QUESTION 10: Can a biomaterial surface be modified to disperse bacterial adherence and biofilms? What are the potential concerns in modifying implant surfaces to combat biofilms?

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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

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

Post Meeting Rationale:

The material surface used for implantation is a significant factor in bacterial colonization leading to PJI. In 1987, Anthony Gristina was the first to propose the concept of a race for the surface, wherein the fate of the biomaterial implant is dependent on a balance between tissue integration and microbial adhesion with biofilm formation. This concept sets the hypothesis that material modifications that improve osseointegration while inhibiting bacterial adhesion would provide a theoretical advantage and eliminate the risk of infection. As a result, there is a wide array of anti-infective surfaces proposed for utilization in orthopaedic implant applications.

Gallo et al. summarized the available options as bactericidal, anti-adhesion surfaces, coatings, and alternative materials. Romanò et al. proposed a newer classification regime that describes antibacterial coating under three distinctive groups:

1. Passive surface finishing/modification
   Surfaces that prevent adhesion without releasing anti-bacterial substances.
2. Active surface finishing/modification
   Surfaces that release anti-bacterial substances.
3. Perioperative antibacterial carriers or coatings
   Carriers or coatings applied during surgery that are antibacterial and either biodegradable or non-biodegradable.
Active surfaces and perioperative coatings provide only temporary solutions while they exhaust their antimicrobials in time. Passive surfaces may not provide the necessary bactericidal properties needed to eliminate the infection while their action is limited to the immediate peri-implant area. The ideal implant surface should have: 1. a strong anti-infective potential, 2. long duration of effect, 3. biocompatibility with mechanical construct and stability, and 4. minimal host response and harm. To achieve that, surfaces can be physically and mechanically prepared, and coated or chemically modified.

One of the main concerns of antimicrobial biomaterials is the possible cytotoxic effect of the surface modification as related to osseointegration and implant survival in vivo. Based on a preliminary literature review, only four laboratory studies and one clinical study reported the side effects of surface modification. Silver surface modifications have shown higher lactate dehydrogenase (LDH) activity as a marker of cell death, as well as lower cell count and alkaline phosphatase (ALP) activity. Nevertheless, such effects are hard to correlate with clinical outcomes. Glehr et al. performed the only clinical study that focused on silver while examining its use in mega-prosthesis. They have documented the presence of heavy metal poisoning symptoms, even though no correlation with the blood silver concentration was observed. Another two in vitro studies used zinc and farnesol (anti-fungi medicine) surface modifications respectively. The results showed lower ALP activity as well as pre-osteoblastic cell damage. Multiple studies thus agree that silver nanoparticles (AgNPs) have the potential to be toxic to many cell types in a dose- and time-dependent manner, especially when inhaled, injected, or ingested. Interestingly, Shen et al. conducted a study which revealed that both cobalt chrome alloys and pure titanium had cytotoxic effects to osteogenic precursor cells and mesenchymal stem cells, while the incorporation of AgNPs reduced this cytotoxicity.

When working with modified surfaces, bacteria can ultimately adapt and develop resistance to the agent used. Antibiotic resistance is an everyday occurrence in clinical practice. Bacteria have also been shown to surmount resistance to the ionic form of silver, and less commonly, to AgNPs. This is because prolonged exposure to AgNPs, unlike silver ions, is less likely to result in resistance genes since AgNPs have broad-spectrum capabilities by targeting multiple sites on or within bacterial cells. Nevertheless, resistance to silver seems to be a slow process and is a less of a problem compared to antibiotic resistance. Concerning though, Kaweeteerawat et al. suggest that AgNPs could potentially enhance bacterial resistance to antibiotics through promoting stress tolerance by induction of intracellular reactive oxygen species causing DNA mutations.

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.
References:


15. Glehr M, Leithner A, Friesenbichler J, et al. 2013. Argyria following the use of silver-


