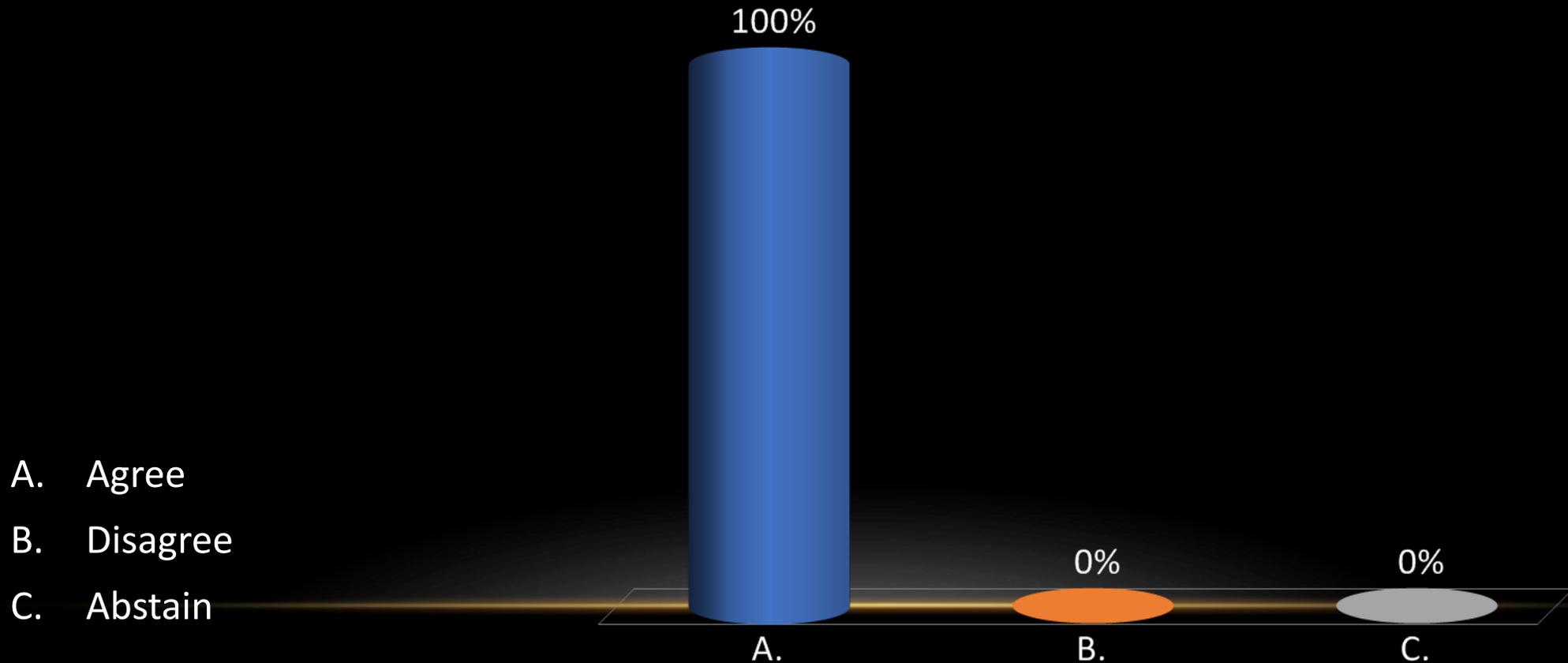
Literature:

- In summary, indications that biofilm forms on bone cement and metallic surfaces 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.

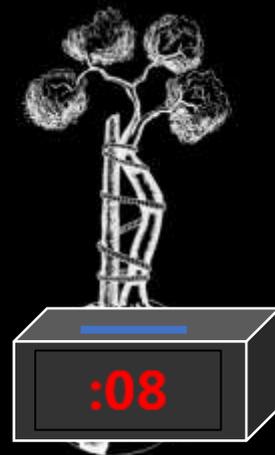


Response: Yes. While the vast majority of studies have been in vitro, there is clinical evidence that majority of bacteria are able to form biofilm on the surface of cement spacer.

Level of Evidence: Strong



- A. Agree
- B. Disagree
- C. Abstain



Biofilm-6 (Former G-32) Does Mycobacterium tuberculosis form a biofilm on implants?

