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Infectious Keratitis: Current Diagnostic Approaches, Antimicrobial Resistance, and Emerging Therapeutic Strategies

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Abstract :

Infectious keratitis (IK) is a vision-threatening ocular disease and one of the leading causes of corneal blindness worldwide. It is caused by a wide range of pathogens, including bacteria, fungi, viruses, and protozoa, with disease prevalence varying according to geographic location, climate, and patient-related risk factors. Common predisposing factors include contact lens wear, ocular trauma, ocular surface disorders, previous ocular surgery, diabetes mellitus, and immunosuppression. Delayed diagnosis or inappropriate treatment may result in severe complications, including corneal scarring, perforation, and permanent vision loss. Accurate identification of the causative pathogen is therefore essential for timely and targeted therapy. Conventional diagnostic methods, including slit-lamp examination, corneal scraping, Gram staining, potassium hydroxide (KOH) preparation, and microbial culture, remain the foundation of clinical diagnosis. However, recent advances in molecular diagnostics, such as polymerase chain reaction (PCR), real-time PCR (RT-qPCR), next-generation sequencing (NGS), and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), have significantly improved diagnostic sensitivity, specificity, and turnaround time. In addition, artificial intelligence (AI)-based imaging systems have shown promising potential for rapid and accurate clinical diagnosis. The increasing emergence of antimicrobial-resistant pathogens has created significant therapeutic challenges, highlighting the need for innovative treatment strategies. Recent developments, including novel antibiotics, antimicrobial peptides, photoactivated chromophore for infectious keratitis–corneal collagen cross-linking (PACK-CXL), bacteriophage therapy, nanoparticle-based drug delivery systems, stem-cell therapy, and immunotherapy, offer promising alternatives to conventional treatment. This review summarizes the current

epidemiology, risk factors, pathogenesis, clinical manifestations, diagnostic advances, and emerging therapeutic strategies for infectious keratitis. Furthermore, it highlights future perspectives aimed at improving early diagnosis, optimizing targeted therapy, and reducing the global burden of corneal blindness associated with this sight-threatening disease.

Keywords :

Corneal ulcer; Bacterial keratitis; Fungal keratitis; Viral keratitis; Acanthamoeba keratitis

Introduction

Infectious keratitis (IK) is a vision-threatening ocular emergency characterized by microbial invasion of the corneal tissue, resulting in inflammation, epithelial disruption, stromal infiltration, ulceration, and, in severe cases, corneal perforation and irreversible blindness. It remains one of the leading causes of corneal opacity and preventable visual impairment worldwide, particularly in low- and middle-income countries where delayed diagnosis and limited access to specialized ophthalmic care contribute to poor clinical outcomes. According to the World Health Organization (WHO), corneal diseases represent one of the major causes of blindness globally, with infectious keratitis accounting for a substantial proportion of corneal blindness. The disease imposes a considerable socioeconomic burden due to prolonged treatment, visual disability, loss of productivity, and the need for surgical interventions such as corneal transplantation[1].

The epidemiology of infectious keratitis varies considerably across different geographical regions and is influenced by climatic conditions, socioeconomic status, occupational exposure, healthcare accessibility, and local microbial ecology[2]. In tropical and developing countries, fungal keratitis is highly prevalent because of agricultural trauma involving plant materials and humid environmental conditions[3]. Conversely, bacterial keratitis predominates in developed countries, where contact lens wear has emerged as the principal predisposing factor. Viral keratitis, predominantly caused by herpes simplex virus (HSV), remains a leading cause of infectious corneal blindness worldwide, whereas *Acanthamoeba* keratitis has become increasingly recognized among contact lens users due to inadequate lens hygiene and exposure to contaminated water sources[4].

The pathogenesis of infectious keratitis involves a complex interaction between microbial virulence factors and the host immune response. Under normal physiological conditions, the corneal epithelium, tear film, antimicrobial peptides, immunoglobulins, and innate immune cells provide an effective defense against invading microorganisms. However, disruption of the epithelial barrier caused by trauma, contact lens wear, ocular surface diseases, previous ocular surgery, or systemic immunosuppression allows pathogens to penetrate the corneal stroma. Following microbial invasion, pathogen-associated molecular patterns (PAMPs) activate pattern-recognition receptors (PRRs), particularly Toll-like receptors (TLRs), on epithelial and immune cells, initiating an inflammatory cascade characterized by the release of pro-inflammatory cytokines, including interleukin-1β (IL-1β), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-8 (IL-8). Although these inflammatory mediators are essential for pathogen elimination, excessive or prolonged inflammation can lead to collagen degradation, stromal necrosis, corneal scarring, and permanent visual impairment[5].

The microbial etiology of infectious keratitis is diverse and includes bacteria, fungi, viruses, and protozoa. Among bacterial pathogens, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, coagulase-negative staphylococci, and *Streptococcus pneumoniae* are the most frequently isolated organisms[6]. Fungal keratitis is predominantly caused by filamentous fungi such as *Fusarium* and *Aspergillus* species, although yeasts including *Candida* species are commonly encountered in immunocompromised individuals. Viral keratitis is primarily associated with herpes simplex virus type 1 (HSV-1), while herpes zoster virus (HZV) represents another important viral pathogen affecting the cornea. In addition, *Acanthamoeba* species are responsible for severe protozoal keratitis, which is frequently associated with delayed diagnosis and poor therapeutic response[7].

Accurate and timely diagnosis is essential for successful management of infectious keratitis because clinical manifestations often overlap among different etiological agents[8]. Conventional diagnostic approaches include slit-lamp biomicroscopy, corneal scraping, Gram staining, potassium hydroxide (KOH) wet mount, Giemsa staining, and microbial culture. Although culture remains the diagnostic gold standard, its sensitivity is limited by prior antimicrobial therapy, inadequate specimen collection, and prolonged incubation time. Consequently, molecular diagnostic techniques have gained increasing importance in recent years. Polymerase chain reaction (PCR), real-time quantitative PCR (RT-qPCR), multiplex PCR, next-generation sequencing (NGS), and matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) have significantly improved the rapid identification of ocular pathogens with higher sensitivity and specificity than conventional methods[9]. Furthermore, recent advances in artificial intelligence (AI) and deep learning algorithms have demonstrated promising performance

in differentiating infectious keratitis from other corneal disorders using slit-lamp photographs and anterior segment imaging[10].

Despite remarkable progress in diagnosis and treatment, antimicrobial resistance has emerged as one of the greatest challenges in the management of infectious keratitis[11]. The widespread and often inappropriate use of topical antibiotics has accelerated the emergence of multidrug-resistant (MDR) pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), fluoroquinolone-resistant *Pseudomonas aeruginosa*, extended-spectrum β-lactamase (ESBL)-producing Gram-negative bacteria, and azole-resistant fungal species. Biofilm formation, horizontal gene transfer, and genetic mutations further compromise antimicrobial efficacy, resulting in prolonged infection, delayed corneal healing, increased healthcare costs, and higher rates of visual loss[12].

