AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 05. MAY ,2026

# PATHOGENETIC MECHANISMS OF STAPHYLOCOCCUS AUREUS IN THE DEVELOPMENT OF BACTERIAL CONJUNCTIVITIS

**Dilafruz Sh. Gulmurotova,**

**Zahro A. Adhamjonova,**

**Dilroz I. Abdumo'minova**

Assistant at the Department of Microbiology, virology and immunology of Tashkent State Medical University, Tashkent, Uzbekistan

E-mail: dilafruzgulmurotova82@gmail.com

Student of Tashkent State Medical University, 2nd Faculty of General Medicine, Group 212A, Tashkent, Uzbekistan

E-mail: zaxroadhamjonova@gmail.com

Student of Tashkent State Medical University, 2nd Faculty of General Medicine, Group 216A, Tashkent, Uzbekistan

F-mail: dilrozabdumominova@gmail.com

https://doi.org/10.5281/zenodo.20178614

**Abstract.** Bacterial conjunctivitis occupies a significant place among infectious diseases of the anterior segment of the eye, and within its etiological spectrum, Staphylococcus aureus is recognized as a particularly relevant pathogen, especially in adults, elderly individuals, and patients with compromised ocular surface defense mechanisms. Contemporary literature indicates that the pathogenicity of this microorganism is not limited to superficial colonization but is mediated through a complex, multi-component virulence system. The adhesion of S. aureus to the conjunctival surface is facilitated by fibronectin-binding proteins, extracellular adherence protein, and clumping factors; subsequently, biofilm formation, tissue invasion, toxin secretion, and immune evasion mechanisms contribute to the persistence and recurrence of the disease. In particular, alpha-toxin, gamma-toxin, Panton–Valentine leukocidin, and enterotoxins enhance epithelial cell damage, promote the release of inflammatory mediators, and intensify local tissue destruction. Molecular studies have demonstrated a high prevalence of genes associated with adhesion, invasion, and immune evasion in ocular S. aureus strains; in certain clinical series, the hld and hlg genes were detected significantly more frequently in infectious strains compared to non-infectious isolates. Recent observations indicate that the proportion of staphylococci in bacterial conjunctivitis and the issue of methicillin-resistant strains remain persistent, thereby limiting the effectiveness of empirical therapy. Thus, the pathogenesis of S. aureus-associated bacterial conjunctivitis should be considered as an integrated system involving adhesion, biofilm formation, toxic injury, induction of inflammation, and antibiotic resistance.

**Keywords:** Bacterial conjunctivitis, Staphylococcus aureus, pathogenesis, virulence factors, adhesion, biofilm, alpha-toxin, gamma-toxin, Panton–Valentine leukocidin, enterotoxin B, antibiotic resistance, MRSA, conjunctival inflammation.

**Introduction.** Conjunctivitis is one of the most common conditions in ophthalmological practice. Although viral etiology predominates among infectious forms in the general population, bacterial conjunctivitis constitutes a substantial clinical proportion, particularly in children. According to available data, a large proportion of acute infectious conjunctivitis cases in pediatric populations may be of bacterial origin, whereas in adults, staphylococcal species, including Staphylococcus aureus, play a major etiological role. In the United States, it has been estimated that up to 6 million cases of acute conjunctivitis occur annually from all causes, underscoring not only the clinical significance of the condition but also its economic and organizational impact on healthcare systems.

S. aureus is an opportunistic pathogen capable of affecting various anatomical structures of the eye, including the eyelid margin, conjunctiva, cornea, and intraocular compartments. Its significance as an ophthalmic pathogen persists despite the presence of normal ocular defense barriers.

The tear film contains lysozyme, lactoferrin, immunoglobulins, antimicrobial peptides, and, together with the mechanical action of blinking, provides primary antimicrobial defense. However, when this protective system is compromised—due to factors such as contact lens use, ocular surface dryness, microtrauma, chronic blepharitis, reduced immune response, or nosocomial contamination—conditions become favorable for S. aureus colonization and invasion.

The initial stage of pathogenesis begins with the firm adhesion of the bacterium to the conjunctival or, more broadly, ocular surface. In this process, microbial surface components of S. aureus—including fibronectin-binding proteins, clumping factors, collagen-binding proteins, and extracellular adherence protein—play a critical role. These factors facilitate bacterial attachment to host extracellular matrix components, promote proximity to epithelial cells, and enable subsequent internalization. Molecular studies of ocular isolates have demonstrated that adhesion-associated genes such as eap and fnbpA are present in nearly all infectious strains, confirming that adhesion constitutes a central step in pathogenesis. Furthermore, increased exposure of fibronectin following ocular surface injury further enhances the attachment capacity of this microorganism.

Following adhesion, biofilm formation represents one of the principal mechanisms determining disease persistence and therapeutic resistance. A biofilm is a structured community composed of bacterial cells, an extracellular polymeric matrix, and a complex three-dimensional architecture. This structure not only anchors bacteria firmly to the surface but also restricts antibiotic penetration, alters metabolic activity, and protects microorganisms from immune cell-mediated clearance. In an ex vivo human corneal model, ocular Staphylococcus aureus biofilms were shown to form more rapidly than on synthetic surfaces, with maturation and dispersion observed within 48 hours.

Moreover, antibiotic susceptibility in the biofilm phase was several-fold lower compared to the planktonic state. These findings provide a microbiological basis for the chronicity, recurrence, and frequent failure of empirical therapy in conjunctivitis.

Another critical component of S. aureus pathogenesis is tissue damage mediated by toxins and secreted enzymes. In ocular infections, alpha-toxin, beta-toxin, gamma-toxin, bicomponent leukocidins, staphylococcal enterotoxins, and proteases are actively involved in amplifying inflammation. Alpha-toxin interacts with ADAM10, forming pores in the host cell membrane, disrupting ionic homeostasis, and leading to epithelial cell necrosis and apoptosis. Experimental models have demonstrated that the application of purified alpha-toxin to the eye induces significant inflammation of the conjunctiva and iris, as well as epithelial destruction and enhanced migration of inflammatory cells. Therefore, S. aureus-associated conjunctivitis cannot be adequately characterized as a purely "superficial infection"; its toxic component plays a decisive role in determining clinical severity and the risk of complications.

Immune evasion mechanisms further ensure the successful persistence of S. aureus. Virulence determinants such as protein A, staphylokinase, leukocidins, and others impair neutrophil function, disrupt opsonophagocytosis, and modulate the inflammatory response in favor of the pathogen. An analysis of ocular strains conducted in 2022 revealed that the hlg and hld genes were significantly more prevalent in infectious isolates compared to non-infectious ones, highlighting the importance of toxin-mediated invasion and inflammation in clinical infection. Additionally, factors such as seb and pvl have been identified in certain conjunctival strains, potentially contributing to more severe and highly pro-inflammatory forms of conjunctival inflammation.

Recent microbiological surveillance studies confirm the predominance of Gram-positive cocci in the etiology of bacterial conjunctivitis and the persistent clinical relevance of S. aureus. For instance, in a retrospective analysis covering the period 2020–2024, Gram-positive cocci accounted for 70.7% of all isolates, with S. aureus representing 17.2%. Notably, the detection rate of this pathogen increased from 0% in 2020 to 28.6% in 2024. In the same study, methicillin resistance was identified in 60.0% of S. aureus isolates, indicating a growing proportion of MRSA-associated conjunctival infections. This trend necessitates the implementation of local antibiotic susceptibility monitoring to guide appropriate therapeutic strategies.

The central scientific challenge lies in the fact that, despite similar clinical presentations, variations in virulence profiles and resistance patterns can significantly influence disease progression and treatment outcomes.

From this perspective, a systematic analysis of the pathogenic mechanisms of Staphylococcus aureus in the development of bacterial conjunctivitis, based on contemporary literature, holds substantial scientific and practical importance. Elucidating the integrated roles of adhesion, biofilm formation, toxin secretion, immune evasion, and antimicrobial resistance will not only deepen the understanding of molecular pathogenesis but also facilitate the identification of novel diagnostic markers and the development of pathogen-targeted therapeutic approaches.

**Objective of the study.** The aim of this literature review is to systematically analyze the pathogenic mechanisms of Staphylococcus aureus in the development of bacterial conjunctivitis based on contemporary scientific evidence, with particular emphasis on its key virulence factors and interactions with the host organism.

**Materials and Methods.** This study was conducted in the form of a systematic literature review.

Data sources and search strategy. Scientific sources were identified using the following international databases: PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar. The search process employed the following key terms: "Staphylococcus aureus conjunctivitis pathogenesis"; "bacterial conjunctivitis virulence factors"; "ocular surface infection staphylococcus mechanisms"; and "MRSA ocular infections."

Inclusion criteria. Articles were selected based on the following criteria: publication within the period 2000–2025; publication in peer-reviewed journals; investigation of the pathogenic mechanisms of S. aureus through experimental or clinical approaches; and availability of full-text access.

Data analysis. The selected articles were analyzed using a content analysis approach. Pathogenetic mechanisms were systematized into the following categories: adhesion and colonization; invasion and tissue damage; the role of toxins and enzymes; biofilm formation; and interaction with the immune system. The results were synthesized based on contemporary molecular-biological and clinical studies.

More than 60 scientific articles were selected and systematically reviewed for analysis.

**Results.** The pathogenic mechanisms of Staphylococcus aureus in the development of bacterial conjunctivitis are characterized by a multi-stage and complex nature, involving interactions with the conjunctival surface, expression of virulence factors, and modulation of the host immune response [18].

Etiological and epidemiological characteristics. According to the analyzed epidemiological data, S. aureus is one of the leading pathogens in ocular infections, accounting for up to 70% of all ocular infections in certain studies. It is also recognized as a major etiological agent in bacterial conjunctivitis, particularly with a higher prevalence among adults. Furthermore, clinical observations indicate that S. aureus-associated cases may constitute up to 40–50% of conjunctivitis patients [21].

Main stages of pathogenesis. Based on the reviewed literature, the pathogenesis of S. aureus-associated bacterial conjunctivitis can be divided into three principal stages:

Adhesion and colonization stage. S. aureus adheres to epithelial cells via MSCRAMMs (microbial surface components recognizing adhesive matrix molecules), including proteins such as ClfA, ClfB, and fibronectin-binding proteins, which ensure stable colonization of the conjunctival surface [23].

Invasion and immune evasion. The bacterium employs proteases, capsular components, and other enzymes to inactivate protective factors in the tear fluid (e.g., surfactant D), thereby facilitating evasion of phagocytosis [30].

Tissue damage and inflammation. Exotoxins produced by S. aureus damage cellular membranes and exert cytotoxic effects, leading to increased release of proinflammatory cytokines and the development of neutrophilic infiltration [20].

Virulence factors and their role. The table below systematizes the principal virulence factors of Staphylococcus aureus involved in the pathogenesis of bacterial conjunctivitis.

Table 1. Virulence factors of Staphylococcus aureus and their pathogenic roles

| ***Virulence factor*** | ***Mechanism*** | ***Pathogenetic effect*** |
|---|---|---|
| MSCRAMM proteins | Adhesion to epithelial cells | Colonization and initiation of infection |
| α-hemolysin (hla) | Pore formation in cell membranes | Cell lysis, epithelial damage |
| PVL (Panton–Valentine leukocidin) | Leukocyte destruction | Suppression of immune response |
| Enterotoxins | Superantigen activity | Strong inflammatory response |
| Proteases | Degradation of conjunctival proteins | Tissue invasion |
| Biofilm | Protection from antibiotics and immune defenses | Chronic infection |

According to available evidence, α-toxin (encoded by the hla gene) is present in nearly all ocular strains and induces pore formation in epithelial cells, leading to cell death. PVL contributes to immune cell destruction, thereby promoting a more severe course of infection [9,24,26].

Inflammation and immune response mechanisms. In conjunctival tissues infected with S. aureus, the innate immune response is rapidly activated. Studies have demonstrated increased production of proinflammatory cytokines such as IL-1β and TNF-α, enhanced neutrophil migration, and recruitment of dendritic cells mediated by chemokines such as CCL20. Clinically, these processes manifest as hyperemia, edema, exudation, and purulent discharge [27].

Biofilm formation and antibiotic resistance. S. aureus possesses a well-established capacity for biofilm formation, which represents a critical factor in its pathogenesis. The microbial biofilm reduces antibiotic penetration, enables evasion of immune responses, and contributes to the development of chronic and recurrent conjunctivitis [13].

The increasing prevalence of MRSA (Methicillin-resistant Staphylococcus aureus) strains is recognized as a major challenge, significantly reducing the effectiveness of standard therapeutic approaches.

**Discussion.** The findings of this literature review indicate that Staphylococcus aureus should not be regarded merely as an etiological agent in bacterial conjunctivitis but rather as a highly adaptive pathogen that actively interacts with the ocular surface microecosystem, epithelial barrier, innate immunity, and inflammatory mediators. Contemporary studies consistently identify staphylococci—particularly S. aureus—as among the most prevalent pathogens in adult bacterial conjunctivitis. This predominance can be explained by the organism’s adhesive capacity, toxigenicity, and ability to develop antibiotic resistance. From this perspective, conjunctivitis should be interpreted not simply as a localized inflammatory condition but as a dynamic biological conflict between host and pathogen.

Analysis of the results demonstrates that the primary and decisive stage of pathogenesis is adhesion to and colonization of the ocular surface. Under physiological conditions, the tear film—comprising lysozyme, lactoferrin, antimicrobial peptides—and mechanical clearance mechanisms limit persistent microbial attachment. However, disruption of epithelial integrity, blepharitis, dry eye syndrome, inadequate contact lens hygiene, or pre-existing ocular surface disorders create a “window of opportunity” for S. aureus colonization. Therefore, from a clinical standpoint, conjunctivitis is more appropriately considered not as an isolated infection but as a process that frequently develops on the background of pre-existing ocular surface dysfunction. This interpretation has direct implications for preventive and therapeutic strategies: beyond antibiotic administration, restoration of ocular surface homeostasis should be regarded as an integral component of management.

One of the most significant findings regarding virulence factors is the central role of α-toxin. Experimental and review studies have demonstrated that α-toxin exerts a direct cytotoxic effect on ocular tissues by forming pores in epithelial cell membranes and amplifying inflammatory responses. This mechanism explains clinical manifestations such as hyperemia, edema, purulent discharge, and, in some cases, progression from superficial involvement to deeper ocular damage. Importantly, tissue injury is determined not only by bacterial load but also by the toxin repertoire of the pathogen. Consequently, identical bacterial burdens may produce different clinical presentations depending on the strain. This highlights the перспективность of molecular characterization of virulence profiles in laboratory diagnostics, beyond conventional bacteriological identification.

Furthermore, the review findings indicate that Staphylococcus aureus pathogenesis involves the simultaneous activation of and evasion from the host immune system. On the one hand, bacterial components and toxins stimulate epithelial cells and innate immune receptors, increasing the secretion of proinflammatory mediators such as IL-1β and TNF-α; on the other hand, the bacterium reduces the efficiency of opsonization and phagocytosis through protein A, proteases, and related factors. As a result, clinical damage often reflects two interacting components: the direct cytotoxic effect of the pathogen and the excessive inflammatory response of the host. This dual mechanism can be conceptualized as a “pathogen-mediated damage + immune-mediated damage” model on the ocular surface. Clinically, this distinction is critical, as in some patients the severity of symptoms may correlate more strongly with the intensity of inflammation than with the bacterial load itself.

Data on biofilm formation represent one of the most clinically relevant—and arguably most persistently resistant—components of this pathogenic process. The S. aureus biofilm enables firm surface adherence while providing partial protection against antibiotics, disinfectants, and immune factors. Studies of staphylococcal isolates from ocular fluids have demonstrated that antibiotic susceptibility in the biofilm phase is several-fold lower than in the planktonic state. Consequently, in recurrent or chronic blepharoconjunctivitis and contact lens-associated infections, standard empirical therapy may prove insufficient. Thus, clinical failure is not always attributable to inappropriate antibiotic selection; in many cases, the underlying issue is the biological “sanctuary” provided by the biofilm itself.

Findings related to antibiotic resistance warrant particular emphasis. The presence of methicillin-resistant S. aureus (MRSA) strains among ocular isolates and the observed reduction in susceptibility to certain antibiotics highlight the limitations of long-standing empirical antibacterial approaches in ophthalmology. In patients with recurrent, prolonged, or previously treated conjunctivitis, continuation of therapy without microbiological evaluation represents a scientifically weak strategy. Importantly, antibiotic resistance should not be viewed as an isolated phenomenon; rather, it is an integral component of a complex biological system involving biofilm formation, virulence, and ecological selection pressures.

Another important conclusion from the literature is the close pathogenic association of S. aureus with the eyelid margin, blepharitis, and blepharoconjunctivitis, particularly in chronic or subacute cases. In certain patients, the clinical diagnosis of “conjunctivitis” may actually reflect alterations in eyelid margin microbiota, meibomian gland dysfunction, and chronic staphylococcal colonization of the ocular surface. Therefore, it is more appropriate to conceptualize the condition not as an isolated conjunctival process but as a disorder of the ocular surface unit. This perspective reinforces the importance of eyelid hygiene, biofilm reduction, and restoration of tear film homeostasis as integral components of therapy.

At the molecular level, regulation of pathogenesis provides further insight into disease variability. In S. aureus, virulence expression is not static; it is dynamically regulated through quorum sensing systems, stress-response pathways, and environmental adaptation. This allows the bacterium to shift between phenotypic states depending on ocular surface conditions, adopting either a highly toxigenic or a biofilm-dominant strategy. From a clinical standpoint, this variability is highly significant: applying a uniform therapeutic approach to all patients represents an oversimplified biological model. Consequently, future strategies targeting virulence inhibition, biofilm disruption, or toxin neutralization are likely to represent promising directions in the management of S. aureus-associated conjunctivitis.

It should also be noted that although a substantial proportion of experimental data has been derived from models of keratitis and other severe ocular infections, many of these findings provide a biological basis for understanding bacterial conjunctivitis. This is because adhesion, toxin expression, inflammation, and immune evasion mechanisms share a common pathogenic platform across different layers of the ocular surface. However, the conjunctiva, cornea, and intraocular tissues are not pathophysiologically identical. Therefore, caution is required when extrapolating findings from severe corneal infections directly to conjunctivitis. From a standpoint of scientific rigor, a strong biological analogy exists, but not all conclusions are directly translatable.

Based on the available literature, the following conceptual model can be proposed.

Table. Integrated interpretation of the pathogenesis of S. aureus-associated bacterial conjunctivitis

| ***Pathogenetic stage*** | ***Main mechanism*** | ***Clinical significance*** |
|---|---|---|
| Colonization | MSCRAMM proteins, epithelial adhesion | Initiation and persistence of infection |
| Barrier disruption | Dry eye, blepharitis, contact lens use, microtrauma | Entry point for infection |
| Toxic damage | α-toxin and other secreted factors | Hyperemia, pain, epithelial injury |
| Immune activation | IL-1β, TNF-α, neutrophil infiltration | Exudation and severity of inflammation |
| Immune evasion | Protein A, enzymes, escape from phagocytosis | Persistence and recurrent course |
| Biofilm formation | Surface adherence, antibiotic protection | Chronicity and treatment resistance |
| Resistance | MRSA and other resistant phenotypes | Reduced effectiveness of empirical therapy |

Overall, the findings of this review indicate that the pathogenesis of S. aureus-associated bacterial conjunctivitis is a multi-stage, interconnected, and phenotypically adaptive process. The key scientific conclusion is that disease severity is determined not merely by the presence of the bacterium but by the combined effects of its virulence repertoire, biofilm-forming capacity, resistance profile, and the condition of the host ocular surface. Therefore, future research in this field should extend beyond etiological identification to include toxin profiling, biofilm biomarkers, and alterations in the ocular microbiome. Otherwise, the pathogen may be identified, yet the mechanisms by which it drives disease will remain insufficiently understood—a limitation that is unacceptable in rigorous scientific inquiry.

**Conclusion.** Based on the analyzed literature, results, and discussion, it can be concluded that Staphylococcus aureus represents a central pathogen in the pathogenesis of bacterial conjunctivitis, characterized by multifaceted virulence properties. Its ability to adhere to the ocular surface, colonize, produce toxins, form biofilms, and modulate the host immune response constitutes the principal biological mechanisms determining disease onset, progression, and severity.

2. Staphylococcus aureus should not be regarded merely as a simple etiological factor in bacterial conjunctivitis, but rather as a highly adaptive and complex pathogen. Its pathogenic potential is significantly enhanced in the context of disrupted physiological defense mechanisms of the ocular surface, including the tear film, antimicrobial proteins, epithelial barrier, and mechanical clearance processes. Therefore, disease development should be evaluated not solely

based on the presence of the bacterium but in conjunction with the local defense status of the host.

3. The initial and decisive stage of disease pathogenesis is the adhesion of the bacterium to the conjunctival epithelium followed by colonization. Adhesins belonging to the MSCRAMM family, fibronectin-binding proteins, and other surface virulence determinants ensure stable bacterial attachment to the ocular surface. This process is particularly enhanced in patients with dry eye syndrome, blepharitis, impaired contact lens hygiene, or microtrauma, significantly increasing the likelihood of infection onset.

4. The toxigenic properties of S. aureus, particularly the expression of α-toxin, proteases, and other exotoxins, play a central role in conjunctival tissue damage. These factors induce cytotoxic changes in epithelial cells, disrupt cellular membranes, and enhance the release of proinflammatory mediators. Clinically, this manifests as hyperemia, edema, purulent discharge, and, in some cases, progression to more severe ocular forms. Thus, disease severity is determined not only by bacterial load but also by the virulence profile of the infecting strain.

5. The host immune response has a dual role in pathogenesis: on the one hand, it contributes to bacterial clearance, while on the other, excessive activation exacerbates tissue damage. Increased production of cytokines such as IL-1β and TNF-α, along with neutrophil infiltration and local inflammatory responses, leads to the intensification of clinical symptoms. Therefore, bacterial conjunctivitis follows a “microbial damage + immune-mediated damage” model rather than being solely a consequence of microbial aggression.

6. Biofilm formation and antibiotic resistance—particularly the presence of methicillin-resistant Staphylococcus aureus (MRSA) strains—represent key factors in the development of chronic, recurrent, and treatment-resistant forms of the disease. Biofilms provide partial protection against antibiotics, antiseptics, and immune factors, thereby reducing the effectiveness of standard empirical therapy. Consequently, future management strategies should not rely solely on antibacterial therapy but should incorporate anti-biofilm approaches, anti-virulence strategies, and individualized microbiological diagnostics as part of a comprehensive treatment concept.

In summary, Staphylococcus aureus-associated bacterial conjunctivitis develops through multi-stage and complex pathogenic mechanisms. A deeper understanding of these processes provides a critical scientific basis for early diagnosis, assessment of disease severity, and the development of targeted therapeutic strategies. Ultimately, the issue extends beyond identifying “which bacterium” is involved; rather, it lies in understanding how it adheres, how it causes damage, and why it persists despite treatment—the full burden of pathogenesis resides precisely within this triad.

**References.**

1. Afzal, M., et al. (2021). Susceptibility of ocular Staphylococcus aureus isolates. Antibiotics. https://pmc.ncbi.nlm.nih.gov/articles/PMC8533015/

2. Afzal, M., et al. (2022). Virulence genes of Staphylococcus aureus associated with ocular infections. Translational Vision Science & Technology. https://pmc.ncbi.nlm.nih.gov/articles/PMC9279920/

3. Archer, N. K., Mazaitis, M. J., Costerton, J. W., Leid, J. G., Powers, M. E., & Shirtliff, M. E. (2011). Staphylococcus aureus biofilms: Properties, regulation, and roles in human disease. Virulence, 2(5), 445–459. https://doi.org/10.4161/viru.2.5.17724

4. Astley, R., et al. (2019). An eye on Staphylococcus aureus toxins: Roles in ocular damage and inflammation. Toxins, 11(6), 356. https://pmc.ncbi.nlm.nih.gov/articles/PMC6628431/

5. Azari, A. A., & Barney, N. P. (2020). Conjunctivitis: A systematic review of diagnosis and treatment. JAMA, 323(10), 1052–1062. https://pmc.ncbi.nlm.nih.gov/articles/PMC7431717/

6. Becker, K., Heilmann, C., & Peters, G. (2014). Coagulase-negative staphylococci. Clinical Microbiology Reviews, 27(4), 870–926. https://doi.org/10.1128/CMR.00109-13

7. Berube, B. J., & Bubeck Wardenburg, J. (2013). Staphylococcus aureus α-toxin: Nearly a century of intrigue. Toxins, 5(6), 1140–1166. https://doi.org/10.3390/toxins5061140

8. Boles, B. R., & Horswill, A. R. (2011). Staphylococcal biofilm disassembly. Trends in Microbiology, 19(9), 449–455. https://doi.org/10.1016/j.tim.2011.06.004

9. Chambers, H. F., & DeLeo, F. R. (2009). Waves of resistance: Staphylococcus aureus in the antibiotic era. Nature Reviews Microbiology, 7(9), 629–641. https://doi.org/10.1038/nrmicro2200

10. Cheung, G. Y. C., Bae, J. S., & Otto, M. (2021). Pathogenicity and virulence of Staphylococcus aureus. Virulence, 12(1), 547–569. https://doi.org/10.1080/21505594.2021.1878688

11. DeLeo, F. R., Otto, M., Kreiswirth, B. N., & Chambers, H. F. (2010). Community-associated methicillin-resistant Staphylococcus aureus. Lancet, 375(9725), 1557–1568. https://doi.org/10.1016/S0140-6736(09)61999-1

12. Durán-Manuel, E. M., et al. (2023). Molecular characterization of bacterial agents causing ocular infections. Pathogens, 12(11), 1294. https://www.mdpi.com/2076-0817/12/11/1294

13. Fleiszig, S. M. J., & Evans, D. J. (2010). Pathogenesis of bacterial keratitis: Studies with Pseudomonas aeruginosa and Staphylococcus aureus. Clinical & Experimental Optometry, 93(4), 245–252. https://doi.org/10.1111/j.1444-0938.2010.00488.x

14. Foster, T. J. (2005). Immune evasion by staphylococci. Nature Reviews Microbiology, 3(12), 948–958. https://doi.org/10.1038/nrmicro1289

15. Foster, T. J., Geoghegan, J. A., Ganesh, V. K., & Höök, M. (2014). Adhesion, invasion and evasion. Nature Reviews Microbiology, 12(1), 49–62. https://doi.org/10.1038/nrmicro3161

16. Gordon, R. J., & Lowy, F. D. (2008). Pathogenesis of methicillin-resistant Staphylococcus aureus infection. Clinical Infectious Diseases, 46(Supplement_5), S350–S359. https://doi.org/10.1086/533591

17. Jefferson, K. K. (2004). What drives bacteria to produce a biofilm? FEMS Microbiology Letters, 236(2), 163–173. https://doi.org/10.1016/j.femsle.2004.06.005

18. Kathirvel, K., et al. (2021). Characterization of virulence genes in ocular MRSA. Experimental Eye Research. https://pubmed.ncbi.nlm.nih.gov/34508729/

19. Kiedrowski, M. R., & Horswill, A. R. (2011). New approaches for treating staphylococcal biofilm infections. Annals of the New York Academy of Sciences, 1241(1), 104–121. https://doi.org/10.1111/j.1749-6632.2011.06281.x

20. Kim, H. K., Cheng, A. G., Kim, H. Y., Missiakas, D. M., & Schneewind, O. (2010). Nontoxigenic protein A vaccine for Staphylococcus aureus. Journal of Experimental Medicine, 207(9), 1863–1870. https://doi.org/10.1084/jem.20092514

21. Kong, C., Neoh, H. M., & Nathan, S. (2016). Targeting Staphylococcus aureus toxins: A potential form of anti-virulence therapy. Toxins, 8(3), 72. https://doi.org/10.3390/toxins8030072

22. Krismer, B., Weidenmaier, C., Zipperer, A., & Peschel, A. (2017). The commensal lifestyle of Staphylococcus aureus. Nature Reviews Microbiology, 15(11), 675–687. https://doi.org/10.1038/nrmicro.2017.104

23. Lee, A. S., de Lencastre, H., Garau, J., Kluytmans, J., Malhotra-Kumar, S., Peschel, A., & Harbarth, S. (2018). Methicillin-resistant Staphylococcus aureus. Nature Reviews Disease Primers, 4, 18033. https://doi.org/10.1038/nrdp.2018.33

24. Lee, J. W., et al. (2021). Staphylococcus aureus keratitis: Incidence and virulence factors. Journal of Clinical Medicine. https://www.mdpi.com/2077-0383/10/4/758

25. Lin, A., Rhee, M. K., Akpek, E. K., Amescua, G., Farid, M., Garcia-Ferrer, F. J., & Varu, D. M. (2019). Bacterial conjunctivitis preferred practice pattern. Ophthalmology, 126(1), P94–P169. https://doi.org/10.1016/j.ophtha.2018.10.020

26. Lister, J. L., & Horswill, A. R. (2014). Staphylococcus aureus biofilms: Recent developments. Microbiology Spectrum, 2(3), 1–11. https://doi.org/10.1128/microbiolspec.MB-0001-2014

27. Lowy, F. D. (1998). Staphylococcus aureus infections. New England Journal of Medicine, 339(8), 520–532. https://doi.org/10.1056/NEJM199808203390806

28. Nakagawa, S., Matsumoto, M., Katayama, Y., Oguma, R., Wakabayashi, S., Nygaard, T., … Matsue, H. (2017). Staphylococcus aureus virulent PSMα peptides induce keratinocyte alarmin release. Nature Communications, 8, 14655. https://doi.org/10.1038/ncomms14655

29. O'Callaghan, R. J. (2018). The pathogenesis of Staphylococcus aureus eye infections. Pathogens, 7(1), 9. https://pmc.ncbi.nlm.nih.gov/articles/PMC5874735/

30. Otto, M. (2014). Staphylococcus aureus toxins. Current Opinion in Microbiology, 17, 32–37. https://doi.org/10.1016/j.mib.2013.11.004

31. Peacock, S. J., de Silva, I., & Lowy, F. D. (2001). What determines nasal carriage of Staphylococcus aureus? Trends in Microbiology, 9(12), 605–610. https://doi.org/10.1016/S0966-842X(01)02254-5

32. Pippin, M. M. (2023). Bacterial conjunctivitis. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK546683/

33. Spaulding, A. R., Salgado-Pabón, W., Kohler, P. L., Horswill, A. R., Leung, D. Y. M., & Schlievert, P. M. (2013). Staphylococcal and streptococcal superantigen exotoxins. Clinical Microbiology Reviews, 26(3), 422–447. https://doi.org/10.1128/CMR.00104-12

34. Tilahun, M., et al. (2025). Prevalence of bacterial eye infections and multidrug resistance. BMC Infectious Diseases. https://link.springer.com/article/10.1186/s12879-025-11095-y

35. Tong, S. Y. C., Davis, J. S., Eichenberger, E., Holland, T. L., & Fowler, V. G. (2015). Staphylococcus aureus infections: Epidemiology, pathophysiology, clinical manifestations, and management. Clinical Microbiology Reviews, 28(3), 603–661. https://doi.org/10.1128/CMR.00134-14

36. Touaitia, R., et al. (2025). Staphylococcus aureus: Pathogenesis, virulence factors, and antimicrobial resistance. Antibiotics, 14(5), 470. https://pmc.ncbi.nlm.nih.gov/articles/PMC12108373/

37. Turner, N. A., Sharma-Kuinkel, B. K., Maskarinec, S. A., Eichenberger, E. M., Shah, P. P., Carugati, M., … Fowler, V. G. (2019). Methicillin-resistant Staphylococcus aureus. Nature Reviews Microbiology, 17(4), 203–218. https://doi.org/10.1038/s41579-018-0147-4

38. Wertheim, H. F. L., Melles, D. C., Vos, M. C., van Leeuwen, W., van Belkum, A., Verbrugh, H. A., & Nouwen, J. L. (2005). The role of nasal carriage in Staphylococcus aureus infections. The Lancet Infectious Diseases, 5(12), 751–762. https://doi.org/10.1016/S1473-3099(05)70295-4

39. Voyich, J. M., Braughton, K. R., Sturdevant, D. E., Whitney, A. R., Said-Salim, B., Porcella, S. F., … DeLeo, F. R. (2005). Insights into mechanisms used by Staphylococcus aureus to avoid innate immune responses. Journal of Immunology, 175(6), 3907–3919. https://doi.org/10.4049/jimmunol.175.6.3907

40. Rooijakkers, S. H. M., van Wamel, W. J. B., Ruyken, M., van Kessel, K. P. M., & van Strijp, J. A. G. (2005). Anti-opsonic properties of staphylokinase. Journal of Experimental Medicine, 201(7), 1057–1065. https://doi.org/10.1084/jem.20042524

41. Clarke, S. R., & Foster, S. J. (2006). Surface adhesins of Staphylococcus aureus. Advances in Microbial Physiology, 51, 187–224. https://doi.org/10.1016/S0065-2911(06)51003-9

42. Geoghegan, J. A., & Foster, T. J. (2015). Cell wall-anchored surface proteins of Staphylococcus aureus. Microbiology Spectrum, 3(3), 1–19. https://doi.org/10.1128/microbiolspec.MB-0008-2014

43. Bubeck Wardenburg, J., & Schneewind, O. (2008). Vaccine protection against Staphylococcus aureus pneumonia. Journal of Experimental Medicine, 205(2), 287–294. https://doi.org/10.1084/jem.20072208

44. Grumann, D., & Nübel, U. (2014). Multilocus sequence typing of Staphylococcus aureus. Infection, Genetics and Evolution, 21, 193–201. https://doi.org/10.1016/j.meegid.2013.10.013

45. Coates, R., Moran, J., & Horsburgh, M. J. (2014). Staphylococci: Colonizers and pathogens. Frontiers in Cellular and Infection Microbiology, 4, 151. https://doi.org/10.3389/fcimb.2014.00151

46. Fey, P. D., & Olson, M. E. (2010). Current concepts in biofilm formation of Staphylococcus epidermidis. Future Microbiology, 5(6), 917–933. https://doi.org/10.2217/fmb.10.56

47. Archer, N. K., Harro, J. M., Shirtliff, M. E. (2013). Clearance of Staphylococcus aureus biofilms. Current Opinion in Microbiology, 16(1), 1–7. https://doi.org/10.1016/j.mib.2012.11.002

48. Schlievert, P. M., & Case, L. C. (2007). Molecular analysis of staphylococcal superantigens. Methods in Molecular Biology, 391, 113–120. https://doi.org/10.1007/978-1-59745-468-1_7

49. Peschel, A., & Otto, M. (2013). Phenol-soluble modulins and staphylococcal infection. Nature Reviews Microbiology, 11(10), 667–673. https://doi.org/10.1038/nrmicro3110

50. Chatterjee, S. S., & Otto, M. (2013). Improved understanding of factors driving methicillin-resistant Staphylococcus aureus epidemic waves. Clinical Epidemiology, 5, 205–217. https://doi.org/10.2147/CLEP.S30370

51. Gordon, R. J., & Lowy, F. D. (2008). Pathogenesis of MRSA infection. Clinical Infectious Diseases, 46(Supplement_5), S350–S359. https://doi.org/10.1086/533591

52. Archer, G. L. (1998). Staphylococcus aureus: A well-armed pathogen. Clinical Infectious Diseases, 26(5), 1179–1181. https://doi.org/10.1086/520289

53. Diekema, D. J., Pfaller, M. A., Schmitz, F. J., Smayevsky, J., Bell, J., Jones, R. N., & Beach, M. (2001). Survey of infections due to Staphylococcus species. Clinical Infectious Diseases, 32(Supplement_2), S114–S132. https://doi.org/10.1086/320184

54. Wertheim, H. F. L., Vos, M. C., Ott, A., van Belkum, A., Voss, A., Kluytmans, J. A. J. W., … Verbrugh, H. A. (2004). Risk and outcome of nasal carriage of Staphylococcus aureus. Lancet, 364(9435), 703–705. https://doi.org/10.1016/S0140-6736(04)16854-2

55. Miller, L. S., & Cho, J. S. (2011). Immunity against Staphylococcus aureus infections. Nature Reviews Immunology, 11(8), 505–518. https://doi.org/10.1038/nri3010

56. Spaan, A. N., Surewaard, B. G. J., Nijland, R., & van Strijp, J. A. G. (2013). Neutrophils versus Staphylococcus aureus. Cellular Microbiology, 15(9), 1493–1502. https://doi.org/10.1111/cmi.12162

57. Callegan, M. C., Engelbert, M., Parke, D. W., Jett, B. D., & Gilmore, M. S. (2002). Bacterial endophthalmitis: Epidemiology, therapeutics, and bacterium-host interactions. *Clinical Microbiology Reviews, 15*(1), 111–124. https://doi.org/10.1128/CMR.15.1.111-124.2002

58. Astley, R. A., Miller, F. C., Mursalin, M. H., Coburn, P. S., & Callegan, M. C. (2019). An eye on Staphylococcus aureus toxins: Roles in ocular damage. *Frontiers in Microbiology, 10*, 1403. https://doi.org/10.3389/fmicb.2019.01403

59. Sharma, S. (2011). Antibiotic resistance in ocular bacterial pathogens. *Indian Journal of Medical Microbiology, 29*(3), 218–222. https://doi.org/10.4103/0255-0857.83905

60. Willcox, M. D. P. (2011). Review of resistance of ocular isolates. *Clinical & Experimental Optometry, 94*(4), 324–337. https://doi.org/10.1111/j.1444-0938.2011.00615.x

61. Bispo, P. J. M., Haas, W., & Gilmore, M. S. (2015). Biofilms in infections of the eye. *Pathogens, 4*(1), 111–136. https://doi.org/10.3390/pathogens4010111