RESEARCHED BY:



Burastero, Giorgio MD, Italy



Komnos, Georgios MD, Greece



Sendi, Parham MD, Switzerland



Literature:

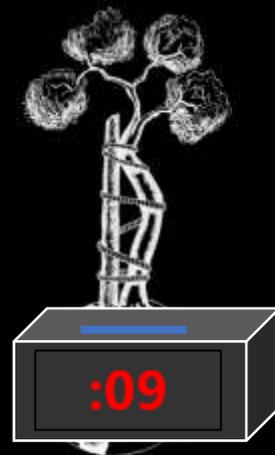
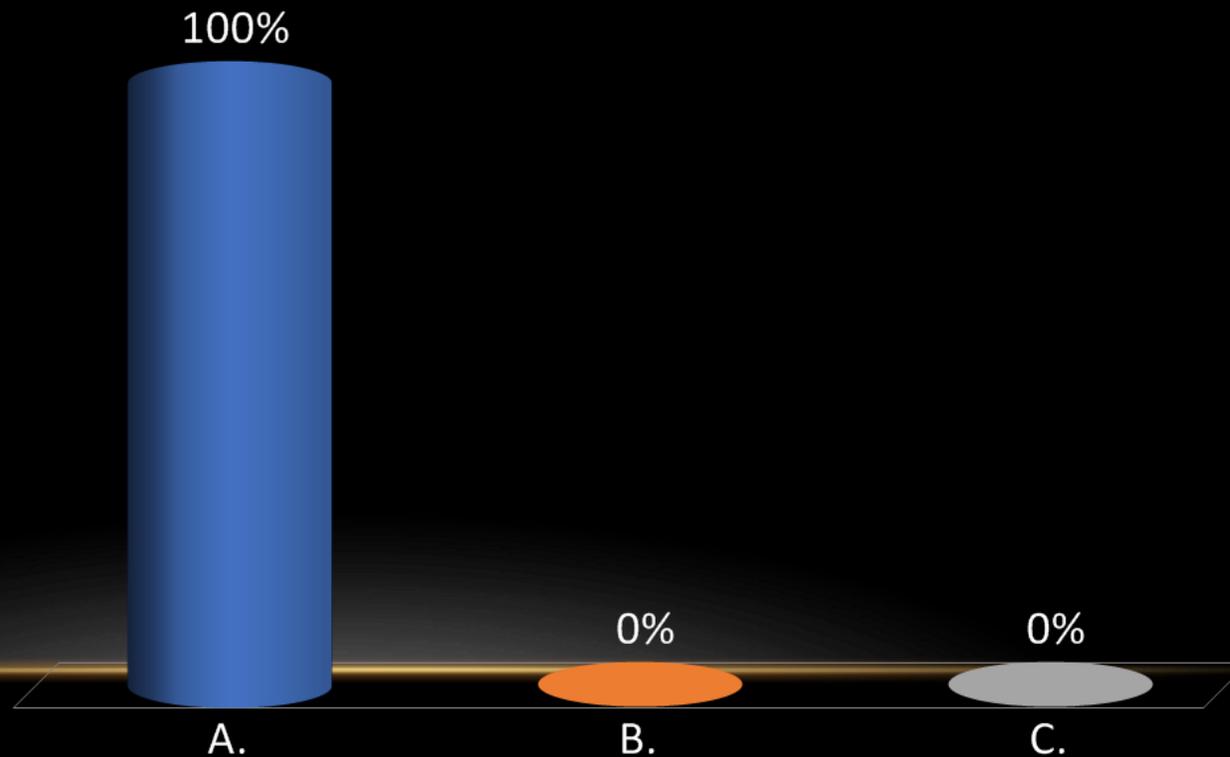
- **The vast majority of studies investigating M.tuberculosis biofilms uses polystyrene plates. A study compared the adherence and the biofilm formation of Staphylococcus epidermidis with those of M. tuberculosis on four types of metal segments.**



Response/Recommendation: Few data from experimental in vitro and in vivo studies and a limited number of case reports indicate that *M. tuberculosis* has a slow, albeit significant, ability to form biofilm on metal surfaces. The group suggests that management of *M. tuberculosis* implant-related infections should be treated using the same principles as that of other implant-related infections.

Level of Evidence: Strong

- A. Agree
- B. Disagree
- C. Abstain



Biofilm-7 (Former G-152) What is the role of the microbial synergy in polymicrobial infections?