In response to these challenges, considerable research efforts have focused on developing innovative therapeutic strategies beyond conventional antimicrobial agents[13]. Emerging approaches include antimicrobial peptides, nanoparticle-based drug delivery systems, bacteriophage therapy, photodynamic antimicrobial therapy, photoactivated chromophore for infectious keratitis–corneal collagen cross-linking (PACK-CXL), stem cell-based therapies, immunomodulatory agents, and precision medicine guided by molecular diagnostics. These novel interventions aim not only to eradicate pathogens more effectively but also to reduce inflammation, preserve corneal integrity, and improve long-term visual outcomes[14].

This review provides a comprehensive overview of the current understanding of infectious keratitis, focusing on its epidemiology, microbial etiology, pathogenesis, clinical manifestations, diagnostic advances, antimicrobial resistance, and emerging therapeutic strategies. In addition, recent developments in molecular diagnostics, artificial intelligence, and novel antimicrobial approaches are discussed to highlight future directions for improving the diagnosis and management of this potentially blinding ocular disease[15].

Epidemiology and Risk Factors

Infectious keratitis (IK) is a major cause of corneal blindness and visual impairment worldwide, particularly in developing countries where delayed diagnosis and limited access to ophthalmic care remain significant challenges[16]. The incidence of IK varies widely, ranging from approximately 2.5 to over 700 cases per 100,000 population annually**,** depending on geographic location, climate, socioeconomic conditions, healthcare availability, and the prevalence of causative pathogens[17]. Tropical and subtropical regions, especially in Asia and Africa, report the highest incidence due to agricultural activities, ocular trauma, and poor hygiene, whereas bacterial keratitis is more common in developed countries because of the widespread use of contact lenses[18].The microbial epidemiology of IK differs across regions. Bacterial keratitis, mainly caused by *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Streptococcus pneumoniae*, predominates in North America and Europe[19]. In contrast, fungal keratitis**,** commonly caused by *Fusarium* and *Aspergillus* species, is more prevalent in tropical countries. Herpes simplex virus (HSV-1) remains the leading cause of viral keratitis globally, while Acanthamoeba keratitis has increased in incidence due to poor contact lens hygiene.Several factors increase susceptibility to infectious keratitis. Contact lens wear is the most important risk factor in industrialized countries, particularly when associated with overnight wear, poor hygiene, or exposure to contaminated water[20]. In developing countries, ocular trauma, especially injuries involving vegetative materials, represents the leading predisposing factor and is strongly associated with fungal keratitis[21]. Additional ocular risk factors include dry eye disease, blepharitis, previous ocular surgery, corneal transplantation, and ocular surface disorders that compromise epithelial integrity.Systemic conditions such as diabetes mellitus, HIV infection, autoimmune diseases, malignancy, and prolonged corticosteroid or immunosuppressive therapy also increase the risk of infection by impairing host immune defenses[22]. Furthermore, microbial virulence factors, including biofilm formation, toxin production, and tissue-invasive mechanisms, contribute to disease severity and antimicrobial resistance .Environmental and behavioral factors—including poor sanitation, low socioeconomic status, delayed medical consultation, inappropriate antibiotic use, and climate-related changes—further influence the occurrence and outcomes of infectious keratitis. Therefore, improving public awareness, promoting proper contact lens hygiene, preventing ocular trauma, and ensuring early diagnosis and treatment are essential strategies for reducing the global burden of this potentially blinding disease[23].

Etiological Agents

Infectious keratitis is caused by a diverse group of microorganisms, including bacteria, fungi, viruses, and protozoa[24]. The distribution of these pathogens varies according to geographical location, climatic conditions, host immune status, and predisposing risk factors. Accurate identification of the causative agent is essential because clinical manifestations often overlap, while treatment strategies differ considerably depending on the pathogen involved. The major etiological agents of infectious keratitis are discussed below.

Bacterial Keratitis

Bacterial keratitis is the most common form of infectious keratitis worldwide and is considered an ophthalmic emergency due to its rapid progression and potential to cause irreversible vision loss[25]. The disease is characterized by corneal epithelial defects accompanied by stromal infiltration, inflammation, ulceration, and, in severe cases, corneal perforation. The predominant bacterial pathogens include *Pseudomonas aeruginosa*, *Staphylococcus aureus*, coagulase-negative staphylococci, *Streptococcus pneumoniae*, and *Moraxella* species. Among these, *P. aeruginosa* is particularly associated with contact lens wear and is capable of causing rapidly progressive corneal destruction through the production of proteases, elastases, exotoxins, and biofilm formation. *S. aureus*, including methicillin-resistant *S. aureus* (MRSA), is frequently isolated from patients with ocular surface diseases or previous ocular surgery[26]. Risk factors include contact lens misuse, ocular trauma, dry eye disease, diabetes mellitus, previous ocular surgery, topical corticosteroid use, and immunosuppression. Prompt diagnosis and initiation of broad-spectrum topical antibiotics are critical to prevent permanent visual impairment.

Fungal Keratitis

Fungal keratitis (keratomycosis) is a severe corneal infection that occurs predominantly in tropical and subtropical regions. It accounts for a substantial proportion of corneal blindness in developing countries, particularly among agricultural workers[27], The most common causative organisms are filamentous fungi such as *Fusarium* and *Aspergillus* species, whereas *Candida* species are more frequently encountered in immunocompromised patients and those with chronic ocular surface disease. Corneal trauma involving vegetative material remains the principal predisposing factor, allowing fungal spores to penetrate the corneal stroma. Other risk factors include prolonged corticosteroid therapy, contact lens wear, diabetes mellitus, and previous corneal surgery. Fungal keratitis typically progresses slowly but may lead to deep stromal invasion, endothelial involvement, corneal perforation, and poor visual

outcomes. Diagnosis is often challenging because fungal cultures require prolonged incubation, making molecular diagnostic methods such as PCR increasingly valuable for rapid pathogen identification[28].

Viral Keratitis

Viral keratitis is primarily caused by herpes simplex virus type 1 (HSV-1) and represents the leading infectious cause of unilateral corneal blindness worldwide. Other viral pathogens include varicella-zoster virus (VZV)**,** adenoviruses, cytomegalovirus (CMV), and, less commonly, Epstein–Barr virus. HSV establishes lifelong latency in the trigeminal ganglion and may reactivate under conditions such as stress, fever, ultraviolet light exposure, or immunosuppression. Recurrent HSV infection can result in epithelial, stromal, endothelial, or neurotrophic keratitis, frequently causing corneal scarring and visual impairment. VZV keratitis usually occurs following herpes zoster ophthalmicus and may produce severe inflammatory complications. Although viral keratitis is generally diagnosed clinically, PCR has become the gold standard for confirming viral DNA in corneal specimens, especially in atypical or recurrent cases. Early administration of antiviral agents significantly improves clinical outcomes and reduces the risk of recurrence[29].

