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Iu.M. Nasieka^{4, 5} , V.S. Chorny^{1, 6} ¹Bogomolets National Medical University, Kyiv, Ukraine²Frantsevich Institute for Problems of Materials Science, NAS of Ukraine, Kyiv, Ukraine³Zhytomyr Ivan Franko State University, Zhytomyr, Ukraine⁴V. Lashkaryov Institute of Semiconductor Physics, NAS of Ukraine, Kyiv, Ukraine⁵National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine⁶State Institution "Institute of Traumatology and Orthopedics, NAMS of Ukraine", Kyiv, Ukraine

Biofilm infection of orthopedic implants: diagnosis, treatment, and prevention

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Abstract. Biofilm infection of orthopedic implants is one of the most challenging problems in modern orthopedics and traumatology, as it combines microbial persistence, limited efficacy of systemic antibacterial therapy, chronic inflammation, impaired osseointegration, implant instability, and functional consequences of treatment. Microorganisms attach to the surfaces of endoprostheses, plates, screws, intramedullary rods, spinal systems, and other fixation devices, forming biofilms that are more tolerant to antibiotics and immune responses than free-living bacteria. This review purposed to summarize current data on the pathogenesis, microbiological spectrum, clinical forms, diagnosis, treatment, prevention, and antibiofilm coating strategies for orthopedic implants. A narrative literature search was performed in four bibliographic databases — PubMed, Scopus, Web of Science, and Google Scholar — and six publisher platforms: Elsevier, Springer Nature, Wiley, Oxford Academic, MDPI, and Frontiers. Eleven keyword groups were used in English and Ukrainian, publications from 2014 to 2026 were prioritized, and 37 sources were included after two-stage screening of titles/abstracts and full texts. The analysis showed that periprosthetic joint infection (PJI) and fracture-related infection (FRI) share the same biofilm mechanism but differ clinically because in FRI, the implant is also required to maintain fracture stability. Key diagnostic elements include deep tissue sampling, sonication of removed implants, histology, and standardized PJI/FRI criteria, whereas superficial swabs are insufficient for final therapeutic decision-making. Effective treatment requires surgical source control, stable fixation or implant revision, dead-space management, soft tissue coverage, and systemic and local antimicrobial therapy. The review identified 12 main groups of antibiofilm or antimicrobial coating strategies, including antibiotic-releasing systems, antibiotic-loaded hydrogels, gentamicin-coated nails, metal-ion coatings, calcium phosphate-/hydroxyapatite-based systems, antimicrobial peptides, chitosan, nanostructured surfaces, and smart pH- or enzyme-responsive coatings. Multifunctional coatings based on bioactive glass, calcium phosphate, hydroxyapatite, silver, antibiotics, hydrogels, or combined systems are especially promising because they can inhibit early bacterial adhesion, reduce biofilm formation, and support osseointegration. However, most available evidence remains preclinical or clinically limited, and further validation is required before routine use in orthopedic traumatology.

Keywords: biofilm; orthopedic implants; periprosthetic joint infection; fracture-related infection; antibiofilm coatings; review

Introduction

Orthopedic implants are an important component of modern musculoskeletal surgery and are used across all its fields. Endoprostheses, plates, screws, intramedullary rods, spinal systems, external and internal fixators can be used to restore limb anatomy, stability, support, and function. Implantation

of a foreign material creates a microenvironment in which the structure's surface can serve as a substrate for bacterial adhesion. After implantation, the material's surface is rapidly covered with plasma proteins, fibrin, extracellular matrix, and cellular components. This conditioning layer can help microorganisms attach to the tissue and begin biofilm formation.



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Для кореспонденції: Чорний Володимир Сергійович, кандидат медичних наук, доцент, кафедра травматології та ортопедії, Національний медичний університет імені О.О. Богомольця, бульв. Тараса Шевченка, 13, м. Київ, 01601, Україна; e-mail: oncoortoped@gmail.com

For correspondence: Volodymyr S. Chorny, PhD in Medicine, Associate Professor, Department of Traumatology and Orthopedics, Bogomolets National Medical University, Taras Shevchenko boulevard, 13, Kyiv, 01601, Ukraine; e-mail: oncoortoped@gmail.com

Full list of authors information is available at the end of the article.

Unlike acute soft tissue infection, implant-associated infection can be latent, chronic, or recurrent. This is due not only to the pathogen's virulence but also to the biofilm's unique features. The biofilm protects bacteria from antibacterial agents, phagocytosis, complement, and other immune responses. Therefore, the typical *in vitro* susceptibility of a pathogen to an antibiotic does not always reflect the drug's actual efficacy once a biofilm has formed.

In clinical practice, biofilm infection can occur in periprosthetic joint infection (PJI), infection after osteosynthesis, fracture-related infection (FRI), infection of other implants, or infection around external fixation devices. Although the general biofilm mechanism is the same, this is not the case in the clinical context. In periprosthetic infection, the problem is infection of a permanent implant, whereas a fixator is a temporary but valuable tool for stabilizing a fracture. Therefore, premature removal of the fixator can lead to loss of stability, nonunion, and the need for complex reconstruction.

The problem is also important because even with surgical intervention and antibiotics, implant-associated infection is not eliminated. When a biofilm forms, treatment often requires repeated interventions, prolonged antibacterial therapy, revision osteosynthesis or arthroplasty, soft tissue reconstruction, and local antimicrobial measures. For FRIs, international recommendations focus on debridement of the fracture, its stabilization, and control of bone and soft tissue defects.