RESEARCHED BY:



Shubnyakov, Igor MD, Russia



Tan, Timothy MD, USA



Bonilla León, G. A MD,
Colombia



Literature:

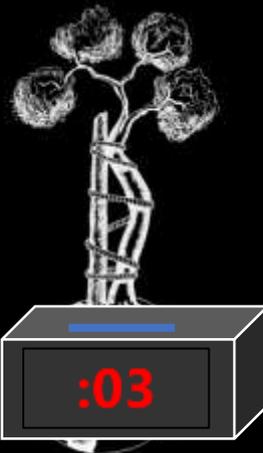
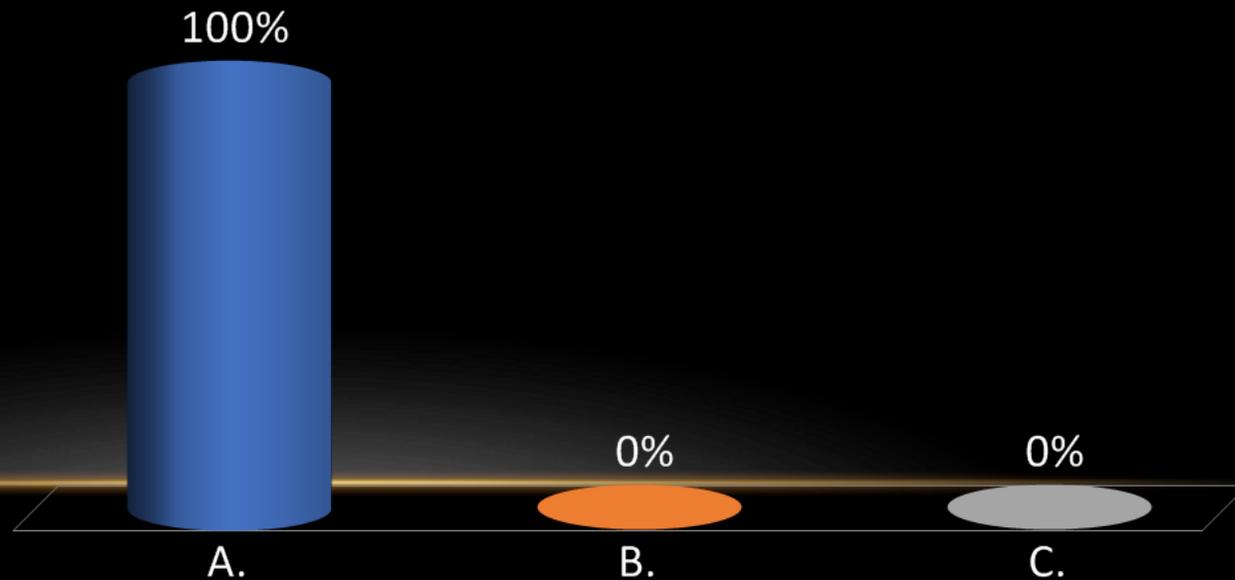
- **Several mechanisms of microbial synergy have been proposed in order to explain microorganisms interactions during polymicrobial infections: Metabolite cross-feeding: reported as the consumption of metabolic end-products by one of the microbial communities involved and optimization of local environment with the metabolic end-products.**



Response: In polymicrobial infections, a complex environment may be formed in which microbiological interactions exist between microorganisms. Scientific evidence exists to show that combinations of bacterial species may exist whereby these can protect each other from antibiotic action via the exchange of virulence and antibiotic resistance genes, and this may be evident in adverse outcomes for polymicrobial orthopaedic implant-related infections. It is also probable that polymicrobial infections may be more likely in patients with poor immunity and tissue healing.

Level of Evidence: Strong

- A. Agree
- B. Disagree
- C. Abstain



Biofilm-8 (Former G-96) Is the mapping of biofilm to a particular component or anatomical location an important consideration in management of implant related infections?

RESEARCHED BY:



Stoodley, Paul MD, USA



Ehrlich, Garth D MD, USA



Literature:

