Review Article

Acanthamoeba keratitis: from pathophysiology to prevention, a contemporary clinical perspective

Pelin Kiyat [1] and Melis Palamar [2]

[1] *Buca Seyfi Demirsoy Training and Research Hospital Department of Ophthalmology, Izmir Democracy University, Izmir, Turkiye*
[2] *Department of Ophthalmology, Ege University, Izmir, Turkiye*

ABSTRACT

Background: Acanthamoeba keratitis represents a devastating corneal infection caused by free-living protozoan organisms. This condition has evolved from an extraordinarily rare disease to a significant public health concern, with increasing global incidence. The infection predominantly affects contact lens wearers and poses substantial diagnostic and therapeutic challenges. This narrative review aims to provide analysis of current knowledge regarding Acanthamoeba keratitis, including epidemiology, pathogenesis, diagnostic approaches, treatment strategies, and prevention methods, to guide clinicians in optimal patient management.

Methods: This review was conducted through a literature search of PubMed-indexed journals from January 2000 to August 2025, incorporating current information on pathophysiology, clinical features, diagnosis, therapy, and outcomes of Acanthamoeba keratitis. Keywords included "Acanthamoeba keratitis", "contact lens-related keratitis", "Acanthamoeba diagnosis", and "Acanthamoeba treatment". English-language publications including original articles, reviews, case reports, and clinical studies were included based on relevance to current diagnostic and therapeutic practices, with an emphasis on recent advances in the field.

Results: Contact lens wearers comprised the vast majority of cases, with soft contact lens users representing the predominant affected population. Peak occurrence involves young adults aged 20–40 years, with water-based transmission through contaminated domestic supplies representing a significant risk pathway. Clinical manifestations commonly include epithelial abnormalities, stromal infiltration, and ring infiltrates in advanced cases. Traditional culture methods evidence limited sensitivity (33–67%), while advanced diagnostic approaches include polymerase chain reaction (PCR) and in vivo confocal microscopy (IVCM) achieving superior accuracy (sensitivity 77–100%, specificity 84–100%). First-line therapy employs biguanides and diamidines with prolonged administration. Advanced treatment options include oral miltefosine for refractory cases, azole antifungals, and surgical interventions ranging from epithelial debridement to corneal transplantation. Early diagnostic recognition represents the strongest predictor of visual recovery, with diagnostic delays associated with poor prognosis.

Conclusions: Acanthamoeba keratitis management requires high clinical suspicion, rapid diagnosis using advanced techniques such as IVCM and PCR, and prolonged antimicrobial therapy. Early diagnosis remains the most important predictor of visual recovery. Prevention through proper contact lens hygiene and water exposure avoidance is paramount. Future research priorities include development of novel antimicrobial agents and enhanced prevention strategies.

KEYWORDS

acanthamoebas, acanthamoeba keratitides, contact lens, diagnose, routine diagnostic test, polymerase chain reactions, confocal microscopy, miltefosine, azole, surgical procedure

Correspondence: Pelin Kiyat, Buca Seyfi Demirsoy Training and Research Hospital, Kozagac Mah., Ozmen Sok, No:147, Buca / Izmir, Turkiye. Email: pelinkiyat@hotmail.com, ORCID iD: https://orcid.org/0000-0002-3581-7059.

How to cite this article: Kiyat P, Palamar M. Acanthamoeba keratitis: from pathophysiology to prevention, a contemporary clinical perspective. Med Hypothesis Discov Innov Ophthalmol. 2025 Fall; 14(3): 146-162. https://doi.org/10.51329/mehdiophthal1528

Received: 08 August 2025; Accepted: 19 September 2025

Copyright © Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (https://creativecommons.org/licenses/by-nc/4.0/) which permits copy and redistribute the material just in noncommercial usages, provided the original work is properly cited.