What is the scientific novelty and relevance of this review? Most reviews address either periprosthetic joint infection or biofilm formation in general. At the same time, for orthopedic traumatology it is important to analyze biofilm infection both as a microbiological problem and as a function of three components: the microorganism, the implant surface, and osseointegration. This three-component model demonstrates why, in FRI, treatment cannot be limited to eliminating pathogens alone.

It is relevant to combine three areas: modern biofilm infection of orthopedic implants, the features of FRI in traumatology, and the possibilities of various antibiofilm coatings. This is especially relevant for the development of bioactive glass materials and calcium phosphate (CaP) and hydroxyapatite (HA) coatings with antimicrobial agents, as these coatings can also be used to modify bacterial attachment, biofilm formation, and osseointegration.

It is important to evaluate them in a broader context: cytocompatibility, effect on osteoblasts, coating stability, mechanical properties of the bone-implant system, antibacterial properties, potential for clinical application, and level of evidence.

The purpose. This review article aims to analyze the existing scientific literature on biofilm infections of orthopedic implants in orthopedics and traumatology, regarding pathogenesis, microbiological spectrum, clinical forms, diagnostic criteria, treatment options, and prevention. An additional aim is to analyze antibiofilm coatings for orthopedic implants in terms of their mechanisms of action, advantages, limitations, level of evidence, and potential applications in traumatology.

Materials and methods

The research was performed as a narrative literature review of biofilm infection of orthopedic implants. The literature search was conducted in the PubMed, Scopus, Web of Science, and Google Scholar databases, as well as in the scientific collections of the publishers Elsevier, Springer Nature, Wiley, Oxford Academic, MDPI, and Frontiers. The following search terms and their combinations (in English and Ukrainian) were used: “biofilm”, “orthopedic implant”, “periprosthetic joint infection”, “fracture-related infection”, “implant-associated infection”, “sonication”, “antibacterial coating”, “antibiofilm coating”, “calcium phosphate coating”, “bioactive glass”, and “osseointegration”. Publications in English and Ukrainian were included in the analysis. Original clinical studies, experimental works, systematic reviews, meta-analyses, consensus documents, and clinical guidelines were considered. Preference was given to sources from the last 5–10 years (2014–2026); however, earlier fundamental works were also included when of methodological or conceptual significance. Source selection was carried out in two stages, based on relevance and scientific significance: titles and abstracts were assessed first, followed by full texts, in accordance with the inclusion and exclusion criteria. As a result of the selection, 37 sources were included in the review, among them classic works on biofilms, the Infectious Diseases Society of America (IDSA) guidelines on periprosthetic infection, the European Bone & Joint Infection Society (EBJIS) definition of PJI, consensus documents on FRI, and studies on the sonication of removed implants [1–16].

Inclusion criteria: relevance to orthopedic implant-associated infection; data on biofilm, diagnosis, treatment, prevention, or implant coatings; scientific significance of the source. Exclusion criteria: publications without an abstract, duplicates, sources without a clear methodology, works unrelated to orthopedic implants, or studies that did not provide data relevant to the review topic.

Since the article is a narrative rather than a systematic review, a quantitative meta-analysis was not performed. The subject matter was used to categorize the sources into the following areas: biofilm pathogenesis, microbiological spectrum, clinical types of infection, diagnosis, treatment, prevention, and antibiofilm coatings.

Results

Biofilm: definition and pathogenesis

A biofilm is a community of microorganisms attached to a biological or artificial surface within an extracellular polymeric matrix. The matrix consists of polysaccharides, proteins, lipids, extracellular DNA, ions, and other components that provide mechanical stability, protection, intercellular communication, and attachment to the surface.

Biofilm formation occurs in stages. The first step is the initial adhesion of bacteria to the implant surface. This process depends on the material's properties: roughness, hydrophilicity, electrostatic charge, chemical composition, and micro- and nanotopography. After implantation, the surface of the structure is rapidly covered with plasma proteins and extracellular matrix, thereby promoting bacterial

recruitment. The second stage is irreversible adhesion, during which microorganisms begin to produce a matrix and form microcolonies. The third stage is biofilm maturation with the formation of a complex 3D structure. At this stage, some cells may disperse, creating conditions for the spread or recurrence of infection [1, 2, 13].

It is important to distinguish between antibiotic resistance and antibiotic tolerance in a pathogen. Resistance is due to genetically fixed mechanisms that allow bacteria to grow in the presence of an antibiotic. Tolerance in a biofilm can develop without genetic resistance and may be explained by low metabolic activity, limited drug diffusion, persister cells, and the protective role of the matrix. Current research emphasizes that persister cells can radically alter their metabolic pathways, evading the effects of even the newest antibiotics, thereby necessitating the development of innovative coatings that target these resistant subpopulations [13]. For example, in a clinical setting, an antibiotic shows activity on a standard antibiogram but fails to eliminate the infection in the presence of an implant [2, 17].

In addition to its microbiological aspects, a biofilm also affects the tissue response. Prolonged inflammation around the implant interferes with local vascularization, osteoblast activity, bone remodeling, and the formation of a stable bone-implant contact. In traumatology, this is especially important, since the infectious environment can impair reparative osteogenesis, increase the risk of nonunion, and cause mechanical damage to the fixator.

In biofilm infections, the interactions among bacteria, immune cells, and the implant surface become more complex. Neutrophils and macrophages can play important roles in local inflammation, but microorganisms cannot be completely removed from the surface. This creates a paradox: the inflammatory response persists, yet effective control of the infection cannot be achieved. This is why biofilm infection usually has no pronounced symptoms or a wave-like course.