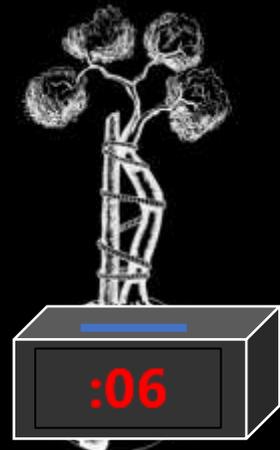
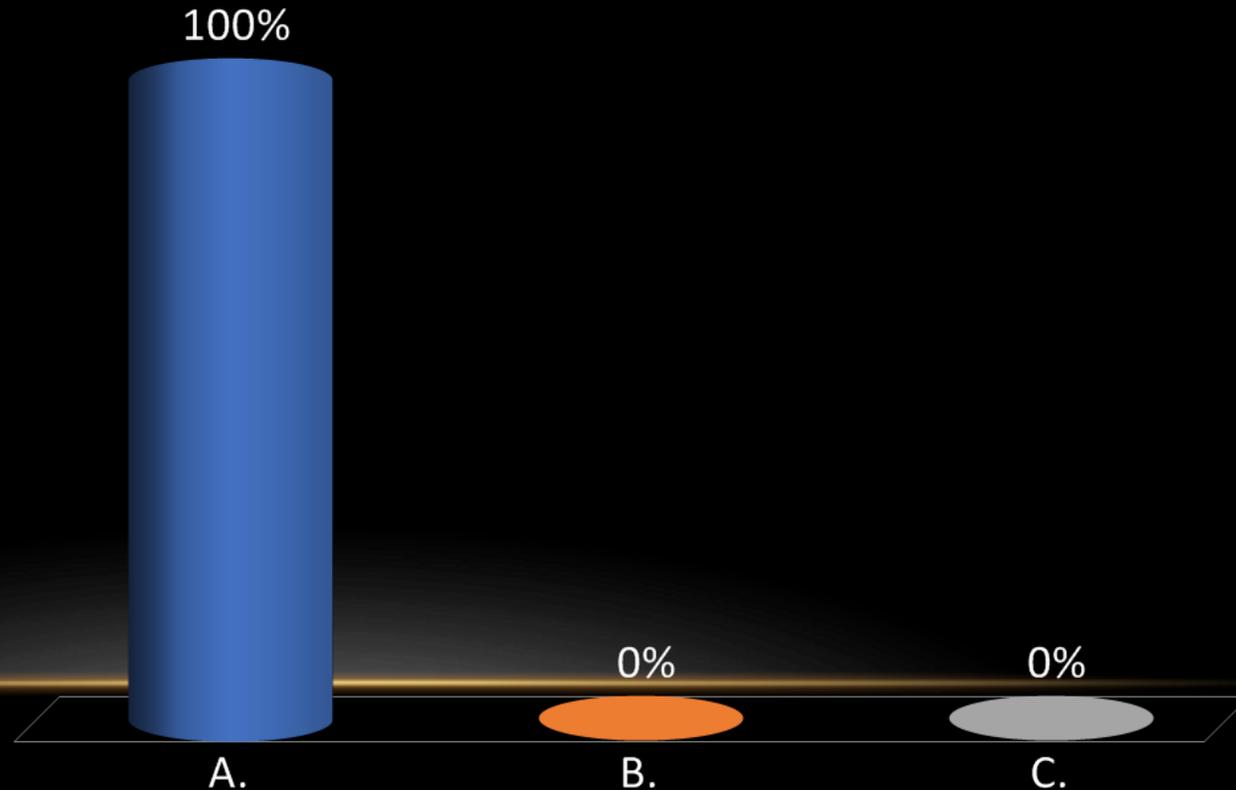
- **Given the limited number of studies evaluating the location of biofilms on specific components isolated from PJI patients, either clinically or in the laboratory, we conclude that there is no strong evidence that biofilms formation favors either a specific location or material type in total joint arthroplasty.**



Response: At present, mapping of biofilms is only possible in the laboratory, not in the clinical setting. Therefore, it is of unknown clinical importance in relation to management of implant-related infections.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



Biofilm Disruption



Biofilm-9 (Former G-106) Is there evidence that interference with bacterial communication by blocking quorum sensing molecules can minimize biofilm formation in vivo?

RESEARCHED BY:



McLaren, Alex MD, USA



Ehrlich, Garth D MD, USA



Literature:

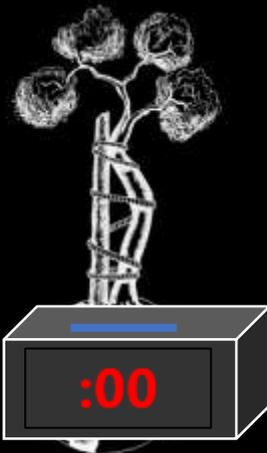
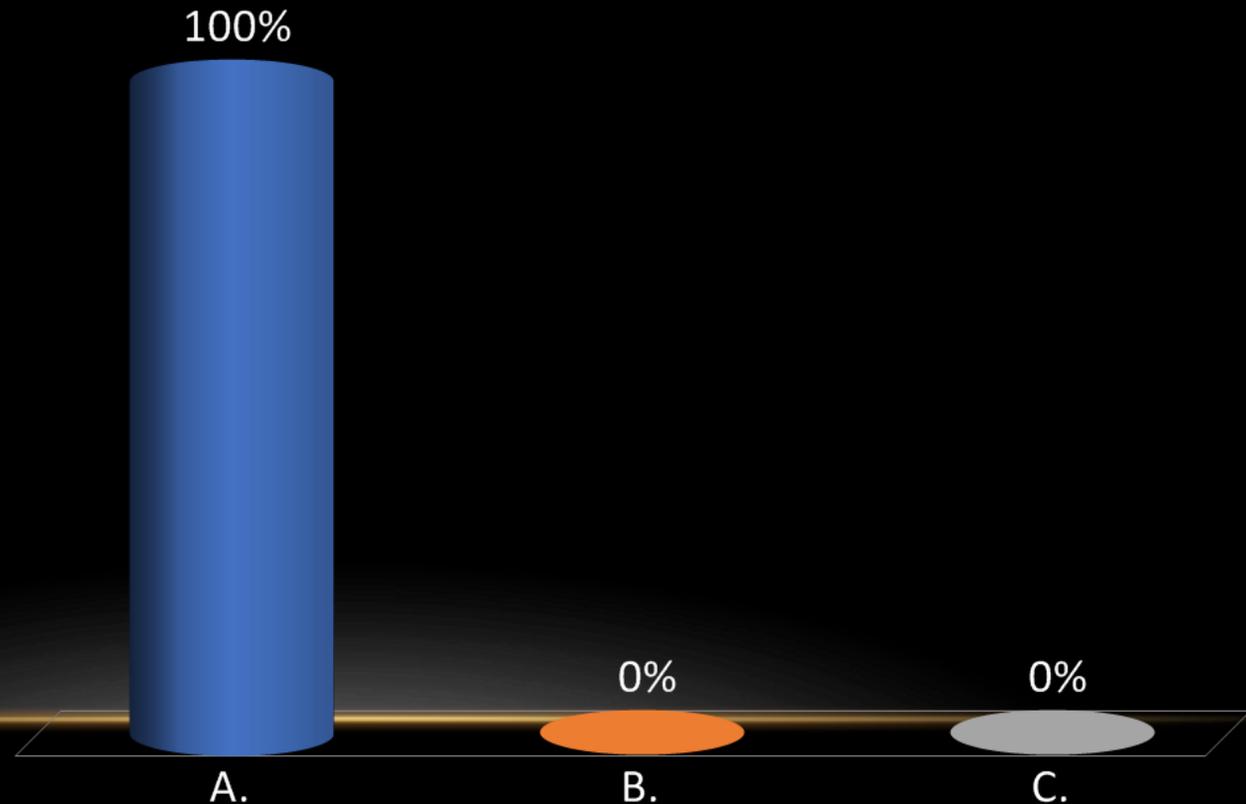
- **While there is extensive in vitro and in silico work being done and reported on quorum sensing and anti-quorum sensing molecules, otherwise known as quorum quenching, there are limited in vivo data and none of the anti-quorum sensing strategies are ready for widespread clinical application.**



Response: *In vivo* animal studies have demonstrated that interference with quorum sensing signals/molecules in some infections leads to decreased biofilm formation. There are contradictory results in *Staphylococcus* species. However, there are no clinical studies demonstrating this phenomenon.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Biofilm-10 (Former G-6) Can a biomaterial surface be modified to dispel bacterial adherence and biofilms? What are the potential concerns in modifying implant surfaces to combat biofilms?