INTRODUCTION

Acanthamoeba keratitis constitutes an uncommon yet devastating corneal infection affecting patients worldwide. It is caused by Acanthamoeba, free-living amoeba distributed ubiquitously across environmental sources including water, soil, and air, with *Acanthamoeba castellanii* and *Acanthamoeba polyphaga* constituting the two main, most common pathogenic species [1]. The pathological process advances through progressive corneal inflammatory responses, leading to epithelial damage and ulceration, potentially resulting in significant vision impairment absent timely diagnosis and treatment [2]. Clinical significance derives from its increasing frequency and the difficulties associated with diagnosis and management, as symptoms often resemble other types of infectious keratitis. This makes early and accurate recognition challenging [1, 3].

The initial cases were reported in 1974 and 1975, with incidence increasing in the 1980s and 1990s in parallel with the widespread adoption of contact lens use [4]. Between 2009 and 2016, the mean incidence of Acanthamoeba keratitis more than doubled compared with the preceding seven years, reaching 8.3 cases annually, including six bilateral cases, as reported by McKelvie t al. [5]. At least 24 amoebic protozoa species of Acanthamoeba have been recognized, with keratitis representing the main ophthalmic manifestation [6]. These organisms exist widely in environmental water sources such as tap water and swimming pools [6, 7]. Contact lens wearers face the highest risk, with history of contact lens use documented in over 90% of recent cases, though the condition also develops in non-lens users following contaminated water contact or in immunocompromised individuals [1, 4, 6–8].

The serious visual complications associated with this infection require comprehensive understanding from ophthalmologists. This narrative review synthesizes current evidence and recent developments to improve clinical diagnosis, optimize treatment approaches, and enhance prevention strategies. We examine epidemiological patterns, risk factors, disease mechanisms, diagnostic methods, therapeutic options, and outcome predictors outlined in literature while highlighting evidence-based prevention measures for reducing disease burden in at-risk populations.

METHODS

This review was conducted through a comprehensive literature search incorporating current information on pathophysiology, clinical features, diagnosis, medical and surgical therapy, and outcomes of Acanthamoeba keratitis. The review utilized established academic sources and focused on evidence-based approaches to its management. A comprehensive literature search was conducted using PubMed database. The search strategy employed the following keywords: “Acanthamoeba keratitis”, “contact lens-related keratitis”, “Acanthamoeba diagnosis”, and "Acanthamoeba treatment”, combined using Boolean operators (AND, OR). The time interval covered publications from January 2000 to August 2025, with inclusion of seminal earlier studies when historically significant. Types of records included were original research articles, systematic reviews, meta-analyses, case series, case reports, and clinical trials. The search was restricted to English-language publications, although key studies in other languages were included if English abstracts were available and content was deemed essential. Conference abstracts, letters to editors without substantial data, and duplicate publications were excluded to ensure quality and relevance of the included literature. Literature was selected based on relevance to current diagnostic and therapeutic practices, with an emphasis on recent advances in the field.

RESULTS and DISCUSSION

Epidemiological Patterns

Acanthamoeba keratitis has evolved from an extraordinarily rare condition affecting fewer than two individuals per million lens wearers two decades ago to a significant public health concern [1]. Current global statistics reveal 23,561 annual cases, translating to 2.9 per million population and representing 2% of all corneal infections worldwide [1, 9]. This remarkable escalation stems from enhanced diagnostic capabilities, increased physician awareness, and substantial expansion of contact lens markets globally [1].

Furthermore, disease prevalence varies dramatically across continents. American healthcare systems have documented outbreak scenarios connected to point-of-use contamination of lens solutions [10]. Infection rates in Europe continue to climb [11, 12], an upward trend indicating worldwide spread driven by contact lens popularity [12–15]. Peak occurrence involves young adults aged 20–40 years [1], typically affecting healthy patients, though those with weakened immunity or existing ocular surface disorders encounter greater vulnerability [1, 16]. Regional variations in disease etiology reflect contact lens usage patterns. In India, Acanthamoeba keratitis represents approximately 1% of corneal ulcer cases [17], contrasting with much higher prevalence in nations with extensive contact lens adoption [15, 18].

A recent Turkish study of 60 suspected keratitis cases identified Acanthamoeba in 11.66% (n = 7) of patients through polymerase chain reaction (PCR) analysis, revealing T4 and T5 genotypes, with T5 representing the first documented occurrence in Turkiye. Contact lens use was confirmed as the predominant risk factor in this study [19]. Importantly, in regions with limited contact lens utilization the majority were non-contact lens wearers, accounting for 99.1% of individuals with culture-proven Acanthamoeba keratitis [20]. Environmental studies examining tap water sources reveal clear associations between domestic water contamination and disease development [21, 22].

Life Cycle and Pathogenesis

When conditions favor growth—adequate food sources, neutral pH, and approximately 30°C temperatures—the metabolically active trophozoite form undergoes mitotic reproduction [23], being motile at this stage and measuring 25–40 μm in diameter, and initiating corneal tissue invasion [24, 25]. Adverse environmental pressure prompts encystment [26–28]. The resulting protective capsules feature dual-wall construction and measure 15–28 μm in diameter [27]. This survival mechanism allows the parasite to withstand hostile environments that would destroy the vulnerable active form [23]. The ability to produce disease depends on structural and enzymatic mechanisms, with cyst formation representing the most critical feature, as this dormancy process activates during hostile environmental circumstances. The cystic forms exhibit remarkable resilience against temperature variations, conventional disinfection protocols, and radiation exposure while maintaining osmotic tolerance [28–30].

Tissue invasion mechanisms involve acanthopodia-mediated attachment to both biological and synthetic surfaces, while pseudopods give motility and facilitate intercellular penetration pathways [31]. Successful pathogenesis requires intimate cellular contact with host tissues through specialized adhesion molecules [32]. Multiple enzymatic factors contribute to tissue destruction, including neuraminidase, elastase, diverse proteolytic enzymes, glycosidases, and superoxide dismutase, which collectively enable amoebic invasion and subsequent disease manifestation [32–34].

Risk Factors

The development of Acanthamoeba keratitis evidences strong associations with contact lens wear, which nearly 90% of patients do [1]. Infection likelihood increases when users engage in risky behaviors including cleaning lenses with tap water, using outdated or inappropriate cleaning products, ignoring replacement schedules, and practicing prolonged wearing patterns [15, 35]. Overnight lens wear systems create particular hazards by limiting corneal oxygen access and establishing optimal growth conditions for the pathogen [1]. Additional lens-related risk factors encompass insufficient disinfection procedures, poor hygiene standards, and minor trauma from handling procedures [4, 35].

Soft contact lenses dominate the infection pattern across multiple studies, though all lens varieties carry risk [4, 5, 36]. Ross et al. [36] showed that soft lens users comprised 82.1% (n = 69) of 84 affected individuals and 17.9% (n = 15) wore rigid contact lens. Two-four-week daily wear systems were involved in 55.1% (n = 38) of cases and extended wear in 30.4% (n = 21), yet despite expectations of complete safety daily disposable lenses still accounted for 10.1% (n = 7) of patients with Acanthamoeba keratitis [36]. McKelvie et al. [5] reported similar findings, with 90% (n = 48) of cases of Acanthamoeba keratitis involving soft lens wearers where monthly replacement lenses constituted 60.4% (n = 29) of cases, weekly disposable 12.5% (n = 6), and daily disposable 12.5% (n = 6). This confirms that even daily disposable lenses cannot guarantee complete protection [5].

Water-based transmission pathways create substantial infection risks, as the pathogen thrives in household water systems, public swimming areas, and spa facilities. Direct ocular contamination occurs when tap water comes into contact with lenses during cleaning or storage procedures; studies show direct linkage between contaminated domestic water supplies and infection development [21, 22, 37, 38]. Physical eye damage and underlying surface abnormalities establish additional vulnerability pathways. Foreign body injuries or lens-handling trauma create pathogen access routes into corneal tissue [39], while patients with compromised immunity face elevated infection probability [1, 40, 41].

Clinical Presentations

Acanthamoeba keratitis presents as a progressive corneal inflammatory disorder that creates significant diagnostic challenges through its non-specific clinical features, often resembling other infectious keratitis forms [40, 42]. Patients typically experience ocular pain, conjunctival hyperemia, photophobia, and excessive lacrimation [4, 40], although the characteristic severe pain disproportionate with clinical findings may be absent in some cases [43].

Disease progression follows a pattern over weeks to months, starting with epithelial changes and advancing through stromal layers before potentially developing the distinctive ring infiltrate [4, 40]. Current classification systems identify five sequential stages: epithelial inflammation, epithelial inflammation with perineuritis, anterior stromal disease, deep stromal involvement, and ring infiltrate formation, while limbitis and scleritis indicate advanced disease [4, 44].

Initial manifestations include punctate epithelial erosions, gray-dirty epithelium, pseudodendritic patterns, and perineural infiltrates (Figure 1). These features closely resemble viral keratitis, particularly herpes simplex infections, leading to frequent initial misdiagnoses [4, 40, 42, 45]. Additional early signs encompass conjunctival follicles, subepithelial opacities mimicking adenoviral infection, irregular epithelial defects, and microcyst formation [46]. Interestingly, unusual clinical presentations have also been documented in the literature. A case report described negative fluorescein staining as an early sign of Acanthamoeba keratitis, presenting as Y-shaped linear epitheliopathy with ridge-like epithelial irregularity in a contact lens wearer, highlighting the importance of detecting negative fluorescein staining in early diagnosis [47].

Advanced disease involves deeper stromal inflammation with ulceration, anterior chamber reactions, hypopyon formation, and endothelial dysfunction (Figure 2). Radial infiltrates along corneal nerves become increasingly prominent, producing the intense pain characteristic of progressive infection. Multiple stromal infiltrates help distinguish Acanthamoeba keratitis from typically unifocal bacterial keratitis. Wessely immune ring may appear occasionally [40, 46, 48] (Figure 3).

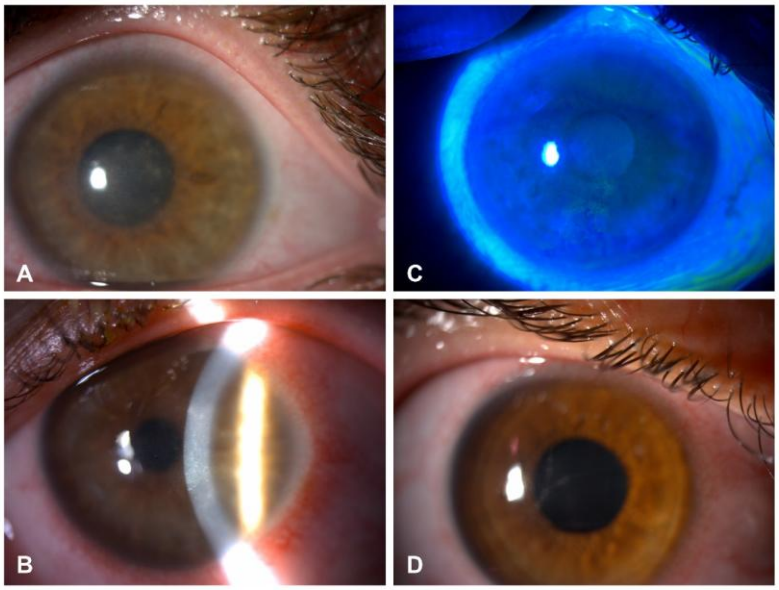

Figure 1. Initial manifestations of Acanthamoeba keratitis. (A) Gray-dirty epithelium showing loss of corneal transparency. (B) Gray-dirty epithelium with punctate epitheliopathy. (C) Pseudo-dendriform lesion. (D) Perineural infiltration showing inflammatory cell accumulation around corneal nerve fibers, a characteristic feature of Acanthamoeba keratitis.