Microbiological spectrum

The common pathogens of orthopedic implant infections are staphylococci, especially *Staphylococcus aureus*, and coagulase-negative staphylococci (*Staphylococcus epidermidis*). *S.aureus* more often presents with a more acute

course, a strong local inflammatory reaction, a purulent process, and early postoperative infections. Coagulase-negative staphylococci are responsible for low-symptom, chronic, and severe infections [13, 17], as well as infections caused by *Enterococcus faecalis*, Gram-negative bacteria — in particular *Pseudomonas aeruginosa* and members of the *Enterobacterales* — and fungal pathogens (*Candida* spp). In traumatology, the pathogen spectrum is broader because of open fractures, primary wound contamination, necrotic tissue, repeated surgery, and external fixation.

Polymicrobial infections require special attention. They are more common in open fractures, severe soft tissue damage, after repeated revision interventions, or in patients with a prolonged hospital stay. In such situations, a superficial swab cannot be a reliable basis for choosing therapy. Care should be taken to obtain several deep-tissue samples using sterile instruments before starting or changing antibacterial therapy [7].

Not only the type of pathogen is important but also its ability to form a biofilm. Microorganisms with low virulence can cause slow infections with minor laboratory changes, whereas highly virulent pathogens present a more acute picture of purulent inflammation. Interpretation of microbiological results should take into account the clinical situation, the number of positive samples, histological correspondence, and confirmatory criteria of infection.

Clinical forms of implant-associated infections

The most studied form of biofilm infection is periprosthetic joint infection. It occurs after hip, knee, shoulder, or other joint replacement surgery. Depending on the time of onset, the virulence of the pathogen, and the route of infection, PJI may have an acute postoperative, chronic low-grade, or hematogenous course. EBJIS proposed a three-tier diagnostic system: infection is unlikely — all criteria negative; infection is likely — two positive criteria; infection is confirmed — at least one confirmatory criterion present. An important nuance regarding “likely”: clinical signs or elevated C-reactive protein (CRP) alone are insufficient — they must be combined with another positive test (synovial fluid, microbiology, histology, or radionuclide examination) [11, 12, 14].

Fracture-related infection is another important form of infection. It is a response to osteosynthesis and is associated

Table 1. Comparison of periprosthetic joint infection and fracture-related infection

Criterion	PJI	FRI
Primary implant	Joint endoprosthesis	Plate, screw, rod, nail, fixation device
Implant function	Replacement of joint function	Fracture stabilization
Key problem	Infected permanent implant	Infected fixator required for healing
Biofilm	On endoprosthesis components	On the fixator, necrotic bone, and in soft tissue cavities
Surgical strategy	DAIR, one-stage or two-stage revision	Retention, replacement, or removal depending on healing
Diagnostic criteria	EBJIS, IDSA, ICM	FRI consensus criteria
Feature	The implant is usually permanent	The fixator can be removed after healing

Notes: DAIR — debridement, antibiotics, and implant retention; ICM — International Consensus Meeting.

with fracture fixators. In FRI, unlike PJI, the implant is not only a substrate for the biofilm but also a device for fracture healing. Therefore, the decision on its removal or retention should be made taking into account the stability of fixation, bone consolidation, the condition of the soft tissues, and the virulence of the bacteria [6–10, 15].

International recommendations for FRI propose two main surgical procedures: debridement with implant retention and implant removal/replacement. If the fracture has not united but the fixation is stable, debridement can be performed while retaining the construct. If the fracture has united, removal of the implant facilitates elimination of the biofilm. If the fixation is unstable, the construct should be revised, or the fixation method replaced [8, 15].

Other groups include infections of spinal implants, pins, and external fixation rods, as well as post-reconstructive infections of bone defects. In all these cases, the biofilm complicates elimination of the pathogen. Still, the choice of treatment depends on the location, the function of the implant, the possibility of its removal, and the risk of loss of stability.

Diagnosis

Diagnosis of biofilm infection of orthopedic implants should be made at multiple levels. No single clinical, laboratory, or instrumental indicator can definitively confirm or exclude infection. This is especially relevant in low-grade infections, when fever, marked leukocytosis, or elevated C-reactive protein may be absent.

For FRI, an international group of experts proposed dividing the criteria into confirmatory and suggestive ones. Confirmatory criteria indicate the presence of infection. These include a fistula or wound defect communicating with the bone/implant, pus, isolation of the same pathogen from at least two deep samples, and histological (or microscopic)

evidence of infection. Suggestive criteria indicate infection but do not confirm it on their own; further investigation is required [7].

If a deep tissue sample is taken, microbiological analysis should be performed. Superficial swabs should not be used when making the final choice of antibiotic therapy, as they may reflect colonization of the wound or skin. It is best to obtain several individual samples from different areas of the infectious focus using sterile instruments. Sample collection should be performed before initiating empirical antibacterial therapy, unless sepsis or another emergency is present.

Sonication of removed implants is a useful method for diagnosing biofilm infection. The method involves ultrasonic treatment of the implant in a sterile fluid, thereby releasing microorganisms from the biofilm. The classic study by Trampuz et al. showed that sonication of removed hip and knee endoprostheses can be useful for detecting infection in complex cases [4].

Molecular methods, such as polymerase chain reaction (PCR), multiplex PCR, 16S rRNA sequencing, and metagenomic sequencing, can be useful when culture is negative. However, they must be interpreted with caution due to the risk of contamination when identifying DNA from nonviable bacteria, the difficulty of interpreting polymicrobial results, and the lack of full standardization in routine orthopedic practice.

Imaging methods also play an important role. X-ray and computed tomography can assess fixation stability, as well as osteolysis, sequestra, nonunion, or implant malposition. Magnetic resonance imaging (MRI) with metal-artifact reduction techniques can be useful for evaluating soft tissues, abscesses, and osteomyelitis, but this depends on the type of implant, the imaging protocols, and the level of interpretive experience.