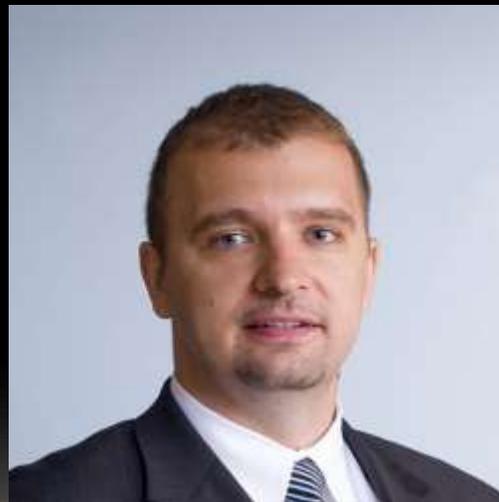
RESEARCHED BY:



Zhou, Yixin
MD, China



Kheir, Matthew
MD, USA



Antoci, Valentin
MD, Moldova



Zagra, Luigi
MD, Italy



Literature:

- **Metanalysis 0, Prospective/Randomized 0, Retrospective 68**

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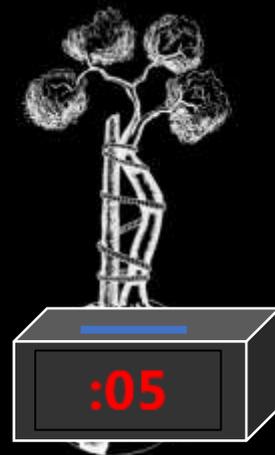
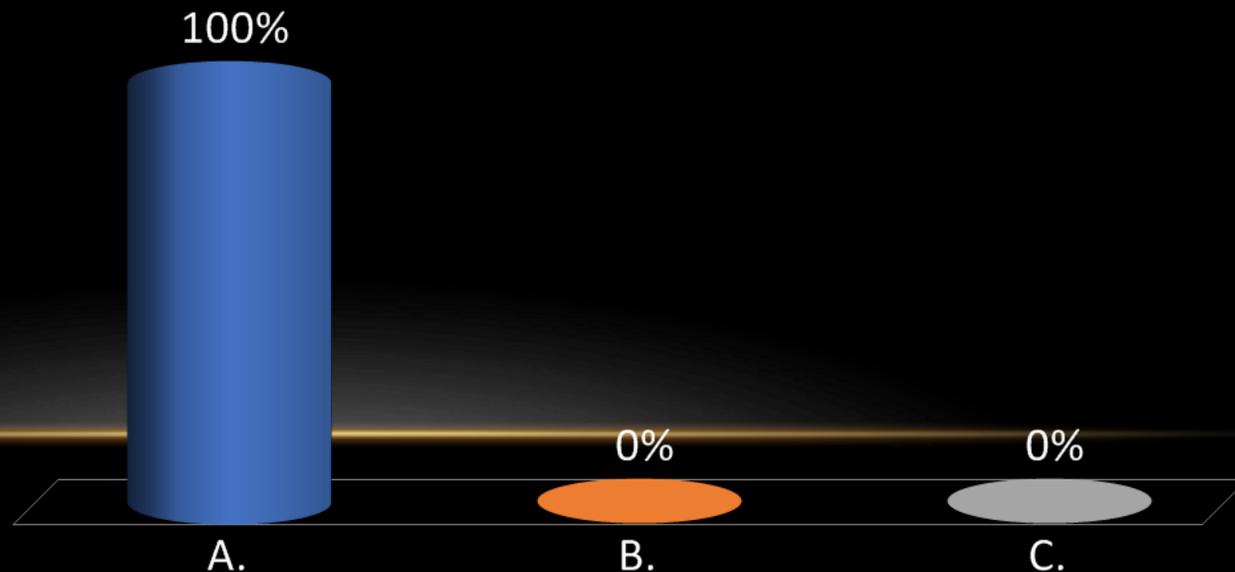
In conclusion, bacterial biofilms are difficult for antimicrobial agents to penetrate. Preventing biofilms and bacterial adherence is probably the only effective way to address the problem of PJI. Silver nanoparticles and iodine are gaining increasing popularity especially for their anti-adhesion, anti-infective, and minimal bacterial resistance properties. Nevertheless, further investigation of the long-term outcomes of patients with modified surfaced implants is warranted.



Response: The purpose of the surface modification is to decrease perioperative bacterial adherence and thus prevent biofilm formation. This has been shown in in vitro studies and in vivo animal models. There have been numerous strategies devised to alter surfaces. Such modified surfaces may interfere with the expected osseointegration, mechanical stability, and long-term implant survivability. The duration of long-term anti-infective effects are unknown. To date, no positive in vitro effect has been translated into a clinical setting.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



Biofilm-11 (Former G-149) What is the relevance of Minimum Inhibitory Concentration (MIC) of infecting organisms in biofilm-mediated chronic infection?

