

**EFFECTS OF BACTERIAL BIOFILMS ON RESISTANCE TO HOSPITAL
DISINFECTANTS: A LITERATURE REVIEW****EFEITOS DO BIOFILME BACTERIANO NA RESISTENCIA A DESINFETANTES
HOSPITALARES: REVISÃO DE LITERATURA****EFFECTOS DE LA BIOPELÍCULA BACTERIANA EN LA RESISTENCIA A LOS
DESINFECTANTES HOSPITALARIOS: UNA REVISIÓN BIBLIOGRÁFICA**Rafaela Marques dos Santos ¹, Luís Henrique Nunes de Souza ², Priscila Luiza Mello ³

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ABSTRACT

Introduction: Hospital-acquired infections are intensified by the formation of biofilms on surfaces and medical devices, making microbial elimination difficult. The effectiveness of disinfection depends on selecting the appropriate agent, its concentration, and the required exposure time. Objective: To review the literature on the impact of bacterial biofilm on resistance to hospital disinfectants, addressing biofilm formation, resistance mechanisms, and implications for infection control. Method: A narrative review of recent literature (2018–2024) was conducted in databases such as PubMed, SciELO, LILACS, and Google Scholar, using descriptors related to biofilms, hospital disinfectants, and microbial resistance. Results: Effective biofilm control requires integrating new technologies such as nanoparticles, enzymes, and UV-C light, which can overcome the protective structural barrier. Conclusion: Biofilms confer persistent resistance to disinfectants, making it essential to combine innovative technologies with strict adherence to manual protocols, supported by continuous staff training to ensure effective prevention of healthcare-associated infections.

KEYWORDS: Biofilms. Drug Resistance, Microbial. Infection Control. Disinfectants.**RESUMO**

Introdução: As infecções hospitalares são potencializadas pela formação de biofilmes em superfícies e dispositivos médicos, dificultando a eliminação microbiana. A eficácia da desinfecção depende da escolha adequada do agente, sua concentração e o tempo de exposição. Objetivo: Revisar a literatura sobre o impacto do biofilme bacteriano na resistência a desinfetantes hospitalares, abordando formação, mecanismos de resistência e implicações para o controle de infecções. Método: Realizou-se revisão narrativa da literatura recente (2018–2024)

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em bases como PubMed, SciELO, LILACS e Google Acadêmico, utilizando descritores relacionados a biofilmes, desinfetantes hospitalares e resistência microbiana. Resultados: O controle de biofilmes requer a integração de novas tecnologias, como nanopartículas, enzimas e luz UV-C, capazes de superar a barreira estrutural protetora. Conclusão: O biofilme confere resistência persistente aos desinfetantes, tornando essencial combinar tecnologias inovadoras e rigor na aplicação de protocolos manuais, com treinamento contínuo das equipes para garantir eficácia na prevenção de infecções relacionadas à assistência à saúde.

PALAVRAS-CHAVE: Biofilmes. Resistência Microbiana a Medicamentos. Controle de Infecções. Desinfetantes.

RESUMEN

Introducción: Las infecciones hospitalarias se agravan por la formación de biopelículas en superficies y dispositivos médicos, lo que dificulta la eliminación microbiana. La eficacia de la desinfección depende de la correcta selección del agente, su concentración y el tiempo de exposición. Objetivo: Revisar la literatura sobre el impacto de la biopelícula bacteriana en la resistencia a los desinfectantes hospitalarios, abordando su formación, los mecanismos de resistencia y las implicaciones para el control de infecciones. Método: Se realizó una revisión narrativa de la literatura reciente (2018–2024) en bases como PubMed, SciELO, LILACS y Google Acadêmico, utilizando descriptores relacionados con biopelículas, desinfectantes hospitalarios y resistencia microbiana. Resultados: El control efectivo de las biopelículas requiere integrar nuevas tecnologías, como nanopartículas, enzimas y luz UV-C, capaces de superar la barrera estructural protectora. Conclusión: La biopelícula confiere una resistencia persistente a los desinfectantes, lo que hace esencial combinar tecnologías innovadoras con rigurosidad en la aplicación de los protocolos manuales, junto con capacitación continua del personal para garantizar la prevención eficaz de infecciones asociadas a la atención en salud.

PALABRAS CLAVE: Biopelículas. Farmacorresistencia Microbiana. Control de Infecciones. Desinfectantes.

INTRODUCTION

Healthcare-associated infections (HAIs) constitute one of the major challenges in public health, as they directly impact patient safety and substantially increase hospital costs¹. This scenario results from multiple factors, including the frequent contact of healthcare workers and patients with invasive devices (such as catheters, tubes and mechanical ventilators), which favors the transfer of microorganisms; the ability of these agents to adhere to plastic and metallic surfaces, forming biofilms that are difficult to remove; recurrent failures in cleaning and disinfection processes; and the presence of multidrug-resistant strains selected by the intensive use of antimicrobials in hospitals. Together, these elements turn surfaces and medical devices into potential reservoirs of infection, demanding rigorous prevention and control practices².

Bacterial biofilms play a central role in this process. Defined as communities of microorganisms organized within an extracellular matrix and attached to living or inert surfaces,

biofilms confer increased resistance to adverse conditions, including the action of antimicrobials and disinfectants³⁻⁵. In hospital settings, they can form on catheters, prosthetic devices, surgical instruments and surfaces near patients, favoring the persistence and spread of multidrug-resistant pathogens⁶⁻⁸.

Biofilms are widely recognized as resilient and complex structures, capable of surviving in diverse habitats, including clinical environments⁴⁸. This organization provides important adaptive advantages, such as reduced susceptibility to phagocytosis, dehydration and the action of antibiotics and biocides^{10,11}. Consequently, biofilm-associated infections often require prolonged treatment, the use of high-dose drug combinations and, in severe cases, the replacement or removal of medical devices^{8,12}.

Within disinfection protocols, microorganisms embedded in biofilms exhibit low susceptibility to chemical, physical and biological agents. Studies have shown that their response to biocides usually follows a dose–response pattern, in which higher concentrations tend to be more effective^{13,14}. Even so, biofilms may maintain high tolerance to sanitizing agents under high-concentration conditions, as observed in *Salmonella* spp. and *Enterococcus faecalis* strains^{15,16}. Limitations of physical methods are also relevant: the poor penetration of ultraviolet (UV) radiation into the biofilm matrix reduces the effectiveness of automated disinfection systems¹⁷. In this context, alternative technologies have been investigated, such as violet–blue LED light, which has shown promising results in reducing contamination by methicillin-resistant *Staphylococcus aureus*¹⁸.

Another critical issue is the lack of a universally accepted definition of “disinfectant resistance”, which hinders the standardization of protocols and may limit the attention given to this problem by healthcare professionals and managers^{19,20}. This gap is particularly concerning in hospital environments, where microorganisms often persist on patient-proximal surfaces, organized in biofilms into which disinfectants cannot penetrate effectively^{21,22}.

Hospital-associated biofilms therefore represent a continuous source of multidrug-resistant pathogens, complicating the prevention and control of HAIs. The appropriate choice of disinfectant—among compounds such as quaternary ammonium compounds, alcohols, glutaraldehyde, hydrogen peroxide, peracetic acid, sodium hypochlorite, iodophors and phenolics—as well as the correct specification of parameters such as concentration and contact time, are crucial for the effectiveness of disinfection^{6,2}. In addition, innovative no-touch disinfection technologies have gained prominence as promising alternatives to reduce cross-contamination and enhance safety in healthcare environments^{12,18}.

In this context, understanding how bacterial biofilms interfere with the action of hospital disinfectants is essential to support the development of more effective protocols and to guide the adoption of new technologies in healthcare services..

MATERIALS AND METHODS

This was an expanded narrative review of the literature, conducted with the aim of identifying, describing and synthesizing the available scientific evidence on the effect of bacterial biofilms on resistance to disinfectants used in hospital environments. This design was chosen because it allows the integration of classic and recent studies, which is essential to understand both the conceptual basis and technological advances related to the topic.

The literature search was performed in the PubMed/MEDLINE, SciELO and LILACS databases. Initially, no time limit was applied, in order to include classic studies on biofilm formation, structure and resistance mechanisms. Subsequently, special emphasis was given to more recent publications (approximately 2018–2024), focusing on innovative technologies for control and disinfection in healthcare settings. Articles published in Portuguese, English and Spanish were considered.

In addition to the database search, the reference lists of selected articles were screened (snowballing strategy), which allowed the identification of additional relevant studies.

Original articles, literature reviews and classic experimental studies were included if they directly and specifically addressed: (1) the formation, structure and characteristics of the biofilm extracellular matrix; (2) the resistance of bacterial biofilms to hospital disinfectants (chemical and physical); and (3) technologies and strategies applied to biofilm control in healthcare environments. Theses, dissertations, editorials, letters to the editor, conference abstracts, non-peer reviewed documents and texts not available in full were excluded.

Potentially eligible studies were screened by reading titles and abstracts, followed by full text reading of those considered relevant to the topic. At the end of the process, 48 articles met the inclusion criteria. These studies were analyzed descriptively and critically with regard to their objectives, methodological design, context of application (experimental or clinical), main findings and implications for infection control practice. The synthesis of results sought to integrate structural and physiological aspects of biofilms, mechanisms of resistance to disinfectants and evidence on emerging technologies for their control in hospital environments.

RESULTS

The control of biofilms in hospital environments requires more advanced approaches than

the mere application of conventional disinfectants. The extracellular matrix that composes the biofilm functions as a protective barrier, reducing the penetration of biocides and allowing microorganisms to survive even after routine cleaning. In this scenario, new technological strategies and changes in cleaning practices have been implemented to increase the effectiveness of microbial control²³.

Among the alternatives with the strongest evidence, metallic nanoparticles such as silver and zinc oxide stand out. These particles are able to penetrate the biofilm, destabilize its structure and cause direct damage to the bacterial cell membrane. Studies have demonstrated a significant reduction in the biomass of biofilms formed by *Pseudomonas aeruginosa* and *Staphylococcus epidermidis*, including multidrug-resistant isolates^{23, 24}.

Another strategy involves the use of enzymes capable of degrading the biofilm extracellular matrix, such as Dispersin B, whose application promotes biofilm disruption and increases bacterial susceptibility to antibiotics and disinfectants^{25, 26}. Studies with biosurfactants, such as rhamnolipids, have also shown efficacy in reducing bacterial adhesion to surfaces and in promoting biofilm dispersion, representing a promising alternative for high-touch surfaces in hospitals^{27, 28}.

In addition to chemical and biological solutions, physical technologies have gained prominence. No-touch disinfection systems, especially UV-C and UV-LED light, have germicidal action through the disruption of microbial DNA or RNA. Studies have shown that the use of UV-C devices in hospital rooms significantly reduces microbial load on surfaces and complements manual cleaning, being effective even against multidrug-resistant microorganisms and *Clostridioides difficile*^{29, 30}. Systematic reviews reinforce that automated no-touch disinfection equipment decreases environmental contamination and the risk of hospital infections³¹.

Even with new technologies, the effectiveness of disinfection still depends on the quality of manual processes. Studies demonstrate that biofilms persist on hospital surfaces even after frequent cleaning, indicating that disinfectant alone is not sufficient to remove biofilm. Therefore, a combination of mechanical action (friction), appropriate selection of the chemical agent and adequate contact time is recommended to promote disruption of the physical barrier created by the biofilm^{32, 33}. These strategies, in turn, are only fully effective when associated with continuous education of healthcare professionals, since correct implementation of protocols depends on ongoing training. Studies in intensive care units show that operational failures are key determinants of microorganism persistence on surfaces, even after disinfection³³.

Table 1. Technologies and evidence for the control of biofilms in hospital environments

Cepa	Ativo	Evidência Clínica	Referências
<i>Pseudomonas aeruginosa</i>	Silver nanoparticles	Reduction of biofilm biomass and structural damage, including multidrug-resistant strains.	Rai et al.,2012 (23) Kalishwaralal et al.,2010 (24)
<i>Staphylococcus epidermidis</i>	Silver nanoparticles	Reduction in biofilm density and destabilization of the matrix.	Kalishwaralal et al.,2010 (24)
Various biofilm-forming strains	Dispersin B	Degradation of the extracellular matrix and increased susceptibility to disinfectants.	Kaplan, 2010: (25) Barraud et al., 2015 (26)
<i>S. aureus e S. epidermidis</i>	Biosurfactants (rhamnolipids)	Reduction of bacterial adhesion and biofilm dispersion.	Dusane et al., 2014 (27) Ceresa et al., 2020 (28)
Various microorganisms	UV-C / UV-LED light	Reduction of microbial load and complementary efficacy to manual cleaning.	Andersen et al., 2006 (29) Boyce et al., 2016 (30) Otter et al., 2013 (31)
Biofilms on ICU surfaces	Friction + appropriate chemical agent	Persistence associated with operational failures.	Ribeiro et al., 2019 (33)
Various environmental strains	Continuing education	Training reduces failures and minimizes persistence of biofilms.	Ribeiro et al., 2019 (33)

Source: The authors, 2025

DISCUSSION

BACTERIAL BIOFILM

Biofilm is a community of microorganisms, such as bacteria, capable of living and reproducing as an organized collective entity. In other words, biofilms represent a living biomass with a highly sophisticated social structure, which is still not fully understood by the scientific community. This structure serves both to protect and to enable the expansion of the microbial colony. It is known that there is a symbiotic relationship between prokaryotes and eukaryotes, or between unicellular and multicellular organisms, which is generally mutually beneficial³⁴.

The human body is composed of an extensive and complex microbiome, formed by bacteria, fungi and viruses. Most of this microbiota is located in the gastrointestinal tract, mucous membranes and skin, performing physiological functions that range from metabolism to innate

immunity. However, under certain conditions, uncontrolled growth of these symbiotic microorganisms may result in infections and subsequent biofilm formation³⁴. Throughout their evolution, bacteria have come to exist in two distinct states: the planktonic (free-living) state and the sessile state (adhered to surfaces). The transition between these states is essential for the establishment and persistence of biofilms, particularly in hospital environments and on medical devices³⁴.

The development of the three-dimensional biofilm architecture is a multistep process that involves initial adsorption, cell adhesion, microcolony formation, maturation and dispersion³⁵. Solid-liquid interfaces, such as moist surfaces in contact with blood, secretions or aqueous solutions, create an ideal environment for microbial attachment and growth. The dense association of cells within the biofilm favors the formation of nutrient gradients, genetic exchange and the phenomenon of quorum sensing (QS), which regulates bacterial communication and collective gene expression³⁵.

HOSPITAL DISINFECTANTS

Hospital disinfectants are indispensable tools for controlling pathogenic microorganisms in clinical and hospital environments. Their application aims to reduce microbial load on surfaces, instruments and critical areas, thereby preventing the spread of infectious agents and, consequently, healthcare-associated infections (HAIs)³⁶. Chemical compounds play an essential role in breaking the chain of transmission of resistant pathogens such as *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, which are frequently associated with hospital outbreaks. The main classes of disinfectants include ethyl or isopropyl alcohol, sodium hypochlorite, quaternary ammonium compounds, glutaraldehyde and hydrogen peroxide, each with specific mechanisms of action³⁶.

Alcohol acts by denaturing proteins and dissolving membrane lipids, being effective against vegetative bacteria but poorly active in the presence of organic matter and ineffective against spores. Sodium hypochlorite, widely used because of its cost-effectiveness, acts by oxidizing cellular components and inactivating enzymes, and has a broad spectrum of activity against viruses, fungi and bacteria, although it is unstable when exposed to light and heat. Quaternary ammonium compounds are cationic surfactants that impair cytoplasmic membrane permeability, leading to cell lysis; however, their effectiveness can be reduced in the presence of soaps and anionic detergents³⁶. Glutaraldehyde is a potent alkylating agent capable of destabilizing proteins and nucleic acids, and is indicated for high-level disinfection of

heat-sensitive instruments. Hydrogen peroxide acts through the release of hydroxyl radicals (OH·), which attack membranes, DNA and other vital cellular components, showing excellent performance against spore-forming bacteria and multidrug-resistant microorganisms^{36, 37}.

New formulations have been investigated, including peracetic acid-based compounds, metallic nanoparticles and enzymatic combinations, which aim to enhance antimicrobial efficiency and reduce the environmental impact of conventional disinfectants³⁸. These agents have advantages such as maintaining activity even in the presence of organic matter and biofilms, and reducing the need for high concentrations of toxic products. However, one of the main challenges faced in hospital environments is the reduced effectiveness of these disinfectants in the presence of biofilms. The polymeric extracellular matrix of biofilms acts as a diffusion barrier, hindering the penetration of active substances and allowing the survival of bacteria within the colonies^{34, 37}.

Studies have shown that microorganisms in biofilm may exhibit up to a thousand-fold greater resistance to disinfectants compared to planktonic cells, which highlights the need for combined cleaning protocols, rotational use of agents and the incorporation of complementary technologies such as ozonation, ultraviolet radiation and antimicrobial nanoparticles^{38, 39}. Thus, although disinfectants remain an essential tool for microbiological control, their isolated use is insufficient in environments with established biofilms, reinforcing the importance of integrating physical cleaning, chemical control and continuous staff training^{38, 39}.

EFFECTS OF BIOFILM ON RESISTANCE

Bacterial biofilm is recognized as one of the main factors contributing to microbial resistance to disinfectants and antimicrobials. This resistance is not limited to the presence of specific genes, but results from a combination of physical, chemical and physiological barriers that hinder the penetration and action of biocidal agents^{40, 41} (Figure 1).

The polymeric extracellular matrix (EPS), composed mainly of polysaccharides, proteins and extracellular DNA, functions as a protective shield that retains and neutralizes part of the disinfectants, significantly reducing their effective concentration within the biofilm⁴². As a result, the penetration of active substances is delayed, allowing deeper bacteria to survive even after prolonged exposure to potent biocides. In addition to this physical barrier, the biofilm creates a heterogeneous microenvironment characterized by gradients of oxygen, pH and nutrients. This uneven environment results in different levels of metabolic activity among cells, giving rise to bacterial subpopulations in a dormant or low-metabolism state, which are less susceptible to disinfectants that depend on active cellular processes^{37, 43}.

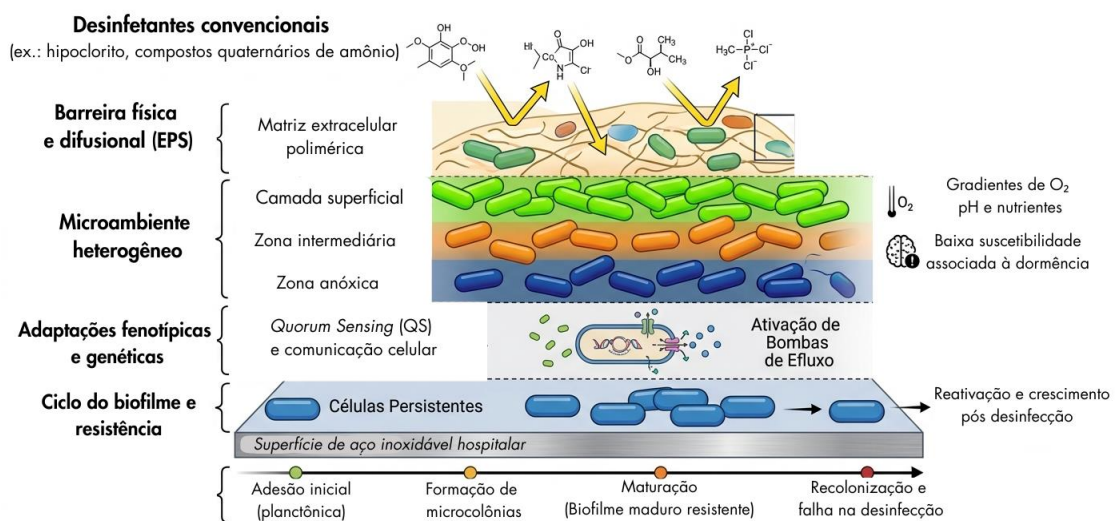
Another crucial factor is phenotypic and genetic adaptation mediated by intercellular communication systems such as quorum sensing (QS). This mechanism regulates the expression of genes related to extracellular matrix production, the synthesis of neutralizing enzymes (such as catalases and peroxidases) and the activation of efflux pumps that expel toxic compounds from the cell interior. Such adaptations make the biofilm a cooperative and highly resilient environment, capable of withstanding multiple antimicrobial agents^{41, 44}.

Cells within biofilms can also give rise to persister cells, a subpopulation that is metabolically inactive and highly tolerant to adverse conditions. Even after disinfection, these cells survive and, when the environment becomes favorable again, resume bacterial growth, facilitating recolonization of the surface and re-establishment of the biofilm^{39, 43}. Planktonic cells, in turn, are those that live in suspension and are not attached to surfaces, and are more vulnerable because they lack the structural and metabolic defenses provided by the biofilm. Therefore, the presence of biofilms in hospital environments represents a constant challenge, hindering microbial eradication and increasing the likelihood of persistent and recurrent infections^{39, 44}.

The effects of biofilm on resistance go far beyond simple chemical tolerance: they involve a set of coordinated mechanisms of protection, communication and survival. This complexity explains why conventional disinfection, although effective at a superficial level, is often unable to completely eliminate microorganisms protected by the biofilm matrix, making it necessary to use new technologies and combined control strategies^{39-41, 44}.

Figure 1. Mechanisms by which biofilm reduces the effectiveness of hospital disinfectants.

Source:



Source: image generated by AI (Nano Banana 2), with modifications by the author (2025).

CLINICAL AND EPIDEMIOLOGICAL IMPLICATIONS

The presence of biofilms in hospital environments represents a critical challenge for infection control. Bacteria within biofilms show drastically reduced susceptibility to disinfectants when compared to the same bacteria in the planktonic state. Studies show that clinical strains exhibit lower susceptibility to disinfectants than reference strains, revealing a higher resistance pattern among hospital isolates⁴⁵. In addition to the low efficacy of disinfectants, the situation is worsened by the fact that many of these biofilm-producing bacteria are also multidrug resistant to antibiotics⁴⁵. The literature demonstrates that biofilms increase antimicrobial resistance through mechanisms such as delayed penetration of the chemical agent and alterations in cellular metabolism⁴⁶.

Healthcare-associated infections (HAIs) are the most frequent adverse events in hospitals and are strongly related to the persistence of microorganisms on critical surfaces. Studies report that the presence of multidrug-resistant agents in intensive care units (ICUs) is associated with increased mortality, prolonged hospital stays, and higher costs for the healthcare system⁴⁷. The scenario becomes even more concerning when environmental contamination is analyzed: in ICUs, biofilms have been identified on 100% of high-touch surfaces, and the proportion of contaminated surfaces remained unchanged even with cleaning performed twice daily⁴⁸. Furthermore, biofilm-associated bacteria can be 100 to 250 times more resistant to biocides compared to planktonic cells⁴⁶.

This resistance is directly related to the extracellular matrix of the biofilm, composed of extracellular polymeric substances (EPS), which form a heterogeneous barrier that hinders both mechanical removal and the penetration of chemical agents. Biofilms in hospitals promote the persistence of pathogenic bacteria, fuel HAI outbreaks, and limit the effectiveness of cleaning and disinfection. In critical environments such as ICUs, biofilm turns seemingly "clean" surfaces into invisible reservoirs of high-risk microorganisms⁴⁸.

CONSIDERATIONS

This expanded narrative review showed that the extracellular matrix of bacterial biofilms confers significant and multifactorial resistance to disinfectants used in hospital settings, limiting the effectiveness of routine hygiene procedures and maintaining a persistent risk for healthcare-associated infections (HAIs). The three-dimensional organization of the biofilm, combined with the formation of heterogeneous microenvironments, the presence of persister cells, and the

activation of bacterial defense mechanisms, makes biofilm-associated microorganisms substantially less susceptible to the action of biocides when compared with planktonic cells.

Evidence from the literature indicates the need for an integrated approach capable of bringing together innovative technologies, such as metallic nanoparticles, depolymerizing enzymes, biosurfactants, and UV-C disinfection systems, which act directly on the structure and resistance mechanisms of the biofilm. However, the success of these technologies depends decisively on the quality of operational processes. Effective biofilm control requires a combination of adequate mechanical action, correct selection of the chemical agent, appropriate contact time, and strict adherence to cleaning and disinfection protocols.

Furthermore, continuous training of healthcare teams is an indispensable element to ensure the consistent application of these strategies in daily practice. Integrating technological innovation with operational excellence and ongoing education constitutes the most promising strategy to reduce the persistence of biofilms in hospital environments and to strengthen patient safety in healthcare services.

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