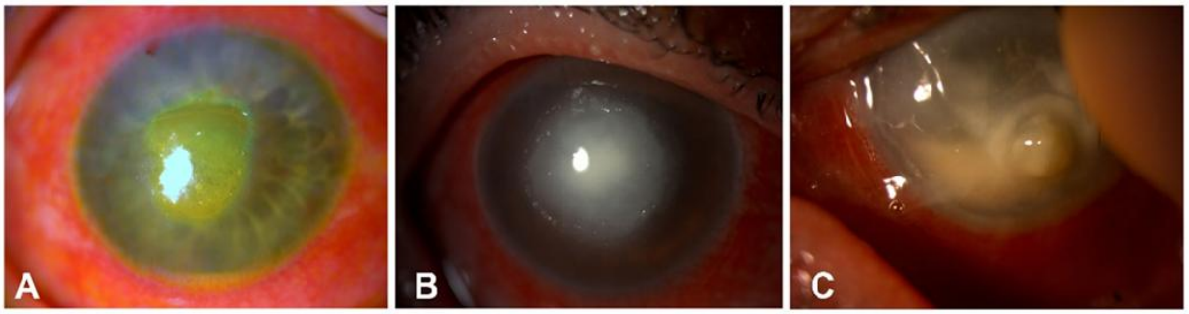

Figure 2. Advanced manifestations of Acanthamoeba keratitis. (A) Extensive epithelial defect with hypopyon formation in the anterior chamber. (B) Stromal keratitis showing deep corneal involvement with inflammatory infiltrates. (C) Suppurative keratitis in end-stage case with severe corneal destruction and purulent inflammation.

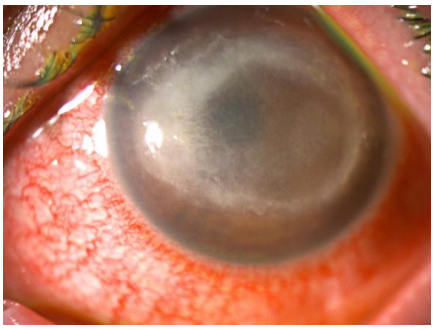

Figure 3. Wessely immune ring in Acanthamoeba keratitis. Characteristic circular inflammatory infiltrate representing an immune-mediated response.

Most cases present unilaterally, with bilateral involvement occurring in only 7.5–11% of patients, primarily contact lens users [46]. Clinical studies show variable presentation frequencies [5, 36, 49]. McKelvie et al. [5] found epithelial abnormalities in 76% (n = 44) of cases, stromal infiltration in 40% (n = 22), anterior chamber reaction in 29% (n = 17), corneal ulceration in 17% (n = 10), pseudodendrites in 14% (n = 8), neurokeratitis in 9% (n = 5), ring stromal infiltrate in 9% (n = 5), hypopyon in 5% (n = 3), and corneal thinning in 2% (n = 1) [5]. Examining 116 patients with Acanthamoeba keratitis, Ross et al. [36] reported epithelial/subepithelial infiltrates in 56% (n = 65) of cases, punctate keratopathy in 52.6% (n = 61), epithelial ulceration in 49.1% (n = 57), ring infiltrate in 29.3% (n = 34), and radial perineuritis in 21.6% (n = 25) [36]. Non–contact lens users with Acanthamoeba keratitis often present with more severe disease, and the absence of typical features such as disproportionate pain, radial keratoneuritis, or ring infiltrate does not rule out the condition in this context. Garg et al. evaluated non-contact lens wearers with Acanthamoeba keratitis and reported ring infiltrates in 33% of cases, whereas radial keratoneuritis was identified in only 2.7% [49]. Complications include secondary glaucoma from trabecular dysfunction and outflow obstruction by inflammatory cells or synechiae formation, along with anterior uveitis, iris atrophy, cataract development, scleral involvement, corneal perforation, and posterior segment extension [4, 46].

Diagnostic Approaches

Traditional Methods

Microscopic examination and culture methods constitute the cornerstone of traditional Acanthamoeba keratitis diagnosis. Culture techniques utilize non-nutrient agar plates with Escherichia coli overlay [50]. When infection is suspected, direct specimen analysis uses various staining approaches. Calcofluor white and potassium hydroxide represent common techniques, while hematoxylin and eosin, periodic acid-Schiff, and Gomori methenamine silver offer additional options [51, 52]. Gram or Giemsa stains show cysts as structures with double walls and clear centers [52]. Potassium hydroxide wet mount works very well with 91.4% sensitivity and 100% specificity, showing cysts as bright structures with double walls [53]. Calcofluor white staining uses a fluorescent dye that sticks to cyst walls, yielding high accuracy but needing special fluorescence microscopes [52, 53].

