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The Association of Intracameral Bacteriophage Administration with Tumor Necrosis Factor Alpha (TNF-α) Expression and Bacterial Viability as a Prophylactic Strategy Against *Staphylococcus aureus*-Induced Endophthalmitis Following Lens Extraction Surgery : A Literature Review

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ABSTRACT
Postoperative infections remain a critical concern following lens extraction procedures, often linked to the presence of *Staphylococcus aureus*. Conventional antibiotic treatments are increasingly challenged by the rise of resistant bacterial strains. This literature review explores the therapeutic potential of *Staphylococcus aureus*-specific bacteriophages in modulating immune response—particularly the expression of Tumor Necrosis Factor-α (TNF-α)—and reducing bacterial viability in ocular surgical contexts. Drawing from a range of peer-reviewed sources, the review examines the dual role of bacteriophages as antimicrobial agents and as modulators of inflammation. Evidence suggests that phage therapy may suppress *Staphylococcus aureus* viability while attenuating pro-inflammatory cytokine production, potentially improving clinical outcomes and minimizing reliance on antibiotics. These findings underscore the need for further in vivo studies and clinical trials to validate phage application as a safe and effective adjunct in ophthalmic surgery.

Keywords: *bacteriophage therapy, Staphylococcus aureus, TNF-α, bacterial viability, lens extraction*

1. INTRODUCTION

Infections occurring after lens extraction represent a serious ocular complication that threatens vision and can lead to permanent damage if not treated promptly and effectively. These infections generally result from microbial contamination by bacteria or fungi and are frequently linked to intraocular surgical procedures, such as cataract surgery. Post-lens extraction infections can develop into endophthalmitis, specifically referred to as postoperative endophthalmitis. This condition is categorized into acute and chronic forms, with chronic cases usually emerging more than six weeks after the surgical intervention. The reported incidence of postoperative endophthalmitis following cataract surgery varies internationally, ranging from 0.025% to 0.136%, with consistent documentation from countries including the United States, France, South Korea, Poland, and Indonesia (Table 1).[1,2]

Table 1. Incidence of Postoperative Endophthalmitis Following Cataract Surgery: Global Data

Source	Incidence
Global Incidence Range	0.025% – 0.136% after cataract surgery
US IRIS Registry (2013–2017)	0.04% within 30 days post-cataract surgery
France / South Korea / Poland	~0.05% incidence

The majority of endophthalmitis cases are caused by gram-positive bacteria, accounting for over 85% of infections, with gram-negative bacteria and fungi comprising smaller proportions. Coagulase-negative Staphylococci are the most frequently isolated pathogens in postoperative cases, followed by *Staphylococcus aureus*, Streptococcus species, Staphylococcus epidermidis, and Enterococcus species. *Staphylococcus aureus* is particularly virulent due to its ability to trigger strong inflammatory responses through its cell wall components and secreted toxins, including toxic shock syndrome toxin-1 (TSST-1) and alpha-toxin. These bacterial factors interact with retinal toll-like receptors (TLRs), promoting cytokine release, immune cell recruitment, and tissue damage, which exacerbate disease severity.[3,4,5]

Cytokines are critical mediators of the immune response in endophthalmitis, acting as signaling molecules that regulate inflammation and immune cell trafficking. Among these, Tumor Necrosis Factor-alpha (TNF-α) plays a central role by enhancing vascular endothelial adhesion and stimulating the production of other proinflammatory cytokines such as interleukin-1 (IL-1) and interleukin-6 (IL-6). Elevated TNF-α levels correlate with disruption of the blood-retina barrier and neutrophil infiltration, leading to increased inflammation and tissue injury. Experimental studies have shown that bacteriophage therapy, specifically with EF24C-P2 phage, can reduce TNF-α expression in bacterial lipopolysaccharide-stimulated cells, demonstrating therapeutic effects comparable to vancomycin.[6]

Assessing bacterial viability is essential for monitoring infection progression and the efficacy of treatments in endophthalmitis. Conventional culture techniques remain standard; however, bacteriophage therapy has emerged as a promising alternative. Bacteriophages are viruses that selectively infect and lyse bacterial cells, and their intracameral administration has shown potential in animal models by suppressing bacterial growth, reducing immune cell infiltration, and preserving retinal function. Additionally, phage therapy has been successfully applied in ocular surface infections, such as corneal abscesses caused by *Staphylococcus aureus*, supporting its expanding role in ophthalmic infections. This literature review aims to explore the impact of intracameral bacteriophage administration on TNF-α expression and bacterial viability, highlighting its potential as a novel therapeutic strategy for managing endophthalmitis.[6]

2. LENS EXTRACTION SURGERY

Lens extraction surgery, particularly extracapsular cataract extraction (ECCE), remains one of the most commonly performed ophthalmic procedures worldwide to treat cataracts. Despite advances in surgical techniques and postoperative care, postoperative infections, especially endophthalmitis, continue to pose significant challenges. ECCE involves removing the lens while leaving the posterior capsule intact, but the procedure still carries a risk of bacterial contamination, primarily from the ocular surface flora, which can lead to severe intraocular infections. Studies have shown that the anterior chamber contamination rates during ECCE are comparable to those in phacoemulsification, though some data suggest a slightly higher contamination risk with ECCE due to the larger incision and more extensive manipulation involved.[7,8,9]

The likelihood of bacteria causing infection during extracapsular cataract extraction (ECCE) depends on several factors, including the condition of the posterior lens capsule and the pathogenicity of the introduced microbes. Research using experimental models has shown that an intact posterior capsule serves as a crucial defense, preventing the infection from reaching the vitreous chamber and thereby greatly lowering the chances of developing bacterial endophthalmitis. Conversely, a compromised posterior capsule can allow even minimal bacterial contamination to result in serious intraocular infections. Frequent bacterial culprits include coagulase-negative staphylococci and species of *Propionibacterium*, both of which are capable of triggering acute or persistent postoperative inflammation. In particular, infections caused by *Propionibacterium acnes* may not become apparent until months after surgery and often necessitate both antibiotic treatment and additional surgical procedures.[10]

Although phacoemulsification has largely replaced extracapsular cataract extraction (ECCE), the risk of postoperative endophthalmitis persists. Factors such as the intraocular lens (IOL) material and structural design significantly affect the likelihood of bacterial colonization. Research indicates that IOLs with polypropylene haptics exhibit greater susceptibility to microbial contamination compared to those made with polymethylmethacrylate haptics. The patient's own ocular surface flora continues to be the predominant source of infectious agents, and contamination during surgery may still occur despite strict adherence to sterile protocols. Furthermore, the emergence of antibiotic-resistant organisms—such as Escherichia coli strains that produce extended-spectrum beta-lactamases (ESBLs)—poses additional treatment challenges and can negatively

impact patient outcomes. These observations underscore the importance of stringent infection prevention strategies, precise surgical execution, and thoughtful selection of IOL materials to reduce the incidence of postoperative infections.[7,9,11]

The incidence of *S. aureus* infections following surgery remains substantial. A retrospective study analyzing elective surgeries in the United States reported a 180-day cumulative incidence of *S. aureus* infections of approximately 1.2–1.35%, including bloodstream infections and surgical site infections, with nearly half of these infections exhibiting methicillin resistance. This high burden of *S. aureus* infections after elective procedures highlights ongoing challenges in infection control and the critical need for enhanced surveillance and novel preventive measures in surgical settings, including ophthalmic surgeries like lens extraction.[13]

Staphylococcus aureus poses a serious threat in postoperative infections following lens extraction due to its ability to trigger severe systemic conditions such as bacteremia and secondary metastatic infections. The occurrence of *Staphylococcus aureus* bacteremia after surgery is associated with considerable rates of illness and death, often advancing to critical complications like infective endocarditis and mediastinitis, especially in surgical patients. Managing these outcomes requires thorough diagnostic efforts and prompt, intensive treatment strategies. The aggressive and invasive behavior of *Staphylococcus aureus* in post-surgical contexts highlights the need for a comprehensive understanding of its epidemiology and virulence to enhance clinical outcomes and patient care.[7,12]

Effective prevention of postoperative *Staphylococcus aureus* infections relies heavily on early identification and prompt intervention. Strategies such as thorough preoperative screening, nasal decolonization using topical agents like mupirocin, and strict adherence to perioperative infection control protocols have proven successful in decreasing infection rates. Nonetheless, *S. aureus* continues to pose a significant clinical burden, highlighting the need for continuous monitoring and the innovation of new preventive and therapeutic methods aimed at enhancing surgical outcomes and minimizing postoperative mortality.[12,13,14]

3. POSTOPERATIVE ENDOPHTHALMITIS

Postoperative endophthalmitis is a severe infection inside the eye that typically arises within a few days to weeks after ocular surgeries, particularly cataract removal. This condition is mainly the result of microbial contamination during surgery, with common culprits including *Staphylococcus epidermidis* and various gram-negative bacteria originating from the ocular surface or surrounding environment. Patients often present with symptoms such as blurred vision, eye pain, redness, sensitivity to light, and occasionally discharge. A characteristic clinical finding is hypopyon—an accumulation of inflammatory cells in the anterior chamber—seen in roughly 70–80% of cases. Clinical examination may reveal conjunctival redness, inflammation within the anterior chamber (cells and flare), vitreous opacities that hinder the view of the retina, and sometimes retinal bleeding or vessel inflammation. The infection can advance quickly within the vitreous body, making early diagnosis and treatment vital to prevent lasting vision damage. It is important to distinguish this condition from other postoperative issues like toxic anterior segment syndrome, as the treatment approaches differ.[17-21]

The standard approach to treating acute postoperative endophthalmitis involves administering broad-spectrum antibiotics directly into the vitreous cavity, with pars plana vitrectomy (PPV) typically reserved for more advanced or severe presentations. Findings from the pivotal Endophthalmitis Vitrectomy Study (EVS) revealed that performing an early vitrectomy can lead to better visual recovery in patients whose vision is limited to light perception at the time of diagnosis, primarily by decreasing the burden of infection and intraocular inflammation. In contrast, individuals presenting with higher baseline visual acuity may not benefit from immediate surgical intervention.[22] Nonetheless, emerging clinical concerns involve the increasing prevalence of bacterial strains resistant to multiple antibiotics, along with pathogens that can form biofilms or survive within host cells. These characteristics reduce the effectiveness of antimicrobial agents by limiting their penetration, thereby increasing the risk of therapeutic failure.[23] Recent improvements in vitrectomy methods and the availability of supportive therapies have made it possible to adopt a more proactive surgical approach early in the disease course for certain patients, aiming to enhance outcomes even in the face of these ongoing challenges.[24,25]

Bacteriophage therapy has gained renewed attention as a viable alternative to conventional antibiotics, particularly in addressing infections caused by multidrug-resistant (MDR) bacteria. These viruses, known as bacteriophages or phages, selectively target and destroy bacterial cells while sparing human tissues and beneficial microbial communities, making them a precise tool for eliminating pathogenic bacteria, including resistant strains. Due to their specificity, phages minimize unintended effects and preserve the normal microbiota, in contrast to the broad activity of traditional antibiotics. Notably, phages are capable of penetrating biofilms and intracellular environments—areas where bacteria often evade antibiotics—making them effective against chronic and refractory infections. Additionally, phages can work in tandem with antibiotics by enhancing bacterial susceptibility and reducing the required antibiotic dose, thereby improving therapeutic outcomes. Although obstacles such as phage resistance and regulatory complexities remain, progress in phage customization and individualized treatment strategies offers considerable promise for tackling antibiotic resistance and advancing infection control.[26-28]

Staphylococcus aureus

Staphylococcus aureus is a Gram-positive microorganism and a major contributor to a wide range of human infections, from superficial skin conditions to life-threatening illnesses such as septicemia, pneumonia, and infective endocarditis. It is a common component of the human microbiota, colonizing sites like the skin, nasal cavity, and gastrointestinal tract in roughly 30% of individuals without causing symptoms. However, when physical or immune barriers are compromised—as can occur during invasive medical procedures such as lens extraction surgery— *Staphylococcus aureus* may transition from a harmless colonizer to a pathogenic agent. In the context of ocular procedures, this bacterium can enter the eye intraoperatively or postoperatively, leading to severe complications like acute postoperative endophthalmitis.[29-33]

The virulence of *Staphylococcus aureus* stems from its production of various pathogenic factors, including coagulases, cytotoxins such as alpha-hemolysin and Panton-Valentine leukocidin, and surface proteins that enhance its ability to adhere to host tissues and evade immune detection. These mechanisms are especially problematic in surgical settings. During lens extraction procedures, such as cataract surgery, if *Staphylococcus aureus* contaminates the surgical field or intraocular lens, it can quickly establish infection due to its capacity to resist immune clearance and form biofilms on artificial surfaces. Biofilms are particularly concerning in ophthalmology because they can form on intraocular lenses or surgical instruments, making the infection more difficult to eradicate with standard antibiotic therapy. [29,30,32]

The emergence of methicillin-resistant Staphylococcus aureus (MRSA) has significantly complicated infection control in both community and hospital settings, particularly impacting ocular surgeries such as lens extraction. MRSA can cause aggressive endophthalmitis, a severe intraocular infection resistant to conventional antibiotics, leading to poor visual outcomes or permanent vision loss. Despite improvements in surgical techniques and sterilization, MRSA remains a notable cause of postoperative morbidity, with bloodstream infections serving as a source for endogenous endophthalmitis. Early diagnosis and prompt treatment with systemic and intravitreal antibiotics are critical to preserving vision, although outcomes remain guarded due to the organism's virulence and resistance profile. Current research is investigating alternative strategies including bacteriophage therapy, nanotechnology-based drug delivery, and vaccine development to better manage resistant MRSA strains and improve treatment efficacy following intraocular procedures. Tailored antimicrobial approaches and early intervention are essential to prevent serious complications in patients undergoing lens extraction surgery. [34-37]

TNF-α

Tumor necrosis factor-alpha (TNF-α) is a multifunctional pro-inflammatory cytokine that plays a pivotal role in immune modulation and the inflammatory response under both normal and pathological conditions. This cytokine is predominantly synthesized by activated macrophages, T-cells, and natural killer cells and exists in two biologically active forms: a membrane-bound version and a soluble variant produced through enzymatic cleavage by TNF-α-converting enzyme (TACE). Upon binding to its primary receptors, TNFR1 and TNFR2, TNF-α initiates a broad spectrum of intracellular pathways that influence key cellular functions, including survival, proliferation, differentiation, programmed cell death, and necrosis. In ocular surgery, particularly lens extraction procedures, the presence and activity of TNF-α become critically relevant due to its ability to influence intraocular inflammation and postoperative tissue responses.[38-40]

Although TNF-α is essential for maintaining immune defense and tissue equilibrium, dysregulated production or sustained activation can contribute to the pathophysiology of numerous inflammatory and autoimmune diseases, such as rheumatoid arthritis and inflammatory bowel disease. In the context of ophthalmic surgery, excessive TNF-α activity can exacerbate postoperative inflammation and potentially compromise visual recovery. [38,41] During lens extraction surgery, surgical trauma and microbial contamination, such as from *Staphylococcus aureus*, may trigger a local increase in TNF-α levels, intensifying the inflammatory response. This heightened cytokine activity is particularly problematic in cases of postoperative endophthalmitis, where an exaggerated immune reaction can damage ocular tissues, highlighting the importance of modulating TNF-α to preserve visual function and reduce complications.[40]

TNF-α, a key molecule in the inflammatory response, has been identified as a pathological component of autoimmune diseases, leading to the development of TNF-α inhibitors for therapeutic use.[38,42] In the eye, TNF-α is secreted by activated macrophages, astrocytes, and microglial cells in response to intraocular stress and can cause retinal cell apoptosis.[43,44] Studies suggest that inhibiting TNF-α could protect against blood vessel formation after ocular trauma and may have a beneficial effect on non-infectious ocular inflammation.[42,45]

Role of *Staphylococcus aureus* in Endophthalmitis Pathogenesis

Staphylococcus aureus plays a critical role in the pathogenesis of endophthalmitis, a severe intraocular infection that can lead to rapid vision loss or even blindness if not promptly treated. *Staphylococcus aureus* possesses a variety of virulence factors, including toxins and surface proteins, that enable it to invade ocular tissues, evade host defenses, and induce significant inflammation. The infection can occur exogenously, often following ocular surgery or trauma, or endogenously via hematogenous spread from distant infection sites, such as in cases of bacteremia or mastitis.[46-48] Once inside the eye, *Staphylococcus aureus* triggers a robust immune response characterized by the recruitment of neutrophils and the release of pro-inflammatory cytokines, including tumor necrosis factor alpha (TNF-α). TNF-α is a key mediator in the inflammatory

cascade, orchestrating leukocyte infiltration and amplifying the local immune response to contain the infection. However, excessive or dysregulated TNF-α production can exacerbate tissue damage, contributing to the destruction of retinal cells and loss of visual function.[46,49,50] Experimental models have shown that the inflammatory response, driven in part by TNF-α and chemokines such as CCL2 and CCL3, is a double-edged sword: while it helps reduce bacterial load, it also leads to collateral damage of ocular tissues, influencing the severity of visual impairment. Clinical outcomes in *Staphylococcus aureus* endophthalmitis are closely linked to the balance between effective pathogen clearance and the containment of damaging inflammation, with therapeutic strategies often combining antibiotics, corticosteroids, and sometimes surgical intervention to optimize this balance.[49,50]

Staphylococcus aureus is recognized as a major etiological agent of endophthalmitis, a severe intraocular infection that can rapidly progress to vision loss or permanent blindness if not managed promptly. The bacterium's involvement in endophthalmitis is well-documented in both clinical and experimental studies, with *Staphylococcus aureus* being frequently isolated from culture-positive cases, particularly following ocular surgery or trauma.[51,52,54] In a retrospective study, *S. aureus* accounted for over half of endogenous bacterial endophthalmitis cases, with methicillin-resistant strains (MRSA) representing a significant proportion, underscoring the clinical challenge posed by antimicrobial resistance.[54] The rapid onset and aggressive progression of *S. aureus* endophthalmitis highlight the importance of early diagnosis and intervention to prevent irreversible ocular damage and optimize visual outcomes.[51,52]

The pathogenesis of *S. aureus* endophthalmitis is driven by the bacterium's arsenal of virulence factors, including surface adhesins and exotoxins, which enable it to adhere to and penetrate ocular tissues, evade immune responses, and incite robust inflammation. Surface adhesins facilitate attachment to host extracellular matrix components, while secreted toxins such as hemolysins and leukocidins disrupt cellular barriers and promote tissue destruction. Experimental models have demonstrated that both live and heat-inactivated *S. aureus* can induce intraocular inflammation, but the severity and nature of the host response are modulated by specific virulence determinants, indicating a complex interplay between bacterial factors and host immunity. This complexity suggests that neutralizing a single virulence factor may not suffice for effective prevention or treatment, necessitating multifaceted therapeutic strategies.[56]

The host's innate immune response to *Staphylococcus aureus* within the eye is characterized by the rapid recruitment of neutrophils and the production of pro-inflammatory cytokines and chemokines, such as CXCL1, CXCL2, and CXCL10.[53,57] Recent studies using mouse models have shown that CXCL1, in particular, contributes to the early inflammatory response, although its inhibition did not significantly reduce inflammation or improve retinal function in the acute phase.[53] Transcriptomic analyses of infected retinas reveal widespread changes in gene expression, with key inflammatory pathways-including JAK/STAT and IL-17A signaling-being highly activated. These findings underscore the dual-edged nature of the immune response: while essential for bacterial clearance, excessive or dysregulated inflammation can exacerbate retinal damage and worsen visual prognosis.[57]

Staphylococcus aureus endophthalmitis can arise through both exogenous and endogenous routes. Exogenous infections typically follow intraocular procedures, such as cataract surgery or intravitreal injections, or result from penetrating ocular trauma.[51,52] In contrast, endogenous endophthalmitis occurs via hematogenous dissemination from distant infection sites, such as skin abscesses, mastitis, or bacteremia, particularly in immunocompromised individuals or those with underlying systemic illness.[52,54] The clinical presentation and prognosis may vary depending on the route of infection, with endogenous cases often presenting later and being associated with poorer visual outcomes due to delayed diagnosis and more extensive intraocular involvement.[54]

Treatment of *Staphylococcus aureus* endophthalmitis involves a combination of intravitreal antibiotics-commonly vancomycin or daptomycin for MRSA-and, in many cases, surgical intervention such as vitrectomy to remove infectious material and inflammatory debris.[51,55] Adjunctive use of intraocular corticosteroids has been associated with improved visual outcomes in some studies, likely due to their ability to modulate damaging inflammation without compromising bacterial clearance.[51] Despite advances in antimicrobial therapy, the emergence of resistant strains and the potential for rapid, irreversible retinal injury make *Staphylococcus aureus* endophthalmitis a persistent clinical challenge, emphasizing the need for continued research into both preventive strategies and novel therapeutic approaches targeting the intricate host-pathogen interactions within the eye.[54,55,57]

Bacteriophage Therapy: Mechanism and Advantages

Bacteriophage therapy harnesses viruses known as bacteriophages that specifically infect and lyse bacterial cells, offering a targeted approach to combat bacterial infections. The primary mechanism involves phages attaching to specific receptors on the bacterial surface, injecting their genetic material, and commandeering the bacterial machinery to produce progeny phages. This process culminates in bacterial cell lysis, releasing new phages to infect adjacent bacteria. Unlike antibiotics, phages have a unique mode of action that can effectively kill bacteria regardless of their antibiotic resistance status, making them particularly valuable against multidrug-resistant (MDR) pathogens.[58,59]

One significant advantage of bacteriophage therapy is its high specificity. Phages typically target a narrow range of bacterial

species or even specific strains, which minimizes collateral damage to the host's beneficial microbiota. This contrasts with broad-spectrum antibiotics that often disrupt the entire microbial community, potentially leading to dysbiosis and secondary infections. Studies have shown that phage therapy preserves the gut microbiome integrity while effectively reducing pathogenic bacteria, thereby maintaining overall microbial balance and reducing side effects.[60]

Another key benefit is the ability of phages to penetrate and disrupt bacterial biofilms, which are complex communities of bacteria embedded in a protective extracellular matrix. Biofilms are notoriously resistant to antibiotics and immune clearance, contributing to chronic and recurrent infections. Phages can produce enzymes that degrade biofilm components and infect bacteria within these structures, enhancing bacterial eradication where antibiotics often fail. Furthermore, genetic engineering techniques allow modification of phages to express biofilm-degrading enzymes or other antibacterial molecules, broadening their therapeutic potential and overcoming bacterial defense mechanisms.[26]

Phage therapy also offers adaptability through the use of phage cocktails and personalized treatments. Combining multiple phages targeting different bacterial receptors reduces the likelihood of bacterial resistance development. Personalized phage therapy involves isolating the causative bacterial strain from a patient and selecting or engineering phages specifically active against it, optimizing treatment efficacy. This tailored approach, although more costly and complex, has shown promising results in difficult-to-treat infections and can be combined synergistically with antibiotics to improve outcomes.[26,59]

TNF-α, Bacterial Viability, and Inflammation Control

TNF-α, bacterial viability and inflammation control are tightly interconnected processes that significantly influence the outcome of infections. Recent studies have elucidated how immune cells, particularly B-cells and macrophages, modulate bacterial survival through inflammatory signaling. For instance, Salmonella can persist within B-cells by evading inflammasome activation, which prevents pyroptotic cell death and allows chronic infection. However, when B-cells are primed with pro-inflammatory cytokines such as TNF-α, IL-1β, or IFN-γ, they enhance their bactericidal capacity by increasing reactive oxygen and nitrogen species production, thereby reducing intracellular bacterial load. This highlights the critical role of a pro-inflammatory microenvironment in controlling bacterial viability within immune cells.[61]

The balance between pro-inflammatory and anti-inflammatory responses is crucial for effective infection control without excessive tissue damage. While pro-inflammatory cytokines activate antimicrobial mechanisms, concurrent production of anti-inflammatory cytokines like IL-10 can modulate and potentially dampen the immune response. This dual cytokine milieu may prevent hyperinflammation but also risks allowing bacterial persistence. Therefore, understanding the regulatory dynamics between these opposing cytokine signals is essential for developing strategies that optimize bacterial clearance while minimizing immunopathology.[61]

Antibiotic treatment further complicates inflammation control due to differential immune responses elicited by bactericidal versus bacteriostatic drugs. Recent research demonstrates that bactericidal antibiotics, which kill bacteria outright, induce higher levels of pro-inflammatory cytokines such as TNFα compared to bacteriostatic agents that inhibit bacterial growth without killing. This heightened inflammatory response is linked to the release of bacterial DNA upon cell lysis, which activates Toll-like receptor 9 (TLR9) signaling in macrophages, exacerbating inflammation. In contrast, bacteriostatic treatments provoke a more controlled immune response, which may improve survival outcomes by preventing excessive inflammation-driven tissue damage.[62]

The inflammatory response to bacterial viability also involves biofilm formation and bacterial metabolic states that influence immune recognition and clearance. Biofilms protect bacteria from immune effectors and antibiotics, contributing to chronic infections. Immune cells must therefore overcome biofilm-mediated tolerance through both direct antimicrobial activity and modulation of inflammation. Immunometabolic pathways are increasingly recognized as key regulators in this context, where metabolic shifts in immune cells influence their capacity to produce inflammatory mediators and reactive species that affect bacterial viability and biofilm disruption.[63]

Probiotics and gut microbiota modulation represent additional avenues to control bacterial viability and inflammation. Beneficial bacteria can enhance mucosal immunity and restore immune homeostasis by producing anti-inflammatory metabolites and competing with pathogenic bacteria. This approach has shown promise in inflammatory bowel disease and other conditions characterized by dysregulated inflammation and bacterial overgrowth. The interplay between probiotics, bacterial viability, and host inflammation underscores the potential of microbiome-based therapies to fine-tune immune responses and promote infection resolution without excessive inflammation.[64,65]

4. CONCLUSION

This literature review indicates that the potential of intracameral bacteriophage administration as an emerging prophylactic approach to prevent *Staphylococcus aureus*-induced endophthalmitis following lens extraction surgery. The reviewed studies suggest that bacteriophage therapy may reduce bacterial viability within the intraocular environment, potentially mitigating the severity of infection. Additionally, evidence from the literature suggests that bacteriophage administration may modulate host immune responses, including levels of Tumor Necrosis Factor-α (TNF-α), a key cytokine involved in ocular

inflammation. While preliminary findings are encouraging, further standardized in vivo and clinical studies are required to establish the optimal dosage, safety profile, and immunological impact of intracameral bacteriophage use in ophthalmic surgery.

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