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Biofilm-Associated Hospital Infections: Antibiotic Resistance and Therapeutic Approaches

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ABSTRACT: Biofilm-associated infections are an important cause of persistent and recurrent healthcare-associated infections (HAIs), particularly when microorganisms colonize intravascular and urinary catheters, endotracheal tubes, prosthetic joints, cardiac devices and wound surfaces. Biofilms are structured microbial communities embedded in an extracellular polymeric substance (EPS) matrix. Their clinical significance arises from a combination of physical protection, altered microbial physiology, metabolic heterogeneity, stress responses, persister-cell formation and opportunities for horizontal gene transfer. These features can markedly reduce antimicrobial activity and impair host immune clearance. Importantly, biofilm-associated antimicrobial tolerance is not synonymous with heritable antibiotic resistance, although prolonged infection and antibiotic exposure can select for genetically resistant organisms. Conventional susceptibility testing predominantly evaluates planktonic organisms and may therefore fail to represent the response of organisms growing in biofilms. Management depends on the infection site, pathogen, severity, device involvement and feasibility of source control. Appropriate antimicrobial therapy, drainage, debridement and removal or exchange of infected devices remains central components of care. Antibiotic lock therapy and selected biofilm-active combinations have roles in specific clinical circumstances. Emerging strategies—including bacteriophages, matrix-degrading enzymes, quorum-sensing inhibitors, antimicrobial peptides, nanoparticles, surface coatings and photodynamic approaches show promise but remain variably supported by clinical evidence. This review discusses the biology, clinical manifestations, diagnostic challenges, established management principles and investigational therapies relevant to biofilm-associated hospital infections, with emphasis on practical infection prevention and antimicrobial stewardship.

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1. Introduction

Healthcare-associated infections remain a major cause of preventable morbidity, mortality, prolonged hospitalization and increased healthcare expenditure. Their occurrence is influenced by patient vulnerability, invasive procedures, antimicrobial exposure, environmental contamination and the increasing use of complex medical devices. A substantial proportion of clinically important infections involve microorganisms growing in organized communities rather than as freely suspended planktonic cells. These communities, known as biofilms, may develop on living tissues, necrotic material and abiotic surfaces, including catheters, prostheses, drains and respiratory equipment [1,2]. Biofilm growth changes the interaction between microorganisms, antimicrobials and host defenses. The matrix can retain extracellular enzymes and metabolites, modify local diffusion, and create gradients of oxygen, nutrients and pH. Cells in different regions of the same biofilm may therefore have markedly different growth rates and susceptibility profiles. Slow-growing cells and persister subpopulations can survive antimicrobial exposure and repopulate the community after treatment ends [3,4]. This helps explain why device-associated infections may persist despite apparently appropriate antibiotic treatment.

The terms resistance and tolerance require careful distinction. Antibiotic resistance generally refers to a heritable increase in the ability to grow at drug concentrations that inhibit susceptible organisms. Biofilm-associated tolerance often reflects a reversible physiological state in which organisms survive antimicrobial exposure without necessarily exhibiting an increased planktonic minimum inhibitory concentration (MIC). Biofilms can nevertheless promote the emergence and spread of genetic resistance through close cell proximity, stress adaptation and horizontal gene transfer [3,5]. This review focuses on biofilm-associated infections encountered in hospitals, the mechanisms underlying treatment failure, diagnostic limitations and established and emerging therapeutic options. It also considers the practical implications for infection prevention and control programmes.

2. Biofilm biology and development

2.1 Definition and composition

A biofilm is a microbial community attached to a surface or present as an aggregate and enclosed within a self-produced or host-influenced matrix. The matrix is commonly described as EPS and may contain polysaccharides, proteins, extracellular DNA (eDNA), lipids and substantial amounts of water. Its composition varies according to the organism, growth conditions, surface, host environment and stage of development [1,6]. In Staphylococcus aureus and Staphylococcus epidermidis, matrix components may include polysaccharide intercellular adhesin, surface-associated proteins, teichoic acids and eDNA. Pseudomonas aeruginosa can produce alginate, Pel and Psl polysaccharides, together with extracellular proteins and DNA. Candida species form fungal biofilms containing yeast, pseudohyphal or hyphal elements within a matrix that includes polysaccharides, proteins and extracellular nucleic acids [6,7]. Mixed-species communities may contain bacteria and fungi, increasing structural and metabolic complexity.

2.2 Stages of biofilm formation

Biofilm development is a dynamic process commonly described in four overlapping stages: initial attachment, irreversible attachment, maturation and dispersal. Initial attachment is influenced by surface chemistry, hydrophobicity, electrostatic interactions, conditioning films and microbial adhesins. Host proteins such as fibrinogen and fibronectin can coat implanted materials and provide binding sites for microbial surface proteins. Reversible attachment may progress to stable adhesion through adhesin expression and production of matrix components [1,6]. During maturation, microorganisms proliferate and organize into three-dimensional structures with channels and spatially distinct microenvironments. Quorum sensing allows cells to coordinate gene expression in response to population density and environmental signals. Cyclic-di-GMP signalling is an important regulator of the transition between motile and sessile lifestyles in many bacteria. Dispersal may occur through enzymatic matrix degradation, changes in signalling, nutrient limitation or host-associated factors. Released cells or aggregates can seed new sites and contribute to bloodstream or tissue dissemination [3,6].