Table 2. Main diagnostic approaches to biofilm infection in orthopedics

Method	Assessment	Advantages	Disadvantages
Clinical examination	Pain, fistula, discharge, instability	Available, initial stage	Low specificity in chronic forms
CRP, erythrocyte sedimentation rate, leukocytes	Systemic inflammatory response	Simple, dynamic monitoring	May be normal in low-grade infection
X-ray/computed tomography	Osteolysis, instability, nonunion	Important for mechanical assessment	Does not always distinguish infection from an aseptic process
Magnetic resonance imaging with metal-artifact reduction	Soft tissues, abscess, osteomyelitis	More suitable for soft tissues	Artifacts, availability
Deep tissue cultures	Pathogen and susceptibility	Basis of etiological therapy	False-negative results after antibiotics
Sonication	Microorganisms from the biofilm	Better able to detect biofilm pathogens	Requires implant removal
Histology	Neutrophil infiltration, microorganisms	Confirmation of deep infection	Depends on the protocol
PCR/16S/metagenomics	Microbial DNA	Useful in culture-negative cases	Contamination, complex interpretation

Treatment

Treatment of biofilm infection of orthopedic implants must be thorough. Intensive antibacterial therapy without surgical control of the source of infection is often insufficient because the biofilm protects microorganisms from the effects of the drugs. The treatment strategy should include surgical debridement, removal of necrotic tissue, assessment of implant stability, correction of fixation, management of dead space, soft tissue coverage, and systemic and local antimicrobial therapy [8–10, 16].

In PJI, several main strategies include DAIR, one- and two-stage revision, resection arthroplasty, suppressive antibacterial therapy in selected cases. The use of these strategies depends on symptom duration, implant stability, soft tissue condition, pathogen type, antibiotic susceptibility, and the patient’s overall condition [5]. In addition, unconventional therapies are increasingly being considered, particularly the use of bacteriophages or enzymatic disruptors of the biofilm matrix as adjuncts for complex and resistant forms of periprosthetic infection [18].

In the case of FRI, the approach depends heavily on the degree of fracture union. If the fracture has united, removal of the implant can eliminate the surface on which biofilm forms. If the fracture has not united but the fixation is stable, debridement with retention of the construct can be considered. If the fixation is unstable, revision, replacement of the fixator, or other stabilization is required [8, 16].

Antibacterial therapy should be etiological. If there is no immediate need for treatment, empirical microbiological examination of deep tissue samples should be initiated. Once culture results are obtained, treatment should be adjusted according to the antibiogram. The consensus on systemic therapy of FRI states that the duration and composition of antibacterial treatment are determined by the

surgical strategy, in which the implant is retained, replaced, or removed [10]. Recent algorithms emphasize the importance of the earliest possible stabilization and transition to adaptive therapy, based on standardized preclinical biofilm assessment models approved by the latest international consensus [15, 16].

Local antimicrobial therapy is important in cases of soft tissue and bone defects, severe damage to the surrounding soft tissues, or a high risk of recurrence. It is not intended to replace systemic therapy and surgical source control but can be an important part of a comprehensive strategy. The use of local antibiotic carriers enables high drug concentrations in the infection zone, which is especially important under conditions of impaired vascularization [9, 19].

Prevention of biofilm infection

Prevention of biofilm infection of orthopedic implants should not be considered a separate measure but a multi-level strategy covering the preoperative, intraoperative, and postoperative stages. This is especially critical in orthopedic traumatology, where the likelihood of infection depends not only on the presence of an implant but also on the nature of the injury, the degree of soft tissue damage, wound contamination, the stability of fixation, the volume of necrotic tissue, and the patient’s general condition.

The first stage of prevention is managing the patient’s condition before surgery, if possible. The risk of infection increases with diabetes, smoking, anorexia, obesity, immunosuppression, anemia, vascular disorders, prolonged hospital stay, and previous surgeries. In traumatology, this stage is often limited by the urgency of the intervention, but even under such conditions it is important to assess the overall risk of infection, the severity of soft tissue damage, and the need for staged surgery, temporary external fixation, or ear-

Table 3. Multilevel prevention of biofilm infection of orthopedic implants

Prevention measure	Advantage/goal	Limitations
Preoperative assessment of risk factors, glycemic control, anemia correction, nutritional support	To reduce systemic susceptibility to infection	In trauma, there is often no time for full optimization
Antibiotic prophylaxis: timely administration of systemic antibiotics before incision	To reduce early bacterial contamination	Does not act fully on an established biofilm
Surgical technique: atraumatic handling, hemostasis, and minimization of operative time	Reduction of tissue ischemia and bacterial adhesion	Depends on the complexity of the injury
Debridement: removal of necrotic tissue, reduction of bacterial load	Necrosis and the presence of cavities sustain infection	Excessive resection may create a defect
Stable fixation: adequate osteosynthesis, avoidance of micromotion	Stability promotes union and infection control	In severe infections, replacement of the construct may be required
Soft tissue coverage: early wound closure, flap surgery if necessary	Vascularized tissues improve delivery of immune cells and antibiotics	Requires a multidisciplinary approach
Local antimicrobial agents: hydrogels, cement, calcium sulfate, antibiotic-coated rods	High local drug concentration	Risk of uneven release or resistance
Antibiofilm coatings: bioactive glass, silver (Ag), iodine, CaP/HA, antibiotics, nanostructures, smart coatings	Inhibition of early adhesion and biofilm formation	Most evidence is preclinical or limited clinical

ly involvement of a plastic surgeon to close soft tissue defects.

The second level is intraoperative prevention. It includes timely systemic antibiotic prophylaxis, minimization of surgical duration, adherence to asepsis, careful handling of soft tissues, adequate hemostasis, reduction of devitalized tissue volume, stable fixation, and anatomically justified wound closure. For open fractures, early debridement, removal of nonviable tissue, reduction of bacterial load, appropriate choice of stabilization method, and closure of soft tissue defects are especially important, and, if necessary, the use of vacuum-assisted closure systems.

The third level is the local antimicrobial strategy. Its rationale is to create a high concentration of the antimicrobial agent directly in the risk zone, where systemic antibiotic therapy may be insufficient because of ischemia, scar tissue, necrosis, the presence of cavities, or impaired microcirculation. For this purpose, antibiotic-impregnated cement, calcium sulfate carriers, bioceramics, hydrogels, rods with antibacterial coatings, and other local delivery systems are used [9, 19].

In the context of prevention, it is important to consider local antibiotic therapy as a supplement to high-quality surgery, not as a replacement. No coating, powder, cement, or hydrogel can compensate for inadequate debridement, unstable fixation, or an unclosed soft tissue defect. A modern approach should combine reduction of bacterial load, a stable mechanical environment, vascularized soft tissue coverage, and local antimicrobial protection in high-risk patients.

Antibiotic-releasing hydrogel coatings are of particular interest. In a multicenter randomized study, Malizos et al. reported that a fast-resorbable antibiotic-loaded hydrogel coating applied during internal osteosynthesis of closed fractures was associated with a reduced rate of postoperative infections without any detected negative effect on fracture union [20]. However, these results cannot be automatically extrapolated to all types of fractures and implants, so additional studies in high-risk traumatology groups are needed.

Antibiofilm coatings for orthopedic implants

Antibiofilm coatings for orthopedic implants are one of the best ways to prevent implant-associated infections [21]. They are based on the idea that the first 24 hours after implantation are a critical period during which competition occurs between bacterial adhesion and the integration of body cells. If bacteria initially colonize the implant surface, a biofilm forms that is much less accessible to antibiotics and the immune response. However, if the surface promotes osseointegration while simultaneously inhibiting bacterial adhesion, the risk of infection is theoretically reduced [22–25].

The ideal coating for orthopedic traumatology should have the following functions:

- inhibit bacterial adhesion;
- prevent biofilm maturation;
- be biocompatible;
- not interfere with osteoblast function;
- not impair the mechanical properties of the implant;
- have predictable release of the active agent;

— not contribute to the development of antimicrobial resistance.

For metal fracture fixators, the coating is also important to avoid compromising the primary stability of fixation and to prevent interference with reparative osteogenesis [26–29].

Antibiofilm coatings are currently classified into anti-adhesive, contact-active, releasing, bioactive, osteointegrative, combined, and stimulus-responsive, each characterized by distinct antimicrobial mechanisms. In a systematic review, Kaspiris et al. examined contact and releasing-type antimicrobial coatings for orthopedic implants. Analysis of the results from *in vitro* and *in vivo* studies showed that coated implants exhibit a broad spectrum of antimicrobial activity, manifested as reduced bacterial growth, inhibition of biofilm formation, and preservation or even enhancement of osseointegration processes [22, 29, 30].

Anti-adhesive coatings are useful for reducing the initial attachment of bacteria to the implant surface. They can work by changing the hydrophilicity, charge, or micro- or nanotopography of the surface. The advantage is the absence of direct antibiotic pressure, but the main limitation is insufficient efficacy at high bacterial loads and in the presence of significant wound contamination.

Contact-active coatings are bactericidal because bacteria come into direct contact with the surface. These include surfaces with antimicrobial peptides, quaternary ammonium compounds, cationic polymer groups, or other functional molecules. Their advantage is lower systemic release of the active substance. Contact-active coatings may be less effective when proteins, cell debris, or fibrin are present on the surface.

Releasing coatings contain antibiotics, metal ions, or other antimicrobial agents that gradually penetrate the surrounding tissues. Their advantage is the ability to create a high local drug concentration, much higher than the systemic level. Antibiotic hydrogels, gentamicin-coated nails, antibiotic-containing polymer coatings, silver-containing coatings, and iodine coatings are examples of this method [31]. However, the main problem is control of release: too rapid release can provide a short-term prophylactic effect, whereas subtherapeutic concentrations at the end can theoretically promote the acquisition of resistance by microorganisms [20, 22–24, 29, 32].

Silver-based coatings are among the most studied. Silver ions exhibit broad-spectrum antimicrobial activity and can target bacterial membranes, proteins, enzymes, DNA, and other components. However, silver has a narrow therapeutic window: its antimicrobial activity must be sufficient to inhibit bacteria but not cytotoxic to bone tissue cells. A systematic literature review by Li et al. on the side effects of antibacterial coatings in orthopedics emphasizes that safety is not only a major issue in the treatment of infection but also a determinant of patient outcomes [33]. To overcome this limitation, current developments focus on creating multilayer silver coatings that optimize the ion-release profile, providing a significant reduction in bacterial colonization without the risk of cytotoxicity to the surrounding tissues [34].

Iodine-containing coatings are widely used in antiseptics but are also associated with adverse reactions and the risk

of allergic reactions. Copper- and zinc-based coatings are known for their strong antimicrobial activity and osteomodulating effects but are still studied primarily in preclinical settings due to the risk of dose-dependent toxicity and the lack of clinical data. In orthopedics and traumatology, calcium phosphate-based coatings are especially useful, as they can not only deliver antimicrobial agents but also promote osseointegration. A strong bond between metal and bone tissue is key for fracture fixators in calcium phosphate-based coatings and is extremely important [25–28].

However, a calcium phosphate or hydroxyapatite base alone does not always provide a sufficient antibacterial effect. Therefore, the most promising systems are modified ones: HA/Ag, CaP/Ag, CaP/antibiotic, HA/zinc, HA/copper, CaSO₄/peptides, or multilayer coatings. This enables the combination of osteoconductive activity with local antibacterial action [26–28, 34, 35].

Analysis of trends in the development of antimicrobial surfaces over the past decade confirms a gradual transition from monotherapeutic solutions to the creation of so-called “smart” or stimulus-responsive surfaces that respond to changes in local pH or to bacterial enzymes [25, 29]. Therefore, for coatings of calcium-containing metal fixators, the best approach is to consider them not only as antibacterial but as bifunctional or multifunctional; a coating that prevents early bacterial adhesion, prevents biofilm formation, promotes osseointegration, improves the mechanical stability of the bone-implant system, and does not harm bone cells.

Discussion

Bioactive glass S53P4 deserves special attention. It is a synthetic bone-graft substitute that combines osteoconductive and antibacterial properties. Bioactive glass has its own antimicrobial action without the use of antibiotics. The peculiarity is that pH and osmotic pressure damage bacterial cells and inhibit their growth by disrupting their membranes. Another important aspect is the absence of resistance development by microorganisms, confirmed in particular for *S.aureus* and *S.epidermidis*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* [36].

There is a need to expand research and the evidence base with high-quality randomized studies, since the available data come mainly from *in vitro* work. An important aspect of fractures is the combination of the osteostimulating and antibacterial effects of S53P4 in complex cases, in bone defects during reconstruction, and as a first stage in preventing biofilm formation [37].

Antibiofilm coatings are a promising direction but should not be considered a replacement for the principles of high-quality surgery. Their role is to reduce the risk of bacterial adhesion and biofilm formation, especially in high-risk patients. The most promising for traumatology are multifunctional coatings that combine antibacterial and osteointegrative properties. In such situations, calcium phosphate antimicrobial agents and bioactive glass have a strong theoretical and experimental basis for further study and for several experimental models, since they have been little studied in

Table 4. Types of antibiofilm coatings: mechanism of action, advantages, limitations, and level of evidence

Coating type	Mechanism of action	Advantages	Limitations	Level of evidence
Antibiotic release	Local release of antibiotics	High local concentration	Burst release, risk of resistance	Moderate
Antibiotic-loaded hydrogel	Resorbable gel with antibiotic	Versatility of application	Short duration of action	Moderate
Gentamicin-coated nail	Gentamicin polymer coating	Standardized system	Fixed antibiotic	Moderate
Silver-containing coatings	Ag ⁺ , membrane and DNA damage	Broad spectrum	Cytotoxicity, argyria	Moderate
Iodine-containing coatings	Antiseptic oxidative effect	Broad spectrum	Allergic reactions	Low/moderate
Copper/zinc-containing coatings	Ionic effect, oxidative stress	Antimicrobial potential	Dose-dependent toxicity	Low
CaP/HA	Osteoconduction	Osseointegration	Weak intrinsic antibacterial effect	Moderate for osseointegration
HA/Ag or CaP/Ag	Osteoconduction + Ag ⁺	Promising for fixators	Balance of Ag and cytocompatibility	Low/moderate
Antimicrobial peptides	Membrane damage	Potential against biofilms	Degradation, cost	Low
Chitosan	Cationic interaction with the membrane	Biocompatibility	Mechanical stability	Low/moderate
Nanostructured	Change of topography	Antibiotic-free prevention	Complex standardization	Low
Smart coatings	Release triggered by pH/enzymes	Personalized concept	Preclinical level	Low

this context. Great attention should be paid to the translational validity of experimental models. Determining the zone of inhibition of bacterial growth *in vitro* is insufficient to assess a coating's clinical potential. For a reliable assessment of osseointegration under conditions of biofilm infection, it is advisable to use standardized *in vivo* models with prior sample-size calculation, clearly defined endpoints, and assessment of mechanical stability, histological bone-implant contact, bacterial load, and local toxicity. For traumatology, it is also important to study the effect of the coating on bacterial adhesion, mature biofilm formation, osteoblast viability, histological bone-implant contact, pull-out strength, local toxicity, and coating stability after mechanical loading.

The practical significance of this review is its emphasis on the need for early detection of biofilm in implant-associated infections. For the clinician, it is important to obtain not only superficial swabs or nonspecific laboratory markers but also deep tissue samples, histology, and sonication, and to use standardized PJI/FRI criteria.

For the traumatologist, infection control and fracture stability are not the same thing. Osteosynthesis, tissue necrosis, dead space, and soft tissue coverage defects can lead to persistent infection despite appropriately selected antibiotic therapy.

A relevant direction is the study of coatings not only for antibacterial activity but also for various other parameters: biofilm formation, cytocompatibility, osseointegration, mechanical properties, morphometry, and systemic effect.

Periprosthetic and fracture-related infections share the same biofilm mechanism but differ in clinical presentation. The modern understanding of biofilm infection of orthope-

dic implants should shift from the simple bacteria-antibiotic model to a more complex one, bacteria-biofilm-implant-tissue environment-mechanical stability. This model better explains why clinical elimination of infection is often impossible without surgical source control and why the stability of fixation in FRI has both mechanical and infectious significance. This interaction is best regarded as a conceptual model of biofilm infection of orthopedic implants (Fig. 1).

Study limitations

The review has several limitations. First, it is a narrative rather than a systematic review; therefore, it does not include a formal PRISMA scheme, risk-of-bias assessment, or quantitative meta-analysis. The literature on antibiotic coatings is heterogeneous; most studies are conducted *in vitro* or in animal models, and there is a lack of high-quality randomized clinical trials. Variations in biofilm models, microbial strains, implant materials, and endpoints complicate comparison of coatings.

Nevertheless, the limitations of these studies point to the need for further research to standardize experimental models and endpoints and to move from a purely antibacterial assessment to a full assessment of the implant-biofilm-bone tissue system.

Research perspectives

Future research should focus on three directions. First, it is important to improve the diagnosis of biofilm infections at early stages: sonication should be standardized, molecular methods should be used in clinical settings, and biomarkers

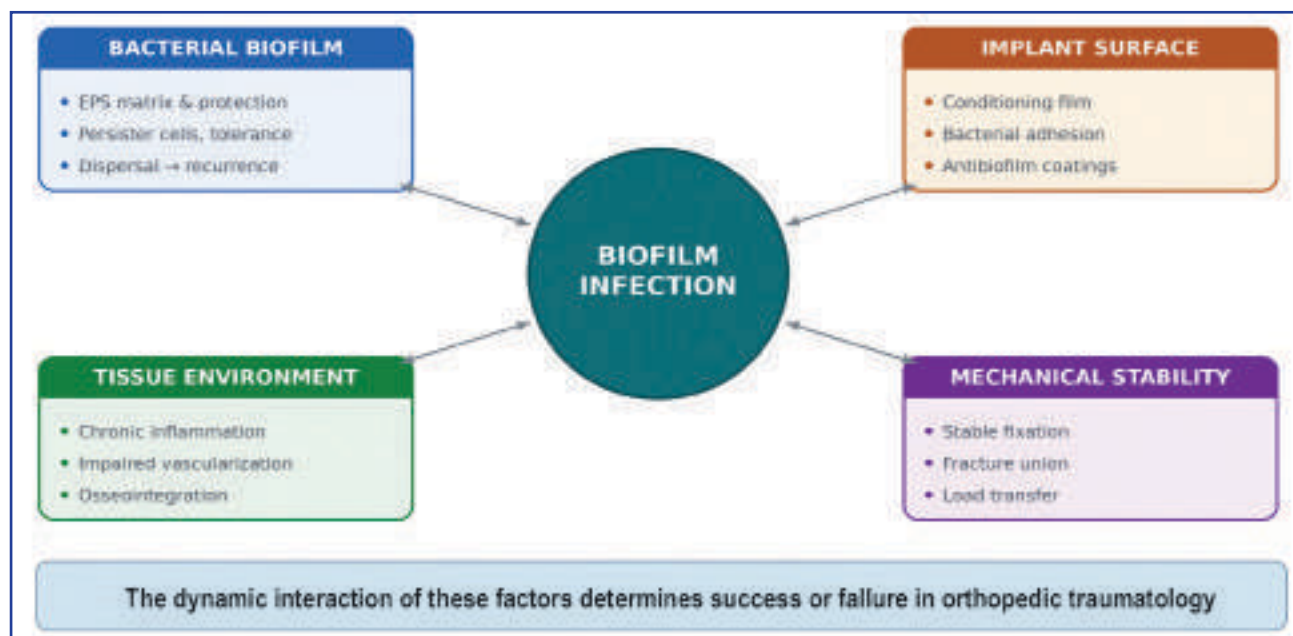


Figure 1. Conceptual model of biofilm infection of orthopedic implants. Biofilm infection is viewed as the result of the interaction of four interrelated components — the bacterial biofilm, the implant surface, the tissue environment, and the mechanical stability of fixation. A disturbance in one of the links (biofilm persistence, implant instability, or tissue devitalization) sustains a vicious circle of infection. In contrast, multifunctional antibiofilm coatings, stable fixation, and wound control promote biofilm suppression, osseointegration, and preservation of limb function

Note: EPS — extracellular polymeric substances.

should be developed to distinguish aseptic inflammation from low-grade infection. The second direction is the personalization of treatment. For FRI, it is important to know whether it is safe to retain the implant or replace it, what the optimal duration of antibacterial therapy is, and how to balance infection control with the reconstruction of bone defects. The third direction is the development of next-generation coatings. The most promising are not only antibacterial but also multifunctional coatings that simultaneously act as anti-adhesives, locally antimicrobially, and biocompatibly, while supporting osseointegration and ensuring the mechanical stability of the bone-implant system.

Conclusions

Biofilm infection of orthopedic implants is a complex clinical and biological process that determines the chronic course, recurrence, and treatment of implant-associated infections. An important pathogenetic feature is the formation of a microbial community on the implant surface, which confers on microorganisms increased tolerance to antibacterial therapy and immune responses. Periprosthetic and fracture-related infection share the same biofilm mechanism but differ in clinical logic. Antibiofilm coatings are a promising approach to prevention, but most technologies have predominantly preclinical or limited clinical evidence. Multifunctional coatings are promising in traumatology, particularly those based on bioactive glass, calcium phosphate, or hydroxyapatite matrices with antimicrobial agents; however, their clinical efficacy requires further validation. The proposed conceptual model emphasizes the need for simultaneous control of the biofilm, implant condition, tissue environment, and mechanical stability of fixation.