Culture methods present significant limitations, including prolonged processing times, false-negative results due to suboptimal sensitivity, and requirements for specialized personnel and equipment. Published studies report sensitivity ranging from 33% to 67%, although specificity may reach 100%, with incubation periods extending up to 10 days [54–56]. Successful organism growth enables antimicrobial susceptibility testing to guide therapeutic selection [57]. Despite limitations, culture techniques remain clinically important. Contemporary diagnostic practice integrates multiple methodologies including PCR, immunofluorescence assays, and in vivo confocal microscopy (IVCM) to achieve enhanced diagnostic speed and improved sensitivity [57].

Molecular Diagnostics

PCR represents a powerful molecular technique for rapid deoxyribonucleic acid (DNA) amplification and pathogen detection in Acanthamoeba keratitis diagnosis. This method evidences higher sensitivity and comparable specificity to culture in detecting pathogen genetic material from ocular specimens [58]. PCR technology detects minimal Acanthamoeba DNA concentrations while delivering rapid results that enable early diagnosis and prompt treatment initiation [57]. Target sequences typically involve the 18S ribosomal DNA regions, a core component of 40S small

subunit, showing extreme sensitivity [55, 59]. The combination of primer pairs was observed to enhance diagnostic accuracy, with sensitivity increasing from 81.0% when a single pair was used to 94.0% when three primer pairs were combined [60]. The Schroeder primers, specifically Jun Dimerization Protein (JDP) 1 and JDP2 targeting the 18S ribosomal ribonucleic acid (rRNA) gene, are demonstrated to provide a reliable amplification system for Acanthamoeba detection across all known genotypes [61].

Molecular diagnostics show particular clinical value in patients with prior antibiotic exposure, where culture methods often produce negative results despite persistent clinical suspicion [33]. Advanced genetic sequencing technologies, including next-generation sequencing platforms, provide comprehensive genetic analysis of corneal specimens, enabling precise species identification and detailed genotype characterization [62].

In Vivo Confocal Microscopy

IVCM provides non-invasive, real-time visualization of corneal architecture through high-resolution layer examination, enabling direct pathogen detection and infection severity assessment [57, 62]. This rapid diagnostic capability allows prompt initiation of treatment protocols, resulting in improved patient outcomes. Organism identification depends on characteristic morphological features within corneal tissues [57, 62].

Acanthamoeba cysts appear as round, highly reflective structures measuring 5–20 μm in diameter with double-walled spherical configurations, displaying high-refractive nuclei surrounded by low-refractile rings and dark borders [63]. Acanthamoeba cysts could be challenging to visualize due to their similarity to damaged keratocyte or leukocytes. Four IVCM image patterns—bright spots, target images, clusters of hyperreflective objects, and trophozoite-like objects—were significantly associated with PCR-positive Acanthamoeba keratitis. Target and trophozoite images showed 100% specificity, 98.2% clusters, and 48.2% bright spots. Using the presence of target, cluster, or trophozoite images for diagnosis yielded a positive predictive value of 87.5% and a negative predictive value of 58.5% [64].

Multiple studies have observed IVCM's diagnostic superiority and clinical utility in Acanthamoeba keratitis management. Performance characteristics evidence superior diagnostic accuracy with sensitivity spanning 88.2–100% and specificity 98.2–100% compared to traditional methods [55, 65]. Lee et al. [66] showed that IVCM implementation alongside culture methods resulted in significantly accelerated diagnosis and enhanced visual outcomes compared to culture-only protocols. Hoffman et al. [50] found that IVCM outperformed both PCR and culture techniques, establishing itself as the most sensitive technique for Acanthamoeba keratitis identification. Recchioni et al. [67] documented considerable enhancements in clinical results when IVCM was utilized as a supplementary diagnostic approach, enabling appropriate patient care and timely clinical decision-making [67].

Several limitations affect clinical implementation of IVCM. Diagnostic accuracy depends heavily on operator experience and image interpretation expertise, creating potential variability in results [68]. There are potential false negatives from inflammatory cell masking in stromal disease, and false positives when macrophages mimic Acanthamoeba cysts [57].

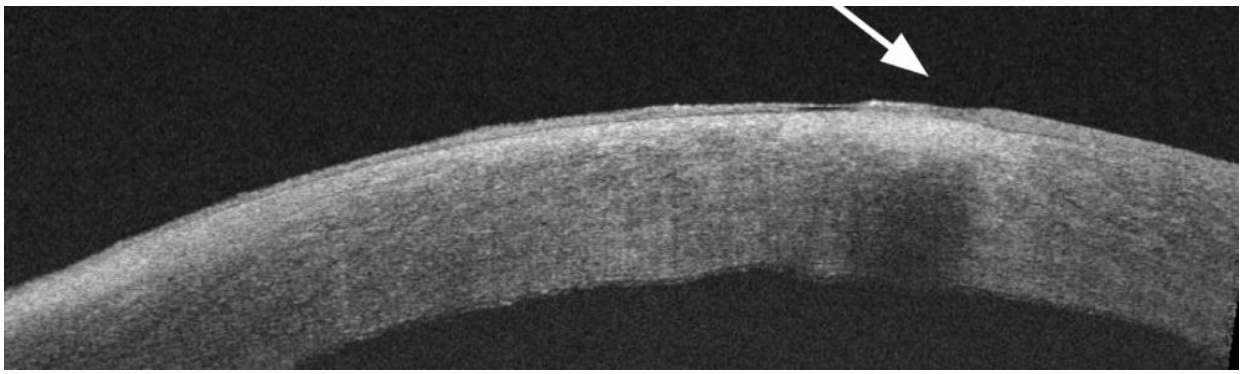

Figure 4. Anterior segment optical coherence tomography (AS-OCT) of Acanthamoeba keratitis, displaying stromal hyperreflectivity.

Anterior Segment Optical Coherence Tomography

Anterior segment optical coherence tomography (AS-OCT) serves as a valuable noninvasive adjunct in Acanthamoeba keratitis evaluation. The technology excels at identifying perineuritis through characteristic reflective oblique bands within deep corneal stroma [69], proving particularly beneficial when stromal edema and infiltrates complicate clinical assessment (Figure 4). However, current AS-OCT systems lack sufficient resolution for direct cyst or trophozoite visualization, limiting their diagnostic scope in organism detection [46].

Machine-Learning Technologies

Artificial intelligence represents a transformative advancement in ophthalmologic diagnostics for Acanthamoeba keratitis detection. Zhang et al. [70] developed KeratitisNet, analyzing slit-lamp photographs. The combination of ResNext101_32x16d and DenseNet169, termed KeratitisNet, achieved the highest performance for diagnosing bacterial, fungal, and herpes simplex keratitis, with an average accuracy of 77.08%. Acanthamoeba-specific detection reached 83.81% accuracy and area under curve of 0.96 [70]. Deep-learning algorithms utilizing IVCM reveal superior characteristics. Essalat et al. [71] developed IVCM-based systems achieving 91.37% sensitivity and 98.25% specificity for diagnosis of Acanthamoeba keratitis. In a retrospective study using 3312 IVCM images from 17 patients with culture-positive Acanthamoeba keratitis, a deep learning–based model achieved sensitivity and specificity of 76% [72]. Koyama et al. [73] adapted a deep-learning architecture originally designed for facial recognition to slit-lamp images, achieving a diagnostic accuracy of 97.9% and an area under the curve of 0.995 for Acanthamoeba keratitis.

Differential Diagnosis

Acanthamoeba keratitis presents significant diagnostic challenges due to clinical features overlapping with other corneal pathologies. Registry data indicate substantial misdiagnosis rates, with cases of Acanthