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*Review Article*

# Biomaterials and technologies in the management of periprosthetic infection after total hip arthroplasty: An updated review

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## ABSTRACT

Although total hip arthroplasty (THA) is considered one of the most efficacious procedures for managing various hip conditions, failures due to different mechanisms are still being reported. Periprosthetic joint infection (PJI) is one of the devastating causes of failure and revision of THA. PJI carries a burden on the patient, the surgeon, and the health-care system. The diagnosis and management of PJIs carry many morbidities and increased treatment costs. The development of PJI is multifactorial, including issues related to the patient's general condition, the surgeon's efficiency, surgical technique, and the implants used. Recent advances in the area of diagnosis and predicting PJI as well as introducing new technologies and biomaterials update for the prevention and treatment of PJI. Local implant coatings, advancement in the bearing surfaces technologies, and new technologies such as immunotherapy and bacteriophage therapy were introduced and suggested as contemporary PJI eradication solutions. In this review, we aimed at discussing some of the newly introduced materials and technologies for the sake of PJI control.

**Keywords:** Periprosthetic joint infection, New technologies, Silver coatings, Biomaterials updates, Revision, Total hip arthroplasty

## INTRODUCTION

"Infection after total joint replacement is a devastating and life-threatening complication for the patient," Sculco.[1] Periprosthetic joint infection (PJI) is considered one of the leading causes for revision total hip arthroplasty (RTHA),[2-5] and its management is associated with a considerable economic and financial burden.[6] The microorganisms source causing PJI could originate from the patient's own flora or an external source such as the operative room environment or surgical instruments; surprisingly, a low volume of microorganisms is needed to establish infection.[7] "The race for the surface" starts after implanting a biomaterial where competition between the host and the microorganisms to occupy the implant surface (colonization); the problems start when the bacteria adhere to the implant with an immediate formation of a "biofilm" leading to extreme resistance of the microorganisms to the host's defense mechanisms and antimicrobial therapy.[8] It had been estimated that about 80% of the bacteria species are capable of biofilm

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formation, including *Staphylococcus aureus*, *Streptococcus*, *Staphylococcus epidermidis*, and *Pseudomonas*.[9] For total hip arthroplasty (THA) to be infected, the microorganism's ability to attach to the implant's surface depends on various factors, such as the microorganism virulence, nutrient availability, the patient immune system competency, and implant-related factors as material surface chemical and physical characteristics.[10]

The strategies for preventing and competing for infection occupy the whole perioperative stages; it starts from the preoperative phase, such as patient optimization and antibiotic prophylaxis administration, some intraoperative strategies including some maneuvers related to the prevention and inhibition of microorganism adhesions to the implants through implant surface modifications such as antibiotic-loaded hydroxyapatite (HA), nanosilver particles, and antiseptic-based coatings, and in the care in post-operative phase by application of proper surgical dressings and watchful wound care.[7,11]

The issues related to the pathogenesis of PJI, development and updates in the biomarkers used for detecting PJI, and the various surgical techniques used for PJI eradication, had been reported extensively in the literature;[7,9,12] in this review, we aimed at discussing some of the advancement and updates related to biomaterials and technologies used for managing PJI.

## WHY THA FAIL RECENTLY?

Although advancements in THA implants and techniques made this procedure one of the most successful surgical interventions introduced in the past decade, failure due to several reasons still occurring and understanding the failure reasons will help improve survival rates.[13] THA revision's main three reasons had been attributed alternatively to aseptic loosening, instability, and PJI in various studies.[2-5] The United Kingdom National Joint Registry reported the same three reasons for a re-revision surgery as well.[14] In contrast, PJI was reported as the leading cause of failure both in revision and re-revision THA according to the Swedish joint registry.[15] In the following, we will report on different strategies and developments made in various aspects of THA surgery to prevent or reduce the occurrence of PJI. In addition, issues related to bearing surfaces, biomaterials updates, and hints on the newly developed technologies will be discussed.

## ROLE OF BEARING SURFACES

For THA, the bearing surfaces could be classified into two major categories, first is the hard-on soft bearings, including metal head-on polyethylene acetabular cup (MoP) or ceramic-on-polyethylene (CoP) bearings.[16] The polyethylene used as a soft bearing could be either conventional, ultrahigh high-molecular-weight polyethylene (UHMWPE),[17] cross-linked polyethylene (XLPE),[18] and highly cross-linked polyethylene (HXLPE).[19] Second is the hard-on hard bearings, including either the metal on metal (MOM), which was limited due to the issue of aseptic lymphocyte-dominated vasculitis-associated lesions,[20] ceramic-on-ceramic (CoC) bearings, which may include either the use of alumina, zirconia, or zirconia toughened alumina,[21] and ceramic on metal where a ceramic femoral head is articulating with a metal acetabular liner.[22]

Regarding the orthopedic implants, HXLPE showed the highest bacterial adherence levels followed by titanium, stainless, and trabecular metal; this adherence is affected by physical implant characteristics such as the surface roughness and the implant chemical structure.[23]

Regarding if the bearing surface influenced the incidence of PJI, several studies evaluated this relation, as in a systematic review by Hexter *et al*., where they evaluated 17 studies to compare the incidence of PJI among different bearing surfaces, mainly MoP, CoP, and CoC, the authors reported an incidence of PJI with the three bearing couples of MoPs 0.85%, 0.38%, and 0.53%, respectively, with no significant difference between the three groups. Therefore, the authors concluded that the idea that a bearing couple will affect the incidence of PJI is not supported.[24]

On the contrary, in the study by Bordini *et al*. including data of 39,206 cementless THA to examine the effect of the bearing surface on the incidence of PJI, the authors showed that the lowest incidence was reported with the CoC bearing couple while the highest incidence occurred with MoM bearings, the authors concluded that bearing surface may influence the occurrence of PJI.[10]

A study by Madanat *et al.* evaluating PJI risk with different bearing surfaces after examining 177,237 primary THA surgeries from the Australian Registry (AOANJRR). The authors reported on three bearing surfaces MoHXLPE, CoHXLPE, and CoC; they found that the former two bearings had a higher revision rate for PJI compared to CoC.[25] The same conclusion derived from the previous study was reported in a study by Pitto *et al.* after evaluating about 98,000 hips from the New Zealand Joint Registry.[26]

### How improving the bearing surface can affect PJI?

Vitamin E was introduced as a blend to stabilize polyethylene by reducing free radicals' production; it showed the ability to prevent the oxidation cascade without affecting polyethylene's mechanical properties.[27] Furthermore, implementing Vitamin E in the material used as bearing surfaces showed its ability to improve the vulnerability of the implanted UHMWPE to infections.[28] In a study by Gomes-

Barrena *et al.* and after 90 min of incubation, they compared the adherence of *S. aureus* and *S. epidermidis* on conventional UHMWPE with and without Vitamin E blending, they found no significant difference in adherence when all strains were analyzed together. However, the authors found high variation when strains were analyzed separately as they found that one of the *S. epidermidis* strains showing significantly less adhesion to Vitamin E-blended UHMWPE. The authors explained this as Vitamin E increased the implant surface hydrophobicity with a decrease in the surface free energy, which might play a role in lowering the bacterial surface adhesion.[29]

Banche *et al.* analyzed three *S. epidermidis* strains growth on conventional UHMWPE samples with and without Vitamin E blending; they found a significantly less adhesion with the Vitamin E-blended samples.[30] In another study, they studied the adherence of two *S. aureus* and two *Escherichia coli* strains,[31] after 48 h of incubation. They found significantly fewer bacteria adherence on the Vitamin E-blended UHMWPE. The last study was reported on two *Candida albicans* strains and showed less fungal adhesion to Vitamin E-blended UHMWPE after incubation for 3, 7, 24, and 48 h.[32]

From the previously reported studies, it seems that the bearing surface may play a role in PJI development, and the introduction of a new bearing surface such as Vitamin E-blended polyethylene may decrease the incidence of PJI.

## ROLE OF BIOMATERIALS

Although the development of PJI in THA is multifactorial, including factors related to the patient such as general condition (ASA class, comorbidities, and age) and issues related to the surgical procedure (approach, length of surgery, and indication for surgery), studies evaluating the effect of the modifications on materials used in the THA implants on development of PJI had been reported.[33] The idea was to introduce new local modalities for PJI prevention and management by optimizing the implant surfaces to guard against biofilm formation and the ability to prolong the intra-articular antibiotic release, which should increase the potency of bacteria eradication.[12] According to the last peri-prosthetic joint infections international consensus meeting held in 2018, a strong recommendation was made related to developing effective local antibacterial surface coatings.[34]

### Local hydrogel coatings

The concept of "race for the surface" dictates that the first few hours after implantation of the prosthetic material are critical for PJI development.[35] Hence originated the idea of local coatings applied to the implant surface like the hydrogels. Implant coatings with a resorbable hydrogel-containing antibiotics (single or combinations) offer optimum drug delivery without interfering with osseointegration.[36] A defensive antibacterial coating (DAC) consisted of hyaluronan, poly-D, and L-lactide has the ability to protect the biomaterials by performing a barrier at implantation time; it is used with antibiotic topically to inhibit early bacterial colonization to the implant and biofilm formation,[37] its use led to a reduction in early post-operative infection rates after TJA.[38] DAC is prepared by mixing 300 mg of hydrogel, 5 mL of sterile water, and liquid-based antibiotics according to the organism's sensitivity previously identified in the cultures. The mixture is then added directly to the implant surfaces about 10 min after mixing.[11]

*In vitro* studies showed significant reductions in bacteria adhesions when used on a sterile titanium disc after being coated with the DAC hydrogel.[39] Animal studies showed the efficacy of DAC hydrogel loaded with an antibiotic to prevent implant-related infection without affecting the bone healing or osseointegration of the implants.[40] When DAC was used as a standalone device, it led to antibiotic concentrations higher than the minimum inhibitory concentration and showed an ability of local antibiotics elution up to 3 days.[38]

In the study by Franceschini *et al.* reporting their early experience of using DAC in 28 patients having chronic PJI underwent cementless two-stage RTHA with a mean follow-up of 2 years, they used vancomycin, rifampicin, or cephalosporin commonly as local antibiotics. They reported two early failures within the first 3 weeks post-revision surgery; the remaining 26 patients did not show signs of reinfection (clinical and laboratory) at the last follow-up, they also reported no implant loosening or ingrowth failure.[11]

### Silver (Ag)-based technologies

The implication of silver in the battle with PJI had various shapes as it could be used as an implant coating nanoparticles;[41] it was incorporated in the wound dressings, which proved efficacy against bacterial infection,[42,43] and could be loaded to the PMMA when it will be used either for primary implant fixation or as a spacer during the two stages revision surgeries.[44] Its efficacy in reducing the incidence of PJI had been proved in some observational studies, even in oncological patients.[45,46] The amount of effectively liberated silver ions to the surrounding tissues to serve its antibacterial function depends on the layer thickness, concentration, and the way of its application to the surface.[47] The liberated silver ions act on bacteria by destroying the peptidoglycan membranes, initiating DNA condensation and ribosome denaturation.[48]

An improvement on silver nanoparticles was introduced by incorporating it into HA and chitosan to produce an antibacterial coating with osseointegration promoting

characteristics; it showed its efficacy in reducing the microorganism (*E. coli* and *S. aureus*) concentration around the implant by about 90%.[49]

Silver nanoparticles combined with titanium dioxide were proposed to function as antibacterial coatings as well as anticorrosive; however, their safety for clinical use is still to be proven.[50]

### *Silver nanoparticles incorporated in implant coatings*

These were introduced as an alternative to nanotubes and drug-eluting antibacterial coatings and are considered as common non-antibiotic antibacterial coatings.[51] It showed activity against several bacterial species such as *S. aureus* and *E. coli* without negatively affecting the surrounding osteoblasts.[52]

Hardes *et al.* carried a prospective case–control study to investigate the efficacy of using the Mutars silver-coated implant (Implantcast, Buxtehude, Germany). They compared 51 patients diagnosed with bone sarcomas who were treated by replacing either the proximal femur or the proximal tibia using Mutars implant with a control group of 74 patients who received uncoated megaprostheses; the authors reported that the infection incidence with the silver-coated implant was 5.9% compared to 17.6% with the uncoated implant.[53]

In a retrospective study by Wafa *et al.*, the authors demonstrated that when using tumor prosthesis, silver-coated implants provided effectiveness in reducing the early post-operative infection in oncological patients or as a second-stage revision after PJI.[54] However, on the contrary, Zajonz *et al*. stated a limited role of the silver-coated implants in preventing infection in patients who underwent a revision for PJIs,[55] with the added possible risk of silver cytotoxicity, inability to coat the whole implant, and the possible high cost.[56]

Wang *et al.* tested a relatively new technology of silver nanoparticles embedded in titania nanotubes forming a contact-killing surface. They incorporated vancomycin into the nanotubes to provide the release-killing effect. They developed an *in vitro* and *in vivo* (Rabbit) PJI model involving methicillin-resistant *S. aureus* (MRSA) to evaluate the antibacterial properties of the hybrid surface technology against planktonic (in body fluids) and sessile (on implant surface) bacteria. The authors reported acceptable antimicrobial and antibiofilm effects against both types of bacteria without considerable silver ion release.[57]

### *Silver incorporated in surgical wound dressing*

A sliver containing dressing is the Aquacel Ag Hydrofiber dressings which act as an antimicrobial dressing composed of weaved cellulose center which when used will follow the contour of the area where it is applied and eliminate any dead space, absorbs exudates, and the release of silver ions which mainly will suppress the bacterial activity and help with wound healing.[58]

Grosso *et al.* in a retrospective study that included 1173 TJA patients, where the authors used Aquacel dressing in 568 patients and the standard gauze dressing or sterile Xeroform dressing in 568 patients, the incidence of acute PJI within the first 3 post-operative months was evaluated, the incidence of PJI in the total cohort was 0.94% (11 patients), nine patients in the usual dressing group (1.58%) compared to only 2 (0.33%) in the Aquacel dressing group. The authors reported a statistically significant difference ($P$ = 0.03), after running a multiple logistic regression model, Aquacel dressing use demonstrated a protective effect with an odds ratio of 0.092.[43]

### Povidone-iodine coating

Iodine was introduced as an antimicrobial coating for titanium hip implants.[59] It offers several advantages, broad antimicrobial activity including tubercle bacilli and fungi. It is not prone to drug resistance development, biologically safe and could be excreted by the kidney. The biological half-life is exceedingly long compared to antibiotic or silver coatings, and it possesses excellent osteoconduction properties.[59,60]

Kabata *et al.* reported on 30 THA using iodine-coated implants. Indications for surgery were revision for PJI in 14, primary THA in 13 patients with immunosuppressive diseases or after pyogenic arthritis, and three were hemiarthroplasty conversions. The authors reported no signs of infection in any patients after a mean follow-up of 33 months, no cytotoxicity, no thyroid function abnormalities, and excellent implant ingrowth and ongrowth with no signs of loosening.[61]

However, some drawbacks were suggested using iodine coatings, mainly cost-related issues as its preparation is time consuming, only used with titanium implants, and the implant size should be determined before surgery which dictates precise preoperative planning.[61]

## NEW AND FUTURE TECHNOLOGIES

After successful biofilm formation by the microorganism, it becomes resistant to mild pH changes. Further use of local antiseptics such as hydrogen peroxide, povidone-iodine, and sodium hypochlorite will be ineffective; an example is *S. aureus* biofilms which showed the ability to survive even after local antiseptics application.[62] Therefore, the following are the new strategies suggested for dealing with PJI, targeting the biofilm, and dealing with the dormant and resistant bacterial strains.

### Cyclodextrin-based drug delivery

Cyclodextrin is a cyclic oligosaccharide cross-linked with an insoluble polymer; it facilitates a prolonged controlled drug release through the formation of inclusion complexes with "pockets."[63] It had been incorporated into several other surgical implants, such as hernia meshes, and vascular grafts or stents, for the sake of delivering antibiotics over a more extended period.[12] Taha *et al*. loaded tobramycin and rifampicin in combination on a grafted cyclodextrin onto HA-coated titanium hip implants, aiming to have a dual drug delivery system to work against *S. aureus* and *Enterobacter cloacae*; they found that this delivery system provided sustained release of both antibiotics.[64] The authors also proved the antibacterial activity of gentamicin-loaded plasma-sprayed HA-coated titanium using cyclodextrin.[65]

### New antibiotics with boosted penetration power

If an antibiotic can penetrate the bone and articular tissues, this was suggested to improve its efficacy against the biofilm;[9] two newly FDA-approved antibiotics, oritavancin and dalbavancin, showed the ability to interrupt bacterial cell wall synthesis and to disrupt bacterial cell membrane.[66] Both agents showed activity against Gram-positive bacteria, including MRSA, methicillin-sensitive *S. aureus* (MSSA), and vancomycin-resistant *S. aureus*. Both agents showed the capability of penetrating the bone and articular tissues;[67] in an *in vitro* model of PJI, both agents showed activity in competing biofilm isolated from *S. aureus* and *S. epidermidis*.[68] Its wide use limitation is the high cost and the selectivity to Gram-positive bacteria only.[9]

### Immunotherapy/monoclonal antibodies

Monoclonal antibodies as a modality of immunotherapy were suggested to provide an adjunct or even an alternative to antibiotics; various investigations are running to assess the possible targets of the antibody-based therapies, an example is antibodies against staphylococcal adhesins, which resulted in inhibiting the microbial adherence to surfaces, with an additional increase in microorganism clearance through opsonophagocytic killing.[69] Another potential target is *S. aureus* cell wall moiety protein A; the use of antibodies targeting this protein showed better opsonization of both MRSA and MSSA, leading to possible clearance by the immune cells; these agents showed an improved mice survival which had MRSA bacteremia both when combined with vancomycin and when used alone.[70]

### Agents targeting dormant state bacteria

Another new strategy is targeted against the dormant bacteria present in the biofilm, called the persister cells (these are less active, which makes them more resilient to antibiotics); the idea is to stimulate these bacteria to initiate a metabolic activity making them more sensitive to antibiotics.[9] In a study by Fux *et al*., they found that a strain of MSSA, when present in the biofilm, was resistant to oxacillin even after the biofilm dispersion. However, stimulation of the bacteria by adding nutrients and fresh media caused sensitivity of the MSSA to the antibiotic.[71] A further innovative approach to attack the dormant bacteria is to use anticancer drugs, which will bind to bacterial DNA and RNA, leading to its unwinding with subsequent death of the bacteria, including mitomycin C and cisplatin, which have shown effectiveness against persister cells.[72] Both drugs had proven to kill the planktonic bacteria and persister cells, including various species such as *E. coli*, *S. aureus*, and *Pseudomonas aeruginosa*.[73] Kwan *et al*. reported mitomycin C's efficacy in eradicating infection in an *in vivo* animal and in *in vitro* wound models, and the authors suggested its possible efficacy in treating resistant clinical infection.[73] Although anticancer drugs are considered by some authors as a choice to enter the "post-antibiotic age," Chowdhury *et al*. alluded to the possible intrinsic toxicity of these drugs when used instead of antibiotics. The authors reported that safety could be guaranteed using low doses and combining them with antibiotics, and the topical application will allow the use of higher concentrations.[72]

### Titanium nanotube arrays

The idea is to provide a local antibiotics delivery using nanotube arrays processed on titanium's surface.[12] *In vitro* studies showed a sustained gentamycin release from nanotube arrays coated titanium alloy surfaces reaching about 11 days.[74] Although this technology appears to be appealing to antibiotics delivery and prevention of PJI, its effect on titanium surfaces osseointegration requires further evaluation.[12]

### Polymers

A sustained release of antibiotics through diffusion and degradation using synthetic polymers such as polycaprolactone, polylactic acid, and polylactic-co-glycolic acid (PLGA) has been evaluated *in vitro* and animal models.[75] PLGA was the most studied and showed greater efficacy for antibiotic delivery than local delivery with PMMA.[75]

### Biodegradable bone graft substitutes

These materials were introduced as an alternative to bone cement, such as calcium sulfate, which is commonly used as a void filler which could be molded to form radiopaque beads, the biodegradable nature (absorbed with 30–60 days) of this material is advantageous as another surgery for removal is not needed.[12] When loaded with antibiotics, calcium sulfate

showed an equivalent or even better elution capabilities than PMMA in *in vitro* studies; another advantage of calcium sulfate over PMMA is the lack of high polymerization temperature during preparation, making adding of heat-labile antibiotic possible.[76]

Using antibiotic-loaded calcium sulfate beads showed promising results from trauma literature in osteomyelitis management, with infection eradication rate up to 86% in some reports.[77] For its use in management PJI, Howlin *et al*. showed the ability of these beads to inhibit *S. aureus* biofilm formation when loaded with tobramycin and/or vancomycin, but not activity had been shown against the already formed biofilm.[78]

However, there is limited evidence to support its regular use in the management of PJI. Flierl *et al*. treated 32 PJI cases with debridement, implant retention, and calcium sulfate beads, they reported treatment failure incidence of 48%.[79] Furthermore, calcium sulfate beads use reported to result in possible hypersensitivity reaction presented as persistent wound discharge and heterotopic bone formation.[80] Another reported complication is hypercalcemia which was reported to occur at a rate of 20% in a series of 15 patients treated by single-stage revision by Kallala and Haddad.[81]

### Bacteriophage therapy

Another possible potential therapy for attacking bacteria that reside in the biofilm is "bacteriophages," these are viruses (naturally occurring) that can attack and kill bacteria selectively without affecting the human cells; it showed activity against active bacteria persister cells.[82] Yilmaz *et al*. assessed bacteriophages' antimicrobial activities in a rat model against MRSA and *P. aeruginosa*; the authors found that it reduced viable bacteria count when administered alone, the effect was even more profound when combined with antibiotic therapy.[83] In an *in vivo* study by Kaur *et al*., where the authors investigated bacteriophages usage as prophylaxis against MRSA in a PJI, they reported that implant coating combining bacteriophages and antibiotics gave the best results regarding an initial lowering in bacterial adhesion to the implant and fewer bacteria count in the adjacent tissues.[84] Furthermore, the bacteriophages therapy provides less cross-resistance to antibiotics, minimal or no adverse reactions, and the ability to penetrate the bacteria, which introduce this therapy as a viable strategy combined with antibiotics.[82]

### Enzymatic therapy

Through degradation of the extracellular polymeric substances, enzymes could improve and augment the elimination and eradication of the PJI biofilm by other antimicrobial agents.[9] An agent such as dispersion B showed complete eradication of biofilm in *in vitro* studies through inhibiting biofilm exopolysaccharide PNAG-producing bacteria.[85,86] The proven enzymatic activity against biofilm makes it possible for biofilm eradication either if used alone or in conjunction with antibiotics.[9,87]

### Photodynamic therapy (PDT)

PDT is a strategy in which light and a photosensitizer dye (toluidine blue as an example) are used. These dyes could be absorbed by bacteria, which is then being activated by oxygen and light exposure with a specific wavelength, ultimately resulting in free radicals production, causing bacterial DNA and plasma membrane damage with subsequent cell death.[88] Some studies showed the efficacy of PDT against some bacteria species such as MRSA, MSSA, *S. epidermidis*, and *P. aeruginosa* in a PJI model where mature biofilms were grown on either moderately roughened or a polished titanium alloy.[89,90] As this strategy proved rapid bactericidal behavior with a very low possibility of bacterial resistance development, it was suggested to be used for sterilizing the infected implant bed and surrounding tissues during revision surgery for PJI.[89]

### Ultrasound therapy

Low-intensity ultrasound (frequency between 20 and 200 kHz), known as sonication, was introduced as a technique for improving the accuracy of diagnosis PJI. However, ultrasound with a high intensity (frequency more than 1 MHz) was introduced as a possible effective technique against bacterial biofilms.[91] In an early study by Ensing *et al*. carried on a rabbit model, the authors showed that pulsed ultrasound combined with gentamicin reduced *E. coli* biofilm more than using gentamicin alone.[92] Microfractures and hematoma formation were among the risks questioned when using a high-intensity ultrasound. To avoid this possible risk, Wanner *et al*.[93] and Yu *et al*.[94] showed *in vitro* studies that a synergistic effect of using a low-intensity ultrasound combined with antibiotics, they showed the possibility of eradicating various bacterial species such as *S. epidermidis*, *S. aureus*, and *E. coli* biofilms.

### Vaccination

The introduction of vaccines as a prophylactic therapy against biofilm was suggested as a promising option, which works through antibodies targeting specific structures, including the cell wall enzymes, biofilm extracellular matrix components, and surface cell proteins.[9] Using antibodies vaccine showed efficacy against MRSA infection biofilm when combined with antibiotic therapy in an animal model;[95] however, in clinical application, Fowler *et al*. reported that using a vaccine against *S. aureus* in patients subjected to cardiothoracic surgery did not reduce the rate of

infection and was associated with increase mortality rates.[96] Further development and improvement are still needed to prove the efficacy and safety of vaccines.

### Inhibition of quorum sensing

The quorum sensing system is an essential chemical signaling pathway through which bacteria communicate and cooperate; it also serves as a regulator of certain processes such as biofilm formation and secreting virulence factors.[97] Inhibition of quorum sensing was introduced as a new method for preventing PJI with the possibility of reducing biofilm formation, leaving the bacteria more susceptible to antibiotics; this inhibition was performed through various strategies such as suppressing synthases responsible for extracellular signaling molecules production or by enzymatic degradation.[9] This technology showed a positive effect in clearing *P. aeruginosa* lung infection and improving survival time in an animal model,[98] making its use in preventing and curing PJI an appealing option; however, data are still deficient in this respect.[9]

## CONCLUSION

Management of PJI after THA had evolved over the years by introducing new concepts and technologies to prevent the occurrence of infection in the first place. The role of bearing surfaces had been examined. Although there is some conflicting evidence of its effect on the incidence of PJI, the use of Vitamin E-blended polyethylene showed fewer bacterial adhesions, which may help in reducing the PJI incidence. Novel modalities such as surface coatings using DAC or silver-containing coatings had been proved to be effective against biofilm formation and led to reducing the incidence of PJI in both *in vivo* and *in vitro* studies. The introduction of new concepts and technologies such as the use of new, more powerful antibiotics, bacteriophage therapy, immunotherapy, vaccines, and ultrasound therapy showed promising results; however, its wide adoption in clinical practice still to be proved.

## AUTHORS' CONTRIBUTIONS

HMB and OF carried out the review conception. AAK and HMB carried out the literature search and drafted the manuscript. OF did the critical revision. All authors read and approved the final manuscript. All authors have critically reviewed and approved the final draft and are responsible for the manuscript's content and similarity index.

## ETHICAL APPROVAL

The authors confirm that this review had been prepared in accordance with COPE roles and regulations. Given the nature of the review, the IRB review was not required.

### Declaration of patient consent

Patient consent was not required as there are no patients in this study.

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### Conflicts of interest

There are no conflicts of interest.

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