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Information about authors

Valentyn O. Kuprii, PhD-student, Department of Traumatology and Orthopedics, Bogomolets National Medical University, Kyiv, Ukraine; e-mail: drkuprii@gmail.com; <https://orcid.org/0000-0003-3026-5053>
Oleksandr A. Burianov, MD, DSc, Professor, Head of the Department of Traumatology and Orthopedics, Bogomolets National Medical University; State Institution "Institute of Traumatology and Orthopedics, NAMS of Ukraine", Kyiv, Ukraine; e-mail: kaftraum@ukr.net; <https://orcid.org/0000-0002-2174-1882>

Vadim A. Ponyatovskyi, PhD, Associate Professor, Department of Microbiology, Virology and Immunology, Bogomolets National Medical University, Kyiv, Ukraine; e-mail: vponiatovskyi@gmail.com; <https://orcid.org/0000-0002-1503-3935>

Vitalii A. Dubok, DSc (Chemistry), Professor, Leading Researcher, Frantsevich Institute for Problems of Materials Science, NAS of Ukraine, Kyiv, Ukraine; e-mail: vdubok17@gmail.com; <https://orcid.org/0000-0002-3494-7775>

Andrii P. Kusyak, PhD (Chemistry), Senior Lecturer, Department of Chemistry, Zhytomyr Ivan Franko State University, Zhytomyr, Ukraine; e-mail: a_kusyak@ukr.net; <https://orcid.org/0000-0003-1005-5497>
Iurii M. Nasieka, DSc (Physics and Mathematics), Senior Researcher, Department of Kinetic Phenomena and Polaritons, V. Lashkaryov Institute of Semiconductor Physics, NAS of Ukraine; Senior Lecturer, Education and Research Institute of Energetics, Automation and Energy Efficiency, National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine; <https://orcid.org/0000-0002-3431-8856>
Volodymyr S. Chorny, PhD, Associate Professor, Department of Traumatology and Orthopedics, Bogomolets National Medical University, Kyiv, Ukraine; e-mail: oncoortoped@gmail.com; <https://orcid.org/0000-0002-3679-0783>

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Купрій В.О.¹, Бур'янов О.А.^{1,6}, Понятовський В.А.¹, Дубок В.А.², Кусяк А.П.³, Насека Ю.М.^{4,5}, Чорний В.С.^{1,6}

¹Національний медичний університет імені О.О. Богомольця, м. Київ, Україна

²Інститут проблем матеріалознавства імені І.М. Францевича НАН України, м. Київ, Україна

³Житомирський державний університет імені Івана Франка, м. Житомир, Україна

⁴Інститут фізики напівпровідників імені В.Є. Лашкарьова НАН України, м. Київ, Україна

⁵Національний університет біоресурсів і природокористування України, м. Київ, Україна

⁶Державна установа «Інститут травматології та ортопедії НАМН України», м. Київ, Україна

Біоплівкова інфекція ортопедичних імплантатів: діагностика, лікування та профілактика

Резюме. Біоплівкова інфекція ортопедичних імплантатів є однією з найскладніших проблем у сучасній ортопедії та травматології, оскільки вона поєднує мікробну персистенцію, обмежену ефективність системної антибактеріальної терапії, хронічне запалення, порушення остеоінтеграції, нестабільність імплантатів і функціональні наслідки лікування. Мікроорганізми прикріплюються до поверхонь ендопротезів, пластин, гвинтів, інтрамедулярних стрижнів, спінальних систем та інших фіксуючих пристроїв, утворюючи біоплівки, які є більш стійкими до антибіотиків та імунних реакцій, ніж вільноживучі бактерії. Цей огляд має на меті узагальнити поточні дані про патогенез, мікробіологічний спектр, клінічні форми, діагностику, лікування, профілактику і стратегії антибіоплівкового покриття ортопедичних імплантатів. Пошук літератури проведено в чотирьох бібліографічних базах даних — PubMed, Scopus, Web of Science і Google Scholar — та шести видавничих платформах: Elsevier, Springer Nature, Wiley, Oxford Academic, MDPI і Frontiers. Використано одинадцять груп ключових слів англійською та українською мовами, публікації з 2014 по 2026 рік були пріоритетними, а 37 джерел включено після двоетапного скринінгу назв/анотацій та повних текстів. Аналіз показав, що перипротезна інфекція суглоба (PJI) та інфекція, пов'язана з переломом (FRI), характеризуються однаковим механізмом утворення біоплівки, але відрізняються клінічно, оскільки при FRI імплантат також необхідний для підтримки стабільності перелому. Ключові діагностичні еле-

менти включають глибокий забір тканин, ультразвукову обробку видалених імплантатів, гістологію та стандартизовані критерії PJI/FRI, тоді як поверхневі мазки недостатні для остаточного прийняття терапевтичного рішення. Ефективне лікування вимагає хірургічного контролю джерел, стабільної фіксації або ревізії імплантатів, усунення «мертвого простору», покриття м'яких тканин і системної та місцевої антимікробної терапії. В огляді було визначено 12 основних груп стратегій антибіоплівкового або антимікробного покриття, включаючи системи, що вивільняють антибіотики, гідрогелі з антибіотиками, цвяхи, покриті гентаміцином, покриття на основі іонів металів, системи на основі фосфату кальцію/гідроксиапатиту, антимікробні пептиди, хітозан, наноструктуровані поверхні, а також «розумні» покриття, чутливі до змін pH або ферментів. Багатофункціональні покриття на основі біоактивного скла, фосфату кальцію, гідроксиапатиту, срібла, антибіотиків, гідрогелів або комбінованих систем є особливо перспективними, оскільки вони можуть пригнічувати ранню адгезію бактерій, зменшувати утворення біоплівки й підтримувати остеоінтеграцію. Однак більшість доступних даних залишаються доклінічними або клінічно обмеженими, і перед рутинним використанням в ортопедичній травматології потрібна подальша валідація.

Ключові слова: біоплівка; ортопедичні імплантати; перипротезна інфекція; інфекція, пов'язана з переломом; антибіоплівкові покриття; огляд