RESEARCHED BY:



Lange, Jeppe MD, Denmark



Townsend, Robert MD, UK



Scarborough, Matthew MD, UK



Literature:

- **Given the plethora of evidence detailed above, there is a clear need to seek alternative approaches to the prevention and treatment of biofilm related infections. The use of local antibiotic delivery systems is widely regarded as a possible means to achieve sufficiently high concentrations of antibiotic to exceed the MBEC.**

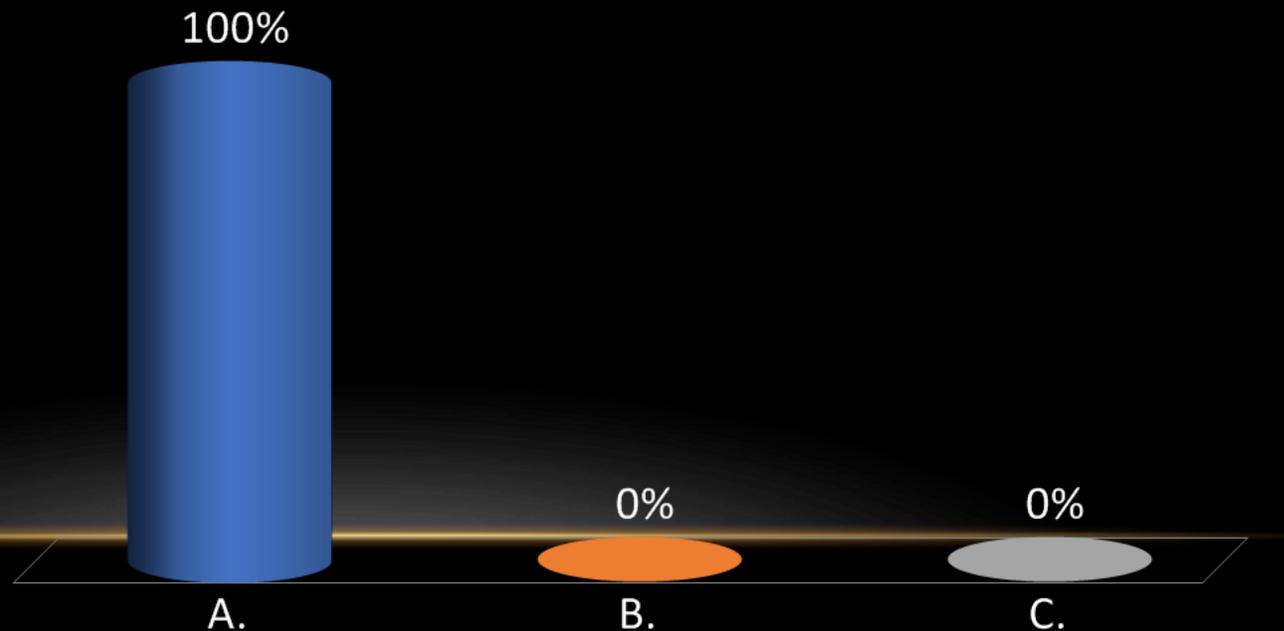


Response: The use of Minimum Inhibitory Concentration (MIC) is limited to (1) defining antibiotics that the microorganism is susceptible to in its planktonic state but cannot be used to guide treatment of biofilm-based bacteria, and (2) selecting long-term suppressive antibiotic regimens where eradication of infection is not anticipated.

Alternative measures of antibiotic efficacy specifically in the context of biofilm-associated infection should be developed and validated.

Level of Evidence: Strong

- A. Agree
- B. Disagree
- C. Abstain



Biofilm-12 (Former G-136) What is the Minimum Biofilm Eradication Concentration (MBEC) of anti-infective agents?

RESEARCHED BY:



Geurts, Jan MD,
Netherlands



Jenny, Jean-Yves MD,
France



Schreurs, Berend W.
MD, Netherlands



Literature:

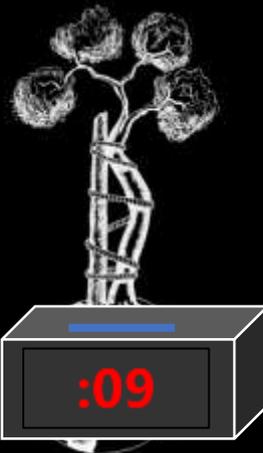
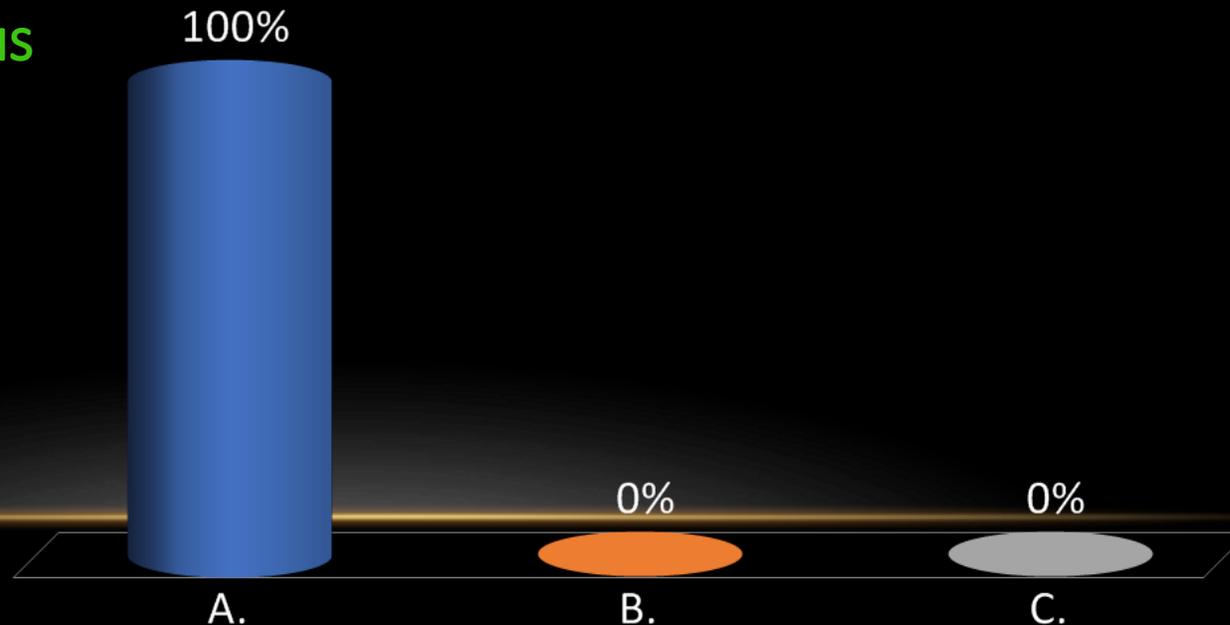
- **There is no antibiotic combination that guarantees bacterial eradication in the biofilm for a given strain of staphylococcus, although antibiotic combinations are generally more effective than monotherapy treatments. The in vitro measurement of the MECB is not a routine use for the moment, remains of the research field with the need to define a standardized methodology for possible use in clinical practice. High biofilm production appears to correlate with a higher complication or failure rate than low or absent biofilm production without statistical demonstration at this time.**



Response/Recommendation: The minimum biofilm eradication concentration (MBEC) of antimicrobial agents is a measure of in vitro antibiotic susceptibility of biofilm producing infective organisms. It is dependent on the surface, medium and the exposure period to an antimicrobial agent. There are no standardized measurement parameters for MBEC. MBEC is currently a research laboratory value and lacks clinical availability. In the group's opinion, there is value in developing a clinically-validated MBEC assay.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



Biofilm-13 (Former G-24) Do bacteriophages have a role in treating multidrug-resistant PJI?

RESEARCHED BY:



Ferry, Tristan MD, France

Pellegrini, Antonio MD, Italy



Literature:

- **Although phage treatment looks promising and safe, further research is needed to understand immunogenicity and answer the remaining questions related to treatment by phage such as timing, duration, methods of delivery, and route of administration. Limitations of present studies include the reduced spectrum of bacteria tested, which are limited to MRSA and *P. aeruginosa*, without considering coagulase-negative staphylococci (CoNS), which substantially contribute to PJI onset.**



Response: Unknown. Although some preclinical and clinical studies have demonstrated a good safety profile as well as promising therapeutic effects using bacteriophages for treating bone and joint infections, further clinical research using bacteriophage therapy in patients with multidrug-resistant PJI is required. There are known obstacles to bacteriophage therapy, including the fact that bacteriophages are neutralized in serum and relevant pathogens contain CRISPR/cas9 immunity against bacteriophage. Phages are usually bacterial strain specific; thus, a cocktail of different bacteriophage lineages may be necessary to effectively treat biofilm-mediated infections.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain