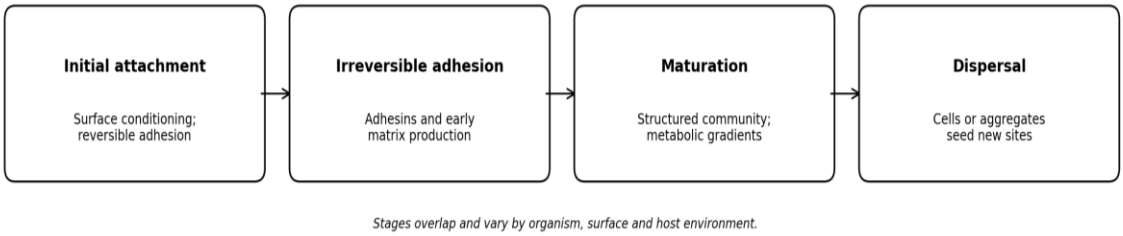


Figure: 1 Stages of microbial biofilm development.

2.3 Biofilms on medical devices

Medical devices provide surfaces that can be rapidly conditioned by host proteins and subsequently colonized by microorganisms. Intravascular catheters may become contaminated during insertion, through migration of skin organisms

along the external surface, or through contamination of hubs and infusates. Urinary catheters facilitate ascending microbial migration and provide a surface for crystalline and non-crystalline biofilm formation. Endotracheal tubes may support biofilms that act as reservoirs for lower respiratory tract pathogens. Orthopaedic implants, cardiac devices and vascular grafts are also vulnerable to microbial adhesion and biofilm development [2,8]. The clinical importance of a device biofilm depends on its location, microbial burden, host response and likelihood of persistent seeding. Not every colonized device causes clinical infection, and positive cultures must be interpreted in the context of symptoms, inflammatory findings and appropriate diagnostic criteria. Conversely, biofilm infection may be difficult to confirm when organisms are intermittently released or are not recovered by routine culture.

3. Major biofilm-associated hospital infections

3.1 Catheter-related bloodstream infections

Central venous catheters are essential for administering medications, fluids, parenteral nutrition and haemodialysis, but they can become colonized by coagulase-negative staphylococci, S. aureus, enterococci, Gram-negative bacilli and Candida species. Biofilm formation on the external or internal catheter surface can result in persistent bloodstream infection. Recurrent positive blood cultures, persistent bacteraemia or fungaemia despite appropriate therapy, and infection involving a long-term intravascular device should prompt assessment for catheter-related infection and other endovascular complications [8,9]. Management requires clinical assessment, appropriately collected peripheral and catheter blood cultures, organism-directed antimicrobial therapy and a decision about catheter removal. Removal is particularly important in severe sepsis, persistent bloodstream infection, infections caused by selected high-risk organisms, or complicated infection. Salvage may be considered in carefully selected patients with limited vascular access or long-term devices, provided that the pathogen, clinical stability and device type support this approach. Antibiotic lock therapy may be used as an adjunct in selected catheter infections; it is not a substitute for systemic therapy when bloodstream infection is present [8,9].

3.2 Catheter-associated urinary tract infections

Indwelling urinary catheters disrupt normal urinary defence mechanisms and provide a surface for ascending microbial colonization. Common organisms include Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, P. aeruginosa, enterococci and Candida species. Urease-producing organisms can increase urinary pH and promote crystalline biofilm formation, causing catheter blockage and urinary retention. Bacteriuria is common with prolonged catheterization and does not, by itself, establish symptomatic infection. Clinical diagnosis should be based on compatible symptoms and signs, microbiological findings and exclusion of alternative explanations [10]. The most effective strategy is to avoid unnecessary catheterization, use aseptic insertion and maintenance practices, maintain a closed drainage system and remove the catheter as soon as it is no longer required. When symptomatic infection occurs, urine should be collected appropriately and antimicrobial treatment selected according to culture results, clinical severity and local susceptibility patterns. Catheter replacement may be appropriate in selected patients with a long-standing catheter, obstruction or suspected catheter biofilm, but routine antimicrobial treatment of asymptomatic bacteriuria is generally inappropriate outside defined exceptions [10,11].

3.3 Ventilator-associated pneumonia and respiratory-device biofilms

Endotracheal tubes can develop biofilms containing organisms such as P. aeruginosa, S. aureus, Acinetobacter baumannii and Enterobacterales. Secretions and biofilm fragments may move into the lower respiratory tract, contributing to microbial exposure and potentially to ventilator-associated pneumonia (VAP). Biofilm presence on an endotracheal tube is not equivalent to a diagnosis of VAP; diagnosis requires clinical, radiological and microbiological assessment. Risk reduction relies on evidence-based ventilator care, minimizing unnecessary ventilation and sedation, appropriate oral care, head-of-bed elevation when suitable, and safe handling of respiratory equipment [12]. Systemic antibiotics are selected according to the suspected pathogens, severity, local antibiogram and culture results. Routine antimicrobial treatment solely to eradicate endotracheal tube biofilm is not established. Specialized tube designs and subglottic secretion drainage may reduce selected risks, but device modifications should be assessed against clinical outcomes, safety and cost.