Acanthamoeba Keratitis

Acanthamoeba keratitis is a rare but potentially devastating protozoal infection that primarily affects contact lens wearers. The disease is caused by free-living amoebae of the genus *Acanthamoeba*, which are widely distributed in soil, freshwater, tap water, swimming pools, and air-conditioning systems[30]. Poor contact lens hygiene, rinsing lenses with tap water, swimming while wearing contact lenses, and corneal trauma are major risk factors. One of the hallmark clinical features is severe ocular pain that is often disproportionate to the clinical findings. As the infection progresses, patients may develop ring-shaped stromal infiltrates, radial keratoneuritis, and progressive corneal ulceration. Diagnosis remains difficult because early clinical manifestations resemble bacterial or fungal keratitis. Laboratory confirmation relies on microscopic examination, culture using non-nutrient agar with *Escherichia coli*, confocal microscopy, and molecular techniques such as PCR. Treatment is prolonged and challenging because *Acanthamoeba* cysts exhibit remarkable resistance to many antimicrobial agents, often necessitating combination therapy and, in advanced cases, therapeutic keratoplasty[31].Overall, the wide diversity of etiological agents highlights the importance of accurate microbiological and molecular diagnosis for guiding targeted therapy. Early pathogen identification improves treatment success, minimizes

unnecessary antimicrobial use, and reduces the risk of complications, including corneal scarring, perforation, and permanent vision loss.

Pathogenesis :

The pathogenesis of infectious keratitis is a complex process involving interactions between invading microorganisms, the host immune response, and environmental or predisposing factors. Under normal conditions, the cornea is protected by several defense mechanisms, including the intact corneal epithelium, tear film, blinking reflex, antimicrobial peptides, immunoglobulin A (IgA), lysozyme, lactoferrin, and resident immune cells. These barriers effectively prevent microbial adhesion and invasion. However, disruption of the corneal epithelium due to trauma, contact lens wear, ocular surface disease, surgery, or immunosuppression allows pathogens to penetrate the corneal tissue and initiate infection[32].

Following epithelial injury, microorganisms adhere to exposed epithelial cells through specific adhesins and surface proteins. Bacterial pathogens such as *Pseudomonas aeruginosa* produce pili, flagella, and adhesins that facilitate attachment and colonization of the corneal surface. Many bacteria also secrete extracellular enzymes, including proteases, collagenases, elastases, phospholipases, and exotoxins, which degrade stromal collagen and promote tissue destruction. Similarly, fungal pathogens invade the corneal stroma through filamentous hyphae that penetrate deeply into collagen layers, whereas viruses infect epithelial cells and establish intracellular replication. *Acanthamoeba* trophozoites attach to corneal epithelial cells through mannose-binding proteins before invading the stroma and transforming into highly resistant cysts under unfavorable conditions[33].

Recognition of invading pathogens by the host immune system is initiated through **pattern** recognition receptors (PRRs) expressed on corneal epithelial cells, dendritic cells, macrophages, and neutrophils. These receptors, particularly Toll-like receptors (TLRs) **and** NOD-like receptors (NLRs)**,** recognize pathogen-associated molecular patterns (PAMPs), including bacterial lipopolysaccharides, fungal β-glucans, viral nucleic acids, and protozoal surface molecules. Activation of these receptors triggers intracellular signaling pathways such as nuclear factor-kappa B (NF-κB) **and** mitogen-activated protein kinase (MAPK)**,** leading to the production of pro-inflammatory cytokines and chemokines[34].

The inflammatory response is characterized by the rapid release of cytokines including interleukin-1β (IL-1β), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), interleukin-8 (IL-8), interferon-gamma (IFN-γ), and interleukin-18 (IL-18)**.** These mediators recruit neutrophils, macrophages, dendritic cells, and natural killer (NK) cells to the site of infection. Neutrophils constitute the primary cellular defense against bacterial and fungal pathogens by eliminating microorganisms through phagocytosis, production of reactive oxygen species (ROS), release of antimicrobial peptides, and formation of neutrophil extracellular traps (NETs). While these immune responses are essential for pathogen clearance, excessive or prolonged inflammation may result in collateral damage to healthy corneal tissue[35].

Matrix metalloproteinases (MMPs), particularly MMP-2 **and** MMP-9, play an important role in corneal tissue remodeling during infection. Excessive production of these enzymes leads to degradation of stromal collagen and extracellular matrix components, resulting in corneal thinning, ulceration, stromal melting, and perforation. Persistent inflammation also promotes fibroblast activation and abnormal collagen deposition, ultimately causing corneal scarring and permanent visual impairment[36].

The pathogenic mechanisms vary among different microorganisms. In bacterial keratitis, rapid multiplication of organisms and secretion of toxins produce acute inflammation and extensive stromal destruction. In fungal keratitis, hyphal invasion extends deeply into the corneal stroma, where fungal cell wall components continuously stimulate chronic inflammatory responses. Viral keratitis, particularly caused by herpes simplex virus (HSV), involves direct viral cytopathic effects combined with immune-mediated stromal inflammation. HSV establishes lifelong latency in the trigeminal ganglion and recurrent reactivation results in repeated episodes of corneal inflammation and progressive scarring. In contrast, *Acanthamoeba* keratitis is characterized by intense inflammatory reactions triggered by trophozoites and cysts, which exhibit remarkable resistance to antimicrobial therapy and frequently cause chronic, recurrent infection[37].

Host-related factors also influence disease severity. Diabetes mellitus, immunodeficiency, malnutrition, aging, prolonged corticosteroid therapy, and systemic immunosuppressive treatment impair innate and adaptive immune responses, allowing microorganisms to proliferate more readily and increasing the risk of severe infection. In addition, biofilm formation by bacterial pathogens enhances resistance to host defenses and antimicrobial agents, contributing to persistent or recurrent keratitis[38].

Overall, the pathogenesis of infectious keratitis results from a dynamic interaction between microbial virulence factors and the host immune response. Although inflammation is essential for eliminating invading pathogens, excessive immune

activation frequently causes corneal tissue destruction, ulceration, scarring, and irreversible vision loss. Understanding these molecular and cellular mechanisms is fundamental for developing targeted therapeutic strategies that not only eradicate pathogens but also modulate inflammation and preserve corneal integrity[39].

Clinical Manifestations :

The clinical manifestations of infectious keratitis (IK) vary depending on the causative microorganism, the extent of corneal involvement, the host immune response, and the duration of infection. Although bacterial, fungal, viral, and protozoal keratitis share several common clinical features, certain characteristic findings may help differentiate among these etiological agents. Early recognition of these manifestations is crucial because delayed diagnosis and treatment can lead to rapid disease progression, corneal perforation, and permanent vision loss.The most common symptoms of infectious keratitis include ocular pain, redness, excessive tearing (epiphora), photophobia, blurred vision, foreign body sensation, mucopurulent or watery discharge, and reduced visual acuity. Patients frequently complain of acute onset of pain accompanied by increasing redness and difficulty opening the affected eye. As the infection progresses, corneal edema and stromal inflammation further impair visual function.On slit-lamp biomicroscopic examination, infectious keratitis typically presents with a corneal epithelial defect associated with stromal infiltration, which is considered the hallmark of microbial keratitis. Additional findings may include conjunctival hyperemia, stromal edema, anterior chamber inflammation, hypopyon, endothelial plaques, Descemet's membrane folds, and, in advanced cases, corneal thinning or perforation. The size, depth, location, and appearance of the corneal infiltrate often provide important clues regarding the underlying pathogen[40].

Bacterial Keratitis

Bacterial keratitis usually presents with a rapid onset of severe ocular pain, redness, purulent discharge, photophobia, and decreased vision. Clinical examination commonly reveals a dense stromal infiltrate with an overlying epithelial defect, marked conjunctival injection, stromal edema, and anterior chamber reaction. A hypopyon may develop in severe infections, particularly those caused by Pseudomonas aeruginosa, which is characterized by rapidly progressive corneal necrosis and stromal melting. Without prompt treatment, bacterial keratitis may progress to corneal perforation within a short period[41].

Fungal Keratitis

Fungal keratitis generally has a more gradual onset than bacterial keratitis and is frequently associated with a history of ocular trauma involving vegetative matter. Patients often present with ocular pain, redness, tearing, photophobia, and progressive visual deterioration. Slit-lamp examination typically demonstrates a dry, gray-white stromal infiltrate with feathery margins, satellite lesions, endothelial plaques, and occasionally a fixed hypopyon. Filamentous fungi such as *Fusarium* and *Aspergillus* often invade deeply into the corneal stroma, making treatment difficult and increasing the risk of corneal perforation[42].

Viral Keratitis

Viral keratitis is most commonly caused by herpes simplex virus type 1 (HSV-1) and typically presents with recurrent episodes of unilateral ocular pain, photophobia, lacrimation, blurred vision, and conjunctival redness. The classic clinical feature is a dendritic corneal ulcer, which stains positively with fluorescein and represents active epithelial infection. Recurrent HSV infection may progress to stromal keratitis, endothelial keratitis, or neurotrophic keratopathy, resulting in corneal scarring and permanent visual impairment. In cases caused by varicella-zoster virus (VZV), pseudodendritic lesions, decreased corneal sensation, and chronic inflammation are frequently observed[43].

Acanthamoeba Keratitis

Acanthamoeba keratitis is characterized by severe ocular pain that is often disproportionate to the clinical findings, making it an important diagnostic clue. Additional symptoms include photophobia, blurred vision, excessive tearing, and foreign body sensation. Early disease may resemble viral or bacterial keratitis, frequently resulting in delayed diagnosis. As the infection advances, slit-lamp examination may reveal radial keratoneuritis, ring-shaped stromal infiltrates, epithelial defects, stromal edema, and anterior uveitis. The disease often follows a chronic course because *Acanthamoeba* cysts are highly resistant to antimicrobial therapy. Although the clinical presentation of infectious keratitis varies according to the causative organism, considerable overlap exists among different pathogens. Therefore, clinical examination alone is often insufficient for establishing a definitive diagnosis. Laboratory investigations, including corneal scraping, microbiological culture, polymerase chain reaction (PCR), real-time PCR (RT-qPCR), confocal microscopy, and next-generation sequencing (NGS), play an essential role in accurately identifying the causative microorganism and guiding targeted antimicrobial

therapy.Prompt recognition of clinical manifestations, combined with early microbiological confirmation, is essential for initiating appropriate treatment, minimizing corneal damage, preserving visual acuity, and reducing the risk of complications such as corneal scarring, perforation, endophthalmitis, and irreversible blindness[45].

Current Diagnostic Approaches :

Early and accurate diagnosis of infectious keratitis (IK) is essential for preventing corneal scarring, irreversible vision loss, and other sight-threatening complications. Because the clinical manifestations of bacterial, fungal, viral, and protozoal keratitis frequently overlap, relying solely on clinical findings may lead to delayed or inappropriate treatment. Therefore, prompt identification of the causative pathogen is critical for selecting targeted antimicrobial therapy and improving patient outcomes[46]. Conventional diagnostic methods, including slit-lamp biomicroscopy, corneal scraping, direct microscopy, and microbial culture, remain the cornerstone of routine clinical practice. These techniques are relatively inexpensive and widely available; however, they have several limitations, including variable sensitivity, prolonged turnaround time, and reduced diagnostic accuracy in patients who have received prior antimicrobial treatment. Recent advances in molecular diagnostics have significantly improved the rapid and accurate detection of ocular pathogens. Techniques such as polymerase chain reaction (PCR), real-time PCR (RT-qPCR), next-generation sequencing (NGS), and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) offer higher sensitivity and specificity than conventional methods, enabling the identification of fastidious, slow-growing, or culture-negative microorganisms[47]. In addition, artificial intelligence (AI)-based image analysis has emerged as a promising diagnostic tool for differentiating various types of infectious keratitis using slit-lamp photographs and other ophthalmic imaging modalities. A multimodal diagnostic approach that combines clinical assessment with microbiological and molecular techniques provides the highest diagnostic accuracy, facilitates early initiation of appropriate therapy, reduces unnecessary antimicrobial use, and ultimately improves visual outcomes in patients with infectious keratitis. The principal diagnostic approaches are summarized below.

Slit-Lamp Examination

Slit-lamp biomicroscopy is the first-line diagnostic tool for evaluating patients with suspected infectious keratitis. It enables detailed examination of the cornea and anterior segment, allowing clinicians to assess the size, depth, location, and characteristics of corneal ulcers and stromal infiltrates. Additional findings such as epithelial defects, conjunctival hyperemia, corneal edema, anterior chamber inflammation, hypopyon, endothelial plaques, and corneal thinning can also be evaluated. Although certain clinical patterns may suggest the causative organism—for example, dendritic ulcers in herpes simplex keratitis or feathery-edged infiltrates in fungal keratitis—clinical examination alone is insufficient to establish a definitive diagnosis because considerable overlap exists among different pathogens[48].

Corneal Scraping

Corneal scraping remains the cornerstone of microbiological diagnosis and should ideally be performed before initiating antimicrobial therapy. Specimens are collected from the base and edges of the corneal ulcer using a sterile blade, spatula, or needle under topical anesthesia. The collected material is used for direct microscopic examination, microbial culture, and molecular diagnostic testing. Adequate specimen collection significantly improves diagnostic accuracy and facilitates early pathogen identification[49].

Gram Stain and Potassium Hydroxide (KOH) Preparation

Direct microscopic examination provides rapid preliminary information regarding the etiological agent. Gram staining is routinely used to differentiate Gram-positive and Gram-negative bacteria while simultaneously assessing the presence of inflammatory cells. It is a simple, inexpensive, and widely available technique that provides immediate guidance for empirical antibiotic therapy.For suspected fungal infections, 10% potassium hydroxide (KOH) wet mount is considered one of the most effective rapid screening methods because it dissolves cellular debris while preserving fungal hyphae and yeast cells. The diagnostic sensitivity can be further improved using Calcofluor White, Giemsa stain, or Periodic Acid–Schiff (PAS) staining. In cases of *Acanthamoeba* keratitis, Calcofluor White and Giemsa staining may help visualize trophozoites and cysts, although their sensitivity remains limited compared with molecular techniques[50].

Culture Techniques

Microbial culture remains the conventional gold standard for confirming the causative organism and determining antimicrobial susceptibility. Corneal specimens are inoculated onto appropriate culture media depending on the suspected pathogen. Blood agar, chocolate agar, and MacConkey agar are commonly used for bacterial isolation, whereas Sabouraud dextrose agar is preferred for fungal pathogens. *Acanthamoeba* is typically cultured on non-nutrient agar seeded with *Escherichia coli*. Culture provides definitive organism identification and enables antimicrobial susceptibility testing (AST), which is particularly important in the era of increasing antimicrobial resistance. However, its limitations include relatively low sensitivity, prolonged incubation time, prior antimicrobial exposure, and false-negative results, especially in viral infections and fastidious organisms[51].

Polymerase Chain Reaction (PCR) and Real-Time PCR (RT-qPCR)

Polymerase chain reaction (PCR) has become an indispensable molecular diagnostic tool for infectious keratitis because of its high sensitivity, specificity, and rapid turnaround time. PCR detects microbial DNA directly from corneal specimens, making it particularly useful when culture results are negative or when patients have received prior antimicrobial therapy. It has demonstrated excellent diagnostic performance for bacterial, fungal, viral, and protozoal pathogens, especially *Herpes simplex virus*, *Varicella-zoster virus*, *Acanthamoeba*, and fungal species. Real-time quantitative PCR (RT-qPCR) further enhances diagnostic accuracy by simultaneously detecting and quantifying microbial DNA during amplification. Compared with conventional PCR, RT-qPCR offers shorter processing time, lower contamination risk, greater analytical sensitivity, and the ability to monitor pathogen load during treatment. Consequently, RT-qPCR is increasingly considered one of the most valuable molecular diagnostic techniques for infectious keratitis[52].

Next-Generation Sequencing (NGS)

Next-generation sequencing (NGS) has emerged as a highly advanced diagnostic platform capable of simultaneously identifying bacteria, fungi, viruses, and protozoa from a single clinical specimen without requiring prior knowledge of the suspected pathogen. Unlike conventional PCR, which targets specific microorganisms, NGS performs comprehensive metagenomic analysis of all microbial DNA present within the sample. This technology is particularly valuable for diagnosing polymicrobial infections, culture-negative keratitis, and infections caused by rare or previously unrecognized pathogens. Despite its excellent diagnostic accuracy, widespread clinical implementation remains limited because of high cost, specialized bioinformatics requirements, and limited accessibility[53].

Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS)

Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS) has revolutionized microbiological diagnostics by providing rapid and highly accurate identification of cultured microorganisms. This technology identifies bacterial and fungal isolates through analysis of unique protein mass spectra that are compared with reference databases. MALDI-TOF significantly reduces laboratory turnaround time from several days to only a few minutes after culture growth and has demonstrated excellent accuracy for identifying bacterial and fungal pathogens associated with infectious keratitis. However, because the technique generally requires prior microbial isolation, it cannot completely replace molecular diagnostic methods[54].

Emerging Therapeutic Strategies

The management of infectious keratitis (IK) has traditionally relied on topical antimicrobial agents, including antibiotics, antifungal drugs, antivirals, and antiamoebic medications. Although these treatments remain the cornerstone of therapy, their effectiveness is increasingly challenged by antimicrobial resistance, poor corneal drug penetration, microbial biofilm formation, prolonged treatment duration, and recurrent infections. Consequently, considerable research has focused on developing novel therapeutic approaches that enhance antimicrobial efficacy, reduce tissue damage, and improve visual outcomes. Emerging strategies include new antimicrobial agents, antimicrobial peptides, corneal collagen cross-linking (PACK-CXL), bacteriophage therapy, nanoparticle-based drug delivery systems, stem-cell therapy, and immunotherapy[55].

New Antibiotics

The increasing prevalence of multidrug-resistant (MDR) pathogens has prompted the development of novel antibiotics with improved antimicrobial activity and enhanced ocular penetration. Recent-generation fluoroquinolones, such as besifloxacin and delafloxacin, demonstrate broader antibacterial spectra and greater efficacy against resistant Gram-positive and Gram-negative organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA). Novel lipoglycopeptides, oxazolidinones, and antimicrobial combinations are also being investigated for severe bacterial keratitis. In addition to developing new agents, optimizing topical drug delivery and antimicrobial stewardship are essential strategies to reduce resistance and preserve antibiotic effectiveness[56].

Antimicrobial Peptides

Antimicrobial peptides (AMPs) are naturally occurring components of the innate immune system that exhibit broad-spectrum activity against bacteria, fungi, viruses, and protozoa. These peptides eliminate pathogens primarily by disrupting microbial cell membranes, thereby reducing the likelihood of resistance development. Examples include human β-defensins, cathelicidin (LL-37), melittin, and lactoferrin-derived peptides. Beyond their direct antimicrobial effects, AMPs possess anti-inflammatory and wound-healing properties that promote corneal epithelial regeneration. Current research focuses on improving peptide stability, minimizing cytotoxicity, and developing sustained-release ocular formulations for clinical application[57].

Photoactivated Chromophore for Infectious Keratitis–Corneal Collagen Cross-Linking (PACK-CXL)

Photoactivated chromophore for infectious keratitis–corneal collagen cross-linking (PACK-CXL) has emerged as a promising adjunctive treatment for infectious keratitis. The technique involves topical application of riboflavin (vitamin B_2) followed by ultraviolet-A (UVA) irradiation, generating reactive oxygen species that exert direct antimicrobial activity while strengthening stromal collagen fibers. PACK-CXL also increases corneal resistance to enzymatic degradation, thereby reducing stromal melting and the risk of perforation. Clinical studies suggest that PACK-CXL may shorten healing time and improve outcomes in bacterial and selected fungal keratitis when combined with conventional antimicrobial therapy. However, evidence regarding its effectiveness in deep fungal or *Acanthamoeba* infections remains limited, and additional randomized controlled trials are required[58].

Phage Therapy

Bacteriophage (phage) therapy represents an innovative biological approach for treating antibiotic-resistant bacterial keratitis. Bacteriophages are viruses that selectively infect

and lyse bacterial cells without affecting human tissues or the normal ocular microbiota. Phage therapy has demonstrated promising activity against MDR pathogens, particularly *Pseudomonas aeruginosa* and *Staphylococcus aureus*, both of which are major causes of bacterial keratitis. Advantages include high specificity, self-replication at the site of infection, and effectiveness against biofilm-producing bacteria. Although preclinical studies have shown encouraging results, further clinical trials are necessary to establish optimal dosing, safety, and regulatory approval[59].

Nanoparticles

Nanotechnology has become one of the most promising approaches for improving ocular drug delivery in infectious keratitis. Nanoparticles—including silver nanoparticles (AgNPs), gold nanoparticles (AuNPs), liposomes, polymeric nanoparticles, solid lipid nanoparticles, and nanogels—enhance drug solubility, prolong corneal residence time, improve tissue penetration, and provide controlled drug release. Silver nanoparticles exhibit intrinsic antibacterial, antifungal, and antiviral activity through the generation of reactive oxygen species, membrane disruption, and inhibition of microbial DNA replication. Nanoparticle-based formulations may reduce dosing frequency, minimize systemic toxicity, and improve therapeutic outcomes, although their long-term ocular safety requires further investigation[60].

Stem-Cell Therapy

Stem-cell therapy has emerged as a regenerative strategy for restoring corneal structure and function following severe infectious keratitis. Mesenchymal stem cells (MSCs) possess anti-inflammatory, immunomodulatory, antimicrobial, and tissue-repair properties through the secretion of growth factors, cytokines, and extracellular vesicles. Limbal stem-cell transplantation has also demonstrated success in patients with limbal stem-cell deficiency resulting from severe corneal infections. Experimental studies suggest that stem-cell therapy accelerates epithelial healing, suppresses excessive inflammation, reduces corneal scarring, and promotes stromal regeneration. However, additional clinical studies are needed to determine long-term efficacy, optimal delivery methods, and safety[61].

Immunotherapy

Excessive inflammatory responses contribute significantly to corneal tissue destruction during infectious keratitis. Consequently, immunotherapy has gained increasing attention as an adjunctive treatment aimed at modulating host immune responses while preserving antimicrobial defense. Potential immunotherapeutic strategies include monoclonal antibodies targeting inflammatory cytokines, cytokine inhibitors, Toll-like receptor modulators, regulatory T-cell therapies, and immunomodulatory biologics. Agents targeting tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6), and interleukin-17 (IL-17**)** are currently under investigation for reducing excessive corneal inflammation and preventing stromal destruction. Future precision medicine approaches may combine molecular pathogen identification with individualized immunomodulatory therapy to optimize clinical outcomes[62].

Conclusion :

Infectious keratitis remains a major cause of corneal blindness worldwide, requiring early diagnosis and prompt treatment to prevent severe complications. Conventional diagnostic methods remain important, while advanced molecular techniques such as PCR, RT-qPCR, NGS, and MALDI-TOF MS have significantly improved the rapid and accurate identification of causative pathogens. The growing challenge of antimicrobial resistance has accelerated the development of innovative therapeutic approaches, including new antibiotics, antimicrobial peptides, PACK-CXL, phage therapy, nanoparticle-based drug delivery, stem-cell therapy, and immunotherapy. Continued advances in molecular diagnostics, artificial intelligence, and targeted therapies are expected to improve disease management, preserve vision, and reduce the global burden of infectious keratitis.

Disclosure statement

No conflict of interest was reported by the author.

References

[1].Shekhawat, N. (2025). Precision Medicine for Diagnosis of Microbial Keratitis. *International ophthalmology clinics*, *65*(2), 20-25.

[2].Ting DSJ, Ho CS, Cairns J, Elsahn A, Al-Aqaba M, Boswell T, et al. 12-year analysis of incidence, microbiological profiles and in vitro antimicrobial susceptibility of infectious keratitis: the Nottingham infectious keratitis study. Br J Ophthalmol. 2021;105:328–33.

[3].González-Dibildox LA, Oyervidez-Alvarado JA, Vazquez-Romo KA, Ramos-Betancourt N, Hernandez-Quintela E, Beltran F, et al. Polymicrobial keratitis: risk factors, clinical characteristics, bacterial profile, and antimicrobial resistance. Eye Contact Lens. 2021;47:465–70.

[4].de Lacerda AG, Lira M. Acanthamoeba keratitis: a review of biology, pathophysiology and epidemiology. Ophthalmic Physiol Opt. 2021;41:116–35.

[5].Ma KK, Ung L, Chodosh J. Evidence-based management of culture-negative microbial Keratitis. Int Ophthalmol Clin. 2022;62:111–24.

[6].Iwen PC, Hinrichs SH, Rupp ME. Utilization of the internal transcribed spacer regions as molecular targets to detect and identify human fungal pathogens. Med Mycol. 2022;40(1):87–109. https://doi.org/10.1080/mmy.40.1.87.109.

[7].Zhang Z, Cao K, Liu J, Wei Z, Xu X, Liang Q. Pathogens and antibiotic susceptibilities of global bacterial keratitis: a meta-analysis. Antibiotics. 2022;11.

[8].Ghenciu, L. A., Faur, A. C., Bolintineanu, S. L., Salavat, M. C., & Maghiari, A. L. (2024). Recent advances in diagnosis and treatment approaches in fungal keratitis: a narrative review. *Microorganisms*, *12*(1), 161.

[9].Gurnani, B., & Kaur, K. (2024). Advances in Diagnosis and Management of Infectious Keratitis. *Current Advances in Optometry*, 19-45.

[10].Joseph, J., & Sharma, S. (2026). Advances in the laboratory diagnosis of non-viral microbial keratitis. *British Journal of Ophthalmology*.

[11].Cabrera-Aguas, M., Khoo, P., & Watson, S. L. (2022). Infectious keratitis: A review. *Clinical & experimental ophthalmology*, *50*(5), 543-562.

[12]. Agarwal, S., Khan, T. A., Vanathi, M., Srinivasan, B., Iyer, G., & Tandon, R. (2022). Update on diagnosis and management of refractory corneal infections. *Indian journal of ophthalmology*, *70*(5), 1475-1490.

[13]. Akter, T., Baishnab, S. M., Damtie, M., Dumpati, S., Eshete, T. B., Irfan, S., ... & Willcox, M. (2025). A review of technological advances in the management of bacterial, fungal, viral, and Acanthamoeba keratitis. *Clinical and Experimental Optometry*, 1-11.