3.4 Surgical-site and chronic wound infections

Biofilms may occur in surgical wounds, chronic ulcers, burns and other damaged tissues. Wound biofilms are often polymicrobial and may include S. aureus, P. aeruginosa, enterococci, anaerobes and fungi. Devitalized tissue, foreign material, poor perfusion, exudate and impaired host immunity create conditions that support persistent microbial communities. Biofilm-associated inflammation can delay granulation and epithelialization, although the presence and clinical significance of biofilm cannot reliably be inferred from appearance alone. Treatment is based on wound assessment, drainage where required, removal of devitalized tissue, correction of contributing factors and systemic antimicrobial therapy when there is clinical evidence of invasive infection. Topical antiseptics or antimicrobial dressings may have a role in selected wound-care plans, but evidence differs by product and wound type. Repeated indiscriminate antibiotic use can select resistant organisms and should be avoided [13].

3.5 Prosthetic joint, cardiac and other implant infections

Prosthetic joint infection (PJI) and infections involving cardiac implantable electronic devices, vascular grafts or other prostheses can be difficult to eradicate because organisms adhere to foreign material and form mature biofilms. Staphylococci are frequent causes, but Gram-negative bacteria, enterococci, fungi and polymicrobial infections also occur. Clinical presentation may be acute, with pain, fever and local inflammation, or indolent, with progressive pain, loosening or impaired function [14]. Management is multidisciplinary and may include debridement, antimicrobial therapy and implant retention in selected cases, one- or two-stage exchange, or removal when feasible. The choice depends on timing, implant stability, soft-tissue condition, pathogen, host factors and surgical feasibility. Rifampicin-containing combinations have a role in selected staphylococcal implant infections when the implant is retained, but rifampicin should not be used alone because resistance can emerge rapidly. Regimens must follow specialist guidance and account for interactions, susceptibility and toxicity [14].

Table: 1 Common biofilm-associated hospital infections and clinical considerations.

Infection setting	Representative organisms	Biofilm-related concern	Core management principle
Central venous catheter infection	Coagulase-negative staphylococci, S. aureus, enterococci, Gram-negative bacilli, Candida	Persistent intraluminal or extraluminal colonization and recurrent bloodstream seeding	Blood cultures, systemic targeted therapy and assess need for device removal or selected salvage
Catheter-associated UTI	E. coli, Klebsiella, Proteus, Pseudomonas, enterococci	Ascending colonization, crystalline biofilm and catheter obstruction	Avoid unnecessary catheter use; remove/replace when indicated and treat symptomatic infection
VAP / respiratory device	P. aeruginosa, S. aureus, A. baumannii, Enterobacterales	Endotracheal tube biofilm and aspiration of contaminated secretions	Apply ventilator prevention practices and diagnose/treat pneumonia clinically
Wound / surgical-site infection	S. aureus, P. aeruginosa, enterococci, anaerobes	Polymicrobial communities in devitalized tissue and foreign material	Source control, wound care and targeted systemic therapy when invasive infection exists
Prosthetic / implant infection	S. aureus, coagulase-negative staphylococci, enterococci, Gram-negative bacilli	Adherent biofilm on implant with potential persistence despite antibiotics	Multidisciplinary surgical strategy plus pathogen-directed antimicrobial therapy

4. Mechanisms of biofilm-associated antibiotic resistance and tolerance

4.1 Restricted and altered antimicrobial penetration

The EPS matrix can slow or bind some antimicrobial molecules, although it is not an impermeable barrier and the effect differs by drug, organism and matrix composition. Charged matrix components may interact with positively charged antibiotics, while extracellular enzymes can inactivate selected agents. More importantly, gradients in oxygen, nutrients, pH and metabolic waste can alter antibiotic activity and microbial physiology across the biofilm [3,5].

4.2 Slow growth and metabolic heterogeneity

Many antibiotics act most effectively on actively growing cells or specific metabolic processes. Cells in nutrient-rich outer regions may grow rapidly, whereas deeper regions may experience nutrient limitation, low oxygen and reduced metabolic activity. Such slow-growing cells may survive exposure to drugs that are highly active against planktonic cells. This is a physiological phenomenon and should not automatically be interpreted as acquired genetic resistance [3,5].

4.3 Persister cells and stress responses

Persister cells are transiently tolerant subpopulations that survive otherwise lethal antimicrobial exposure and can resume growth after drug concentrations decline. Their formation may be influenced by toxin-antitoxin systems, stringent response pathways, oxidative stress, nutrient limitation and other regulatory networks. Persisters can contribute to relapse because surviving cells repopulate the biofilm after treatment, even when the original organism remains susceptible by conventional testing [3,5].

4.4 Efflux pumps, altered targets and enzymatic inactivation

Biofilm growth can increase expression of efflux systems and stress-response pathways. These changes may reduce intracellular drug accumulation or modify susceptibility to selected antimicrobial classes. In genetically resistant organisms, established mechanisms such as beta-lactamase production, target modification, altered permeability and drug-inactivating enzymes operate alongside biofilm-associated tolerance. The combined effect can make treatment particularly difficult in multidrug-resistant organisms [3,5].

4.5 Horizontal gene transfer and polymicrobial interactions

The close proximity of cells within biofilms may facilitate transfer of plasmids and other mobile genetic elements through conjugation, transformation or transduction. eDNA can contribute to matrix structure and may also provide genetic material. Mixed-species communities can exchange metabolites, alter local pH, provide protective enzymes or change the expression of virulence factors. These interactions may influence antimicrobial response, although their clinical effects vary across organisms and infection sites [3,6].

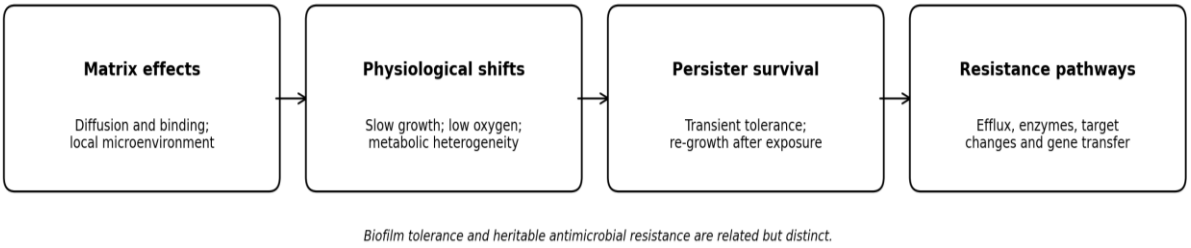


Figure: 2 Major mechanisms contributing to biofilm-associated antimicrobial treatment failure.

5. Diagnostic challenges

5.1 Clinical recognition and microbiological sampling

Biofilm-associated infection should be suspected when an infection is persistent or recurrent, involves an implanted device, responds incompletely to appropriate therapy or is associated with repeated recovery of the same organism. These features are not specific, and clinicians must also consider inadequate source control, incorrect diagnosis, poor antimicrobial exposure, host immunosuppression and an unrecognized metastatic focus. Sampling should target the clinically relevant site and be performed before antimicrobial therapy when this is safe and feasible. Blood cultures, urine cultures, respiratory samples, wound specimens and tissue cultures remain central to routine diagnosis, but they identify recoverable organisms rather than directly demonstrating a biofilm. Superficial swabs may reflect colonization and may not represent organisms within deep tissue or on an implant. In implant-associated infection, multiple separately collected tissue specimens can improve diagnostic interpretation. Sonication of removed devices may dislodge adherent organisms and increase microbiological yield in selected settings [15,16].

5.2 Imaging and specialized methods

Imaging is selected according to the suspected infection and may include ultrasound, computed tomography, magnetic resonance imaging, nuclear medicine techniques or echocardiography. These tests identify structural abnormalities, collections, prosthetic complications or metastatic infection; they do not usually visualize biofilm directly. Microscopy, scanning electron microscopy and confocal laser scanning microscopy can characterize biofilm architecture in research or specialized diagnostic settings, but availability, sample preparation and interpretation limit routine use [15].

5.3 Antimicrobial susceptibility testing

Routine MIC testing is generally performed using planktonic organisms under standardized laboratory conditions. Biofilm susceptibility endpoints include minimum biofilm inhibitory concentration and minimum biofilm eradication concentration, but methods and definitions vary. Biofilm assays are influenced by the surface, inoculum, medium, incubation conditions, biofilm age and endpoint selected. At present, biofilm-based susceptibility testing is not sufficiently standardized for routine treatment decisions in most clinical laboratories [16,17]. Consequently, clinicians should not independently multiply planktonic MIC values or prescribe unvalidated high-dose regimens to compensate for presumed biofilm tolerance. Treatment should be guided by infection-site pharmacology, organism susceptibility, established clinical evidence, source control and specialist consultation. Biofilm testing remains an important research priority, particularly for persistent device-related infections.

6. Established therapeutic approaches

6.1 Source control

Source control is a central principle in the management of biofilm-associated infection. Depending on the site, it may involve drainage of an abscess, debridement of infected or necrotic tissue, removal of an infected catheter, exchange or removal of an infected implant, and correction of obstructed drainage. Antimicrobial therapy alone may fail when a mature biofilm remains on a device or within poorly perfused tissue. The balance between device retention and removal requires individualized assessment of clinical stability, device function, infection severity and available alternatives [8,14].

6.2 Systemic antimicrobial therapy

Antimicrobial selection should be based on the likely or confirmed pathogen, infection site, susceptibility results, severity, renal and hepatic function, drug penetration, allergy history and local resistance patterns. Empirical therapy may be necessary in severe infection, but it should be reassessed and narrowed when microbiological data become available. Prolonged treatment is not automatically beneficial; duration should follow the specific infection syndrome and adequacy of source control. Unnecessary broad-spectrum or extended therapy increases toxicity, Clostridioides difficile risk and

selection pressure for resistance. Combination therapy may be appropriate for defined indications, including selected staphylococcal prosthetic infections or severe infections caused by particular resistant organisms. However, there is no universal antibiotic combination that eradicates all biofilms. Rifampicin has activity against staphylococci in biofilm-associated implant infection but must be combined with another active agent and used in an appropriate clinical context. The choice of companion drug and duration should be made by an infectious diseases and surgical team [14].

6.3 Antibiotic lock therapy

Antibiotic lock therapy involves instilling a concentrated antimicrobial solution into the lumen of a catheter and allowing it to dwell for a specified period. It is intended to expose intraluminal biofilm to high local drug concentrations while limiting systemic exposure. It may be considered as part of a catheter-salvage strategy in selected uncomplicated infections involving long-term catheters. It is not suitable for every pathogen or clinical presentation and should not delay catheter removal when removal is indicated. Protocols vary by catheter type, antimicrobial, compatibility and institutional guidance [8,9].

6.4 Local antimicrobial delivery

Local delivery systems can provide high antimicrobial concentrations at selected sites while limiting systemic exposure. Examples include antibiotic-loaded bone cement or spacers in orthopaedic surgery, local antibiotic carriers and selected wound-delivery materials. Their use depends on the surgical indication, stability of the formulation, elution characteristics, local tissue toxicity and the risk of selecting resistant organisms. Local therapy should complement rather than replace appropriate systemic treatment and surgical management when these are indicated.

6.5 Antiseptics and topical approaches

Antiseptics such as chlorhexidine, iodine-based preparations and selected wound-care agents are used in prevention or management of particular skin, device-site and wound problems. Their role is product- and indication-specific. Concentration, exposure time, tissue compatibility and the presence of organic material influence activity. Antiseptics should not be applied indiscriminately to deep tissues or implanted devices, and topical treatment cannot substitute for systemic therapy in invasive infection [17].

7. Emerging and investigational therapeutic strategies

7.1 Matrix-degrading enzymes

Enzymes that degrade matrix components are being investigated as adjuncts to antimicrobial therapy. DNase can degrade eDNA, dispersin B targets selected polysaccharides, and proteases can disrupt protein-rich matrix structures. By weakening the biofilm scaffold, these agents may improve antimicrobial access or promote detachment. However, matrix composition varies, and disruption can release viable organisms into surrounding tissue or the circulation. Enzyme-based approaches therefore require careful control of delivery, timing and combination with effective antimicrobial therapy [18].

7.2 Quorum-sensing inhibition and anti-virulence approaches

Quorum-sensing systems regulate collective behaviours such as virulence-factor production, matrix synthesis and dispersal. Quorum-quenching compounds may interfere with signal synthesis, signal detection or signal degradation. Anti-virulence approaches aim to reduce pathogenic behaviour without necessarily killing organisms, potentially lowering selective pressure compared with conventional antibiotics. Their activity is species-specific, and compensatory signalling pathways may limit effectiveness. Most candidates remain experimental, and clinical efficacy, dosing and safety require further evaluation [19].

7.3 Bacteriophage therapy

Bacteriophages are viruses that infect bacteria and may be selected for activity against particular pathogens. Some phages can penetrate or disrupt biofilm matrices, and engineered phages may express enzymes that degrade matrix components. Phage-antibiotic combinations are being studied for difficult-to-treat infections, including those involving multidrug-resistant organisms and prosthetic material. Challenges include narrow host range, bacterial resistance to phages, neutralizing antibodies, manufacturing quality, regulatory pathways and the need for rapid pathogen matching. Phage therapy should currently be regarded as an investigational or special-access intervention in many settings, not a routine replacement for standard treatment [20].

7.4 Antimicrobial peptides

Antimicrobial peptides may disrupt microbial membranes, interfere with intracellular targets, modulate host immune responses or affect biofilm development. Naturally occurring peptides such as cathelicidins and defensins provide models for synthetic derivatives with improved stability or selectivity. Their translation is constrained by proteolytic degradation, toxicity, immunogenicity, formulation challenges and cost. Clinical use requires robust evidence of efficacy and safety for the specific product and indication [21].

7.5 Nanoparticles and advanced drug-delivery systems

Metallic and polymeric nanoparticles are being investigated as antimicrobial carriers, matrix-penetrating systems or surface

coatings. Silver, gold, zinc oxide and other formulations have demonstrated antibiofilm activity in selected laboratory models. Nanocarriers may improve local delivery or enable controlled release, but their performance depends on particle size, surface charge, stability, tissue distribution and host toxicity. Potential environmental persistence and manufacturing consistency also require consideration. Evidence from in vitro assays should not be interpreted as proof of clinical benefit [22].

7.6 Antimicrobial surfaces and device coatings

Device engineering offers an opportunity to prevent initial microbial attachment. Hydrophilic or anti-adhesive surfaces, antimicrobial-releasing coatings, contact-killing materials and surface modifications are being evaluated for catheters and implants. A coating may reduce early colonization but lose activity over time, alter device properties or expose organisms to subinhibitory concentrations. Clinical evaluation should measure patient-important outcomes, not only laboratory biofilm biomass. Device coatings should be integrated with insertion and maintenance bundles rather than viewed as a stand-alone prevention strategy [8,23].

7.7 Photodynamic and physical approaches

Antimicrobial photodynamic therapy uses a photosensitizing compound activated by light to generate reactive oxygen species that damage microbial structures. It has been investigated for wounds, oral biofilms and selected superficial infections. Ultrasound-assisted approaches, electrical stimulation and other physical methods are also under study. Limited light penetration, tissue effects, equipment requirements and inconsistent protocols restrict broad application. These methods may eventually serve as adjuncts in selected settings but require clinical validation [24].

7.8 CRISPR-based and other precision strategies

CRISPR-associated systems are being explored as sequence-specific tools to target resistance genes, virulence determinants or essential bacterial sequences. Delivery into target organisms within a mature biofilm remains a major challenge. Other precision approaches include engineered probiotics, targeted nanoparticles and agents designed to alter bacterial metabolism or awaken dormant cells before antimicrobial exposure. These concepts are promising but remain at an early stage of development and should not be presented as established clinical therapies [22,25].

Table: 2 Established and emerging approaches to biofilm-associated infection.

Approach	Proposed role	Current clinical position	Important limitations
Device removal, drainage and debridement	Reduces or removes infected biomass and establishes source control	Established cornerstone when indicated	May be technically difficult or compromise device function
Systemic targeted antibiotics	Treats planktonic and tissue-associated organisms and prevents dissemination	Established; regimen depends on syndrome and pathogen	Biofilm tolerance, toxicity, penetration and resistance
Antibiotic lock therapy	High local antimicrobial exposure within catheter lumen	Selected catheter-salvage situations	Not suitable for all pathogens or complicated infection
Local antibiotic carriers	Delivers antimicrobial locally at selected surgical sites	Established in selected orthopaedic procedures	Variable elution, local toxicity and resistance concerns
Matrix-degrading enzymes	Disrupts EPS to improve antimicrobial access	Investigational / limited specialized use	Matrix variability and risk of organism dispersal
Quorum-sensing inhibitors	Interrupts coordinated biofilm and virulence signalling	Experimental	Pathway redundancy and limited clinical evidence
Bacteriophages	Pathogen-specific bacterial killing and possible matrix disruption	Investigational / special-access use	Narrow host range, resistance and regulatory complexity
Antimicrobial peptides and nanoparticles	Membrane damage, antibiofilm activity or targeted delivery	Predominantly preclinical or early clinical research	Toxicity, stability, delivery and manufacturing
Antimicrobial coatings and photodynamic therapy	Prevents adhesion or damages organisms on accessible surfaces	Selected devices/products or investigational uses	Durability, tissue penetration and variable clinical outcomes

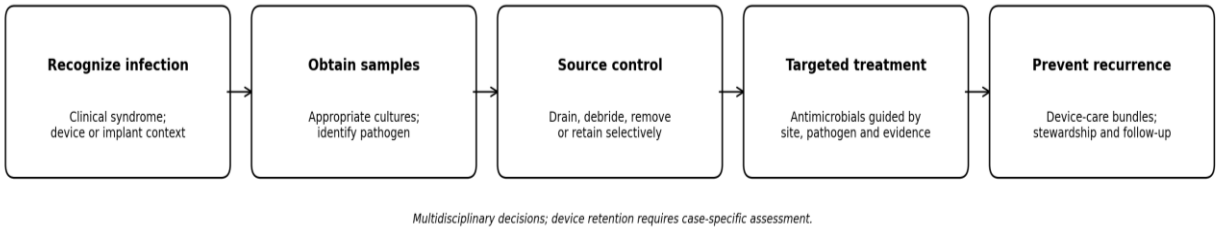


Figure: 3 Integrated clinical approach to suspected biofilm-associated hospital infection.

8. Infection prevention and control

Device-specific prevention also requires attention to the full device lifecycle. Before insertion, clinicians should confirm that the device is necessary and consider fewer invasive alternatives. During insertion, standardized checklists, maximal barrier precautions where indicated, appropriate skin antisepsis and trained personnel reduce opportunities for contamination. During maintenance, dressing integrity, hub and connector disinfection, closed-system integrity and prompt recognition of local or systemic infection should be monitored. Removal should be based on ongoing clinical need rather than an arbitrary schedule. These practices reduce the opportunities for initial colonization and therefore the development of mature biofilm communities [8,10,11].

Preventing biofilm formation is generally more feasible than eradicating a mature device-associated community. Infection prevention programmes should combine evidence-based device indications, trained insertion teams, hand hygiene, aseptic technique, appropriate skin antisepsis, hub disinfection, maintenance bundles and prompt device removal. Compliance should be audited and feedback provided to clinical teams. The CDC guidance for intravascular catheter-related infection emphasizes appropriate catheter selection, aseptic insertion and removal of catheters that are no longer essential [8].

For urinary catheters, facilities should use clear indications, avoid catheterization for staff convenience, maintain unobstructed closed drainage and review catheter necessity daily. CDC recommendations emphasize minimizing catheter use and duration, aseptic insertion and appropriate maintenance. In ventilated patients, prevention bundles should minimize avoidable ventilation, support safe airway care and reduce aspiration risk. Environmental cleaning, equipment reprocessing and adherence to standard precautions remain essential across all clinical areas. Antimicrobial stewardship is integral to biofilm prevention. Unnecessary antibiotic exposure selects resistant organisms and can alter the microbial ecology of hospitals. Stewardship teams should support appropriate empirical choices, timely de-escalation, optimized dosing and syndrome-specific duration. Surveillance data, local antibiograms and outbreak investigation can identify changes in pathogen distribution and resistance patterns. Education should reinforce that device colonization, asymptomatic bacteriuria and positive superficial wound cultures do not automatically require systemic antibiotics [10,11].

In resource-limited healthcare settings, sustainable interventions should prioritize reliable hand hygiene supplies, safe water, sterilization and disinfection systems, adequate staffing, device-care training and surveillance. Novel coatings and advanced diagnostics may not be widely accessible, while basic infection prevention measures can provide substantial benefit when implemented consistently. National infection prevention guidance, including India's National Guidelines for Infection Prevention and Control in Healthcare Facilities, can support facility-level protocols [26].

9. Clinical implications and future directions

Interpretation of biofilm-related evidence should also account for the difference between colonization, contamination and infection. A device culture that is positive after removal may demonstrate microbial attachment, but it does not independently establish that the device caused the patient's illness. Likewise, a positive urine culture in a catheterized patient may represent asymptomatic bacteriuria. Decisions to treat should be based on the clinical syndrome and accepted diagnostic criteria, not on the presumed presence of biofilm alone. This distinction is important for avoiding unnecessary antimicrobial exposure and preventing further selection of resistant organisms [10,16].

Biofilm-associated infection requires a multidisciplinary approach involving microbiologists, infectious diseases physicians, surgeons, pharmacists, nurses, infection prevention specialists and device teams. Treatment decisions should integrate clinical syndrome, microbiology, imaging, device status and feasibility of source control. A positive culture should be interpreted in context, and clinicians should avoid assuming that every persistent infection is caused by biofilm. Alternative explanations—including inadequate drainage, drug underexposure, resistant organisms, poor adherence, noninfectious inflammation and an incorrect diagnosis must be considered. A major research priority is the development of standardized, clinically useful biofilm susceptibility tests. Such tests would need reproducible methods, relevant infection-site models, clinically meaningful endpoints and evidence that results improve patient outcomes. Models should better reflect shear forces, host proteins, immune cells, polymicrobial communities and the pharmacokinetic conditions found in patients. Better methods for rapid identification of biofilm-associated pathogens could support earlier targeted therapy and reduce unnecessary broad-spectrum treatment [16,17].

Clinical trials of antibiofilm agents should distinguish prevention of attachment, inhibition of biofilm maturation, disruption of established biofilm and eradication of viable organisms. These are different biological outcomes and should not be combined under a single label. Studies should include device-free survival, infection recurrence, need for surgery,

mortality, adverse events, antimicrobial exposure and quality of life where appropriate. Laboratory reductions in biomass alone are insufficient to establish clinical effectiveness. Future strategies are likely to combine source control, conventional antimicrobials and targeted antibiofilm interventions. Personalized approaches may consider pathogen genotype, biofilm phenotype, device material, host immune status and drug penetration at the infected site. However, these advances must be supported by controlled clinical evidence, cost-effectiveness analysis and feasible implementation pathways. Clear regulatory standards will be required for phages, enzymes, peptides, coatings and other biologically or technologically complex products [16,17].

Conclusion

At the institutional level, prevention outcomes should be evaluated using standardized infection definitions and denominators appropriate to the device or procedure, such as infections per 1,000 device-days where applicable. Surveillance should be paired with feedback, root-cause review of clusters and assessment of bundle adherence. Such measurement helps distinguish whether an intervention reduces clinically important infection rather than simply reducing device colonization or laboratory biofilm measurements. Biofilm formation is an important contributor to persistent, recurrent and device-associated hospital infections. The biofilm matrix, altered microbial metabolism, persister-cell survival, stress responses and genetic exchange can reduce antimicrobial effectiveness and complicate host clearance. These phenomena must be distinguished from conventional heritable antibiotic resistance, although both can coexist. Routine microbiological testing remains essential but may not fully represent the behaviour of biofilm-associated organisms. Effective management therefore requires accurate clinical diagnosis, pathogen-directed antimicrobial therapy and timely source control, including device removal or debridement when indicated. Antibiotic lock therapy and selected biofilm-active regimens have defined roles, whereas many newer interventions remain investigational. Prevention through appropriate device use, aseptic practice, maintenance bundles, surveillance and antimicrobial stewardship remains the most practical strategy for reducing the burden of biofilm-associated hospital infections. Translation of promising antibiofilm technologies into routine care will depend on standardized testing and well-designed clinical trials demonstrating meaningful patient benefit.

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Author contributions

The first author and the corresponding author's supervisor wrote the initial drafts of the manuscript. All authors contributed to data collection, table design, and manuscript editing, and approved the final version for submission.

Author contributions

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References

1. Flemming HC, Wingender J, Szewzyk U, Steinberg P, Rice SA, Kjelleberg S. Biofilms: an emergent form of bacterial life. Nat Rev Microbiol. 2016;14(9):563-575. doi:10.1038/nrmicro.2016.94.
2. Donlan RM. Biofilms and device-associated infections. Emerg Infect Dis. 2001;7(2):277-281. Doi :10. 3201 /eid 07 02.010226.
3. Liu HY, Prentice EL, Webber MA. Mechanisms of antimicrobial resistance in biofilms. npj Antimicrob Resist. 2024;2:27. doi:10.1038/s44259-024-00046-3.
4. Hall CW, Mah TF. Molecular mechanisms of biofilm-based antibiotic resistance and tolerance in pathogenic bacteria. FEMS Microbiol Rev. 2017;41(3):276-301. doi:10.1093/femsre/fux010.
5. Ciofu O, Moser C, Jensen PØ, Høiby N. Tolerance and resistance of microbial biofilms. Nat Rev Microbiol. 2022;20:621-635. doi:10.1038/s41579-022-00682-4.
6. Flemming HC, Wingender J. The biofilm matrix. Nat Rev Microbiol. 2010;8(9):623-633. doi:10.1038/nrmicro2415.
7. Nobile CJ, Johnson AD. Candida albicans biofilms and human disease. Annu Rev Microbiol. 2015;69:71-92. doi:10.1146/annurev-micro-091014-104330.
8. Centers for Disease Control and Prevention. Intravascular catheter-related infection (BSI) prevention guidelines. Atlanta: CDC; reviewed 2024. Available from: https://www.cdc.gov/infection-control/hcp/intravascular-catheter-related-infection/
9. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America.

Clin Infect Dis. 2009;49(1):1-45. doi:10.1086/599376.
10. Centers for Disease Control and Prevention. Guideline for prevention of catheter-associated urinary tract infections. Atlanta: CDC; 2009, updated 2017. Available from: https://www.cdc.gov/infection-control/hcp/cauti/
11. Centers for Disease Control and Prevention. Clinical safety: preventing catheter-associated urinary tract infections (CAUTIs). Atlanta: CDC; 2025. Available from: https://www.cdc.gov/uti/hcp/clinical-safety/
12. Klompas M, Branson R, Cawcutt K, et al. Strategies to prevent ventilator-associated pneumonia, ventilator-associated events, and nonventilator hospital-acquired pneumonia in acute-care hospitals: 2022 update. Infect Control Hosp Epidemiol. 2022;43(6):687-713. doi:10.1017/ice.2022.88.
13. Malone M, Bjarnsholt T, McBain AJ, James GA, Stoodley P, Leaper D, et al. The prevalence of biofilms in chronic wounds: a systematic review and meta-analysis of published data. J Wound Care. 2017;26(1):20-25. doi:10.12968/jowc.2017.26.1.20.
14. Osmon DR, Berbari EF, Berendt AR, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2013;56(1):e1-e25. doi:10.1093/cid/cis803.
15. Domouchtsidou A, Ioannou P, Lianou A, Tsante KA, Tsakri D, Bonova E, et al. Biofilms in clinical infection: pathophysiology, diagnosis, and the evolving therapeutic landscape. J Clin Microbiol. 2026;64(3):e01042-25. doi:10.1128/jcm.01042-25.
16. Coenye T. Biofilm antimicrobial susceptibility testing: where are we and where could we be going? Clin Microbiol Rev. 2023;36(4):e00024-23. doi:10.1128/cmr.00024-23.
17. Garcia-Maset R, Chu V, Yuen N, Blumgart D, Yoon J, Murray BO, et al. Effect of host microenvironment and bacterial lifestyles on antimicrobial sensitivity and implications for susceptibility testing. npj Antimicrob Resist. 2025;3:42. doi:10.1038/s44259-025-00113-3.
18. Koo H, Allan RN, Howlin RP, Stoodley P, Hall-Stoodley L. Targeting microbial biofilms: current and prospective therapeutic strategies. Nat Rev Microbiol. 2017;15(12):740-755. doi:10.1038/nrmicro.2017.99.
19. Brackman G, Coenye T. Quorum sensing inhibitors as anti-biofilm agents. Curr Pharm Des. 2015;21(1):5-11. doi:10.2174/1381612820666140905114627.
20. Gordillo Altamirano FL, Barr JJ. Phage therapy in the postantibiotic era. Clin Microbiol Rev. 2019;32(2):e00066-18. doi:10.1128/CMR.00066-18.
21. Lei J, Sun L, Huang S, et al. The antimicrobial peptides and their potential clinical applications. Am J Transl Res. 2019;11(7):3919-3931.
22. Makabenta JMV, Nabawy A, Li CH, Schmidt-Malan S, Patel R, Rotello VM. Nanomaterial-based therapeutics for antibiotic-resistant bacterial infections. Nat Rev Microbiol. 2021;19(1):23-36. doi:10.1038/s41579-020-0420-1.
23. Campoccia D, Montanaro L, Arciola CR. A review of the biomaterials technologies for infection-resistant surfaces. Biomaterials. 2013;34(34):8533-8554. doi:10.1016/j.biomaterials.2013.07.089.
24. Cieplik F, Deng D, Crielaard W, et al. Antimicrobial photodynamic therap what we know and what we don't. Crit Rev Microbiol. 2018;44(5):571-589. doi:10.1080/1040841X.2018.1467876.
25. Bikard D, Barrangou R. Using CRISPR-Cas systems in the development of novel antimicrobial therapeutics. Curr Opin Microbiol. 2017;37:155-160. doi:10.1016/j.mib.2017.08.005.
26. Ministry of Health and Family Welfare, Government of India. National guidelines for infection prevention and control in healthcare facilities. New Delhi: National Centre for Disease Control; 2020. Available from: https://ncdc.mohfw.gov.in/