[14]. Soleimani, M., Cheraqpour, K., Sadeghi, R., Pezeshgi, S., Koganti, R., & Djalilian, A. R. (2023). Artificial intelligence and infectious keratitis: where are we now?. *Life*, *13*(11), 2117.

[15]. Kiyat, P., & Palamar, M. (2025). Acanthamoeba keratitis: from pathophysiology to prevention, a contemporary clinical perspective. *Medical Hypothesis, Discovery and Innovation in Ophthalmology*, *14*(3), 146.

[16]. Hoffman, J. J., Burton, M. J., & Leck, A. (2021). Mycotic keratitis—a global threat from the filamentous fungi. *Journal of Fungi*, *7*(4), 273.

[17]. Song, A., Deshmukh, R., Lin, H., Ang, M., Mehta, J. S., Chodosh, J., ... & Ting, D. S. (2021). Post-keratoplasty infectious keratitis: epidemiology, risk factors, management, and outcomes. *Frontiers in Medicine*, *8*, 707242.

[18]. Mirzaei, A., Shahgoli, S. S., Kognati, R., Karaca, E. E., Cheraqpour, K., Alahyari, F., ... & Soleimani, M. (2024). Overcoming Resistance: A Comprehensive Review and Treatment Approach for Acyclovir-Resistant Herpes Simplex Keratitis. *Journal of current ophthalmology*, *36*(4), 342-347.

[19]. Akter, T., Islam, S., Khan, S., Zillur Rahman, K. M., Lubna, M. A., Stapleton, F., & Willcox, M. (2026). Role of cell-associated and secretion-independent virulence factors of Pseudomonas aeruginosa in microbial keratitis and anti-virulence therapeutic strategies. *European Journal of Clinical Microbiology & Infectious Diseases*, 1-13.

[20]. Singh, R. B., Parmar, U. P. S., Woreta, F., Srikumaran, D., Sharma, N., & Jhanji, V. (2025). Global burden, risk factors, causative organisms and antibiotic susceptibility patterns in bacterial keratitis. *The Ocular Surface*.

[21]. Österhed, E., Oldberg, K., & Gustafsson, I. (2025). Aetiology and antibiotic susceptibility of bacterial keratitis at a referral centre in southern Sweden. *Scientific Reports*, *15*(1), 20123.

[22]. Fingerhut, L., Cheng, K. K. W., Ali, A., & Mills, B. (2025). Implications of fungal biofilms in microbial keratitis. In *Fungal Biofilms* (pp. 335-394). Cham: Springer Nature Switzerland.

[23]. Eom, Y. (2025). Contact Lens-associated Microbial Keratitis. *Annals of Optometry and Contact Lens*, *24*(3), 97-109.

[24]. Tew, T. B., Chu, H. S., Hou, Y. C., Chen, W. L., Wang, I. J., & Hu, F. R. (2020). Therapeutic penetrating keratoplasty for microbial keratitis in Taiwan from 2001 to 2014. *Journal of the Formosan Medical Association*, *119*(6), 1061-1069.

[25].. Das, S., Samantaray, R., Mallick, A., Sahu, S. K., & Sharma, S. (2019). Types of organisms and in-vitro susceptibility of bacterial isolates from patients with microbial keratitis: A trend analysis of 8 years. *Indian Journal of Ophthalmology*, *67*(1), 49-53.

[26]. Altamirano D, Martinez J, Leviste KD, Parel JM, Amescua G (2020) Photodynamic therapy for infectious Keratitis. Curr Ophthalmol Rep 8:245–251.

[27]. Arimoto S, Inagaki K, Todokoro D, Suzuki T, Makimura K, Ishino T (2023) Antifungal efficacy of luliconazole in an experimental rabbit model of fungal keratitis caused by Fusarium solani. Mycopathologia 188:775–782.

[28]. Arunachalam D, Namperumalsamy VP, Prajna L, Kuppamuthu D (2021) Human corneal epithelial cells internalize Aspergillus flavus spores by actin-mediated endocytosis. Infect Immun 89.

[29]. Arunga S, Wiafe G, Habtamu E, Onyango J, Gichuhi S, Leck A, Macleod D, Hu V, Burton M (2019) The impact of microbial keratitis on quality of life in Uganda. BMJ Open Ophthalmol 4:e000351

[30]. Aydin B, Cubuk MO, Ucgul A, Ertop M, Ozmen MC, Atalay T, Akata F (2020) Combined Intrastromal Voriconazole and Amphotericin B treatment for persistent fungal keratitis. Eye Contact Lens 46:269–273

[31]. Bagga B, Sharma S, Ahirwar LK, Sheba E, Vaddavalli PK, Mishra DK (2022) Clinical outcomes of rose bengal mediated photodynamic antimicrobial therapy on fungal

keratitis with their microbiological and pathological correlation. Curr Eye Res 47:987–994

[32]. Balakrishnan Sangeetha A, Abdel-Hadi A, Hassan AS, Shobana CS, Suresh S, Abirami B, Selvam KP, AL-Baradie RS, Banawas S, Alaidarous M, Alshehri B, Dukhyil AAB, Dhanasekaran S, Manikandan P (2020) Evaluation of in vitro activities of extracellular enzymes from Aspergillus species isolated from corneal ulcer/keratitis. Saudi J Biol Sci 27:701–705.

[33]. Bautista-Hernandez LA, Gomez-Olivares JL, Buentello-Volante B, Dominguez-Lopez A, Garfias Y, Acosta-Garcia MC, Calvillo-Medina RP, Bautista-de Lucio VM (2019) Negative interaction of Staphylococcus aureus on Fusarium falciforme growth ocular isolates in an in vitro mixed biofilm. Microb Pathog 135:103644.

[34]. Benson S, Kiang A, Lochenie C, Lal N, Mohanan SMP, Williams GO, Dhaliwal K, Mills B, Vendrell M (2023) Environmentally sensitive photosensitizers enable targeted photodynamic ablation of Gram-positive antibiotic resistant bacteria. Theranostics 13:3814

[35]. Bhardwaj SK, Singh H, Deep A, Khatri M, Bhaumik J, Kim K-H, Bhardwaj N (2021) UVC-based photoinactivation as an efficient tool to control the transmission of coronaviruses. Sci Total Environ 792:148548.

[36]. Blango MG, Kniemeyer O, Brakhage AA (2019) Conidial surface proteins at the interface of fungal infections. PLoS Pathogens 15:e1007939.

[37]. Brown ME, Montgomery ML, Kamath MM, Nicholas S, Liu Y, Karamichos D, Fuller KK (2021b) A novel 3D culture model of fungal keratitis to explore host-pathogen interactions within the stromal environment. Exp Eye Res 207:108581.

[38]. Brown L, Kamwiziku G, Oladele RO, Burton MJ, Prajna NV, Leitman TM, Denning DW (2022) The case for fungal keratitis to be accepted as a neglected tropical disease. J Fungi 8:1047

[39]. Calvillo-Medina RP, Reyes-Grajeda JP, Barba-Escoto L, Bautista-Hernandez LA, Campos-Guillen J, Jones GH, Bautista-de Lucio VM (2019) Proteome analysis of biofilm produced by a Fusarium falciforme keratitis infectious agent. Microb Pathog 130:232–241.

[40]. Chatterjee S, Agrawal D (2022) Use of topical Cyclosporine 0.1% in therapeutic penetrating keratoplasty for Fungal Keratitis. Cornea 41:1116–1121.

[41]. Chen X, Li X, Zhang X, Guo X, Qi X, Li S, Shi W, Gao H (2021) Comparison of complications and visual outcomes between big-bubble deep anterior lamellar keratoplasty and penetrating keratoplasty for fungal keratitis. Clin Exp Ophthalmol 49:550–559

[42]. Chen X, Lu D, Liu W, Xie J, Lu Z, Yang H, Yan H, Wang L, Che C (2023) Therapeutic effect of Atractylenolide I on Aspergillus fumigatus keratitis by affecting MyD88/NF-kappaB pathway and IL-1beta, IL-10 expression. Cytokine 162:156112.

[43]. Cheng KKW, Fingerhut L, Duncan S, Prajna NV, Rossi AG, Mills B (2024) In vitro and ex vivo models of microbial keratitis: present and future. Prog Retin Eye Res 102:101287.

[44]. Chi M, Gu L, Zhang L, Lin J, Xu Q, Jiang N, Wang Y, Qi Y, Diao W, Yi W, Zhao G, Li C (2023) Pentoxifylline treats Aspergillus fumigatus keratitis by reducing fungal burden and suppressing corneal inflammation. Eur J Pharmacol 945:175607.

[45]. Chou B, Krishna K, Durkee H, Tribin FE, Ahmed A, Lai J, Aguilar MC, Ferreira BC, Leblanc RM, Flynn HW Jr (2025) Photodynamic antimicrobial therapy with Erythrosin B, Eosin Y, and Rose Bengal for the inhibition of fungal keratitis isolates: an in vitro study. J Photochem Photobiol B Biol 263:113090

[46]. Córdova-Alcántara IM, Venegas-Cortés DL, Martínez-Rivera MÁ, Pérez NO, Rodriguez-Tovar AV (2019) Biofilm characterization of Fusarium solani keratitis isolate: increased resistance to antifungals and UV light. J Microbiol 57:485–497.

[47]. Agarwal S, Khan TA, Vanathi M, Srinivasan B, Iyer G, Tandon R. Update on diagnosis and management of refractory corneal infections. *Indian J Ophthalmol*. 2022;70(5):1475. doi:10.4103/ijo.IJO_2273_21.

[48]. Said DG, Rallis KI, Al-Aqaba MA, Ting DSJ, Dua HS. Surgical management of infectious keratitis. *Ocul Surf*. 2023;28:401–412. doi:10.1016/j.jtos.2021.09.005.

[49]. Ting DSJ, Cairns J, Gopal BP, Ho CS, Krstic L, Elsahn A, et al. Risk factors, clinical outcomes, and prognostic factors of bacterial keratitis: the Nottingham Infectious Keratitis Study. *Front Med*. 2021;8:715118. doi:10.3389/fmed.2021.715118.

[50]. Lamas-Francis D, Navarro D, Mansilla R, de-Rojas V, Moreno C, Dios E, et al. Microbial keratitis in north-western Spain: a review of risk factors, microbiological profile and resistance patterns. *Eur J Clin Microbiol Infect Dis*. 2024. doi:10.1007/s10096-024-04978-6

[51]. Egrilmez S, Yildirim-Theveny Ş. Treatment-resistant bacterial keratitis: challenges and solutions. *Clin Ophthalmol*. 2020;14:287–297. doi:10.2147/OPTH.S181997.

[52]. Kryszan K, Wylęgała A, Kijonka M, Potrawa P, Walasz M, Wylęgała E, et al. Artificial-intelligence-enhanced analysis of in vivo confocal microscopy in corneal diseases: a review. *Diagnostics (Basel)*. 2024;14(7):694.

[53]. Lamas-Francis D, Navarro D, Mansilla R, de-Rojas V, Moreno C, Dios E, et al. Fungal keratitis in Northwestern Spain: epidemiology, risk factors and outcomes. *J Fungi*. 2024;10(10):689.

[54]. Iovieno A, Ledee DR, Miller D, Alfonso EC. Detection of bacterial endosymbionts in clinical acanthamoeba isolates. *Ophthalmology*. 2010;117(3):445–452, 452.e1–3.

[55]. Scruggs BA, Quist TS, Zimmerman MB, Salinas JL, Greiner MA. Risk factors, management, and outcomes of Acanthamoeba keratitis: a retrospective analysis of 110 cases. *Am J Ophthalmol Case Rep*. 2022;25:101372.

[56]. Al-Dhaheri HS, Al-Tamimi MD, Khandekar RB, Khan M, Stone DU. Ocular pathogens and antibiotic sensitivity in bacterial keratitis isolates at King Khaled Eye Specialist Hospital, 2011 to 2014. *Cornea*. 2016;35(6):789–794

[57]. Oliveira-Ferreira C, Leuzinger-Dias M, Tavares-Ferreira J, Torrão L, Falcão-Reis F. Microbiological profile of infectious keratitis in a Portuguese tertiary centre. *J Ophthalmol*. 2019;2019:1–6.

[58]. Dunster E, Johnson WL, Wozniak RAF. Antimicrobial drug-drug interactions in the treatment of infectious keratitis. *Cornea*. 2023;42(12):1555–1561

[59]. Tuft S, Somerville TF, Li JPO, Neal T, De S, Horsburgh MJ, et al. Bacterial keratitis: identifying the areas of clinical uncertainty. *Prog Retin Eye Res*. 2022;89:101031. doi:10.1016/j.preteyeres.2021.101031.

[60]. Ting DSJ, Henein C, Said DG, Dua HS. Amniotic membrane transplantation for infectious keratitis: a systematic review and meta-analysis. *Sci Rep*. 2021;11(1):13007

[61]. Cabrera-Aguas M, Khoo P, Watson SL. Presumed microbial keratitis cases resulting in evisceration and enucleation in Sydney, Australia. *Ocul Immunol Inflamm*. 2023;31(1):224–230.

[62]. Dohse N, Wibbelsman TD, Rapuano SB, Hammersmith KM, Nagra PK, Rapuano CJ, et al. Microbial keratitis and clinical outcomes following penetrating and endothelial keratoplasty. *Acta Ophthalmol*. 2020;98(7):e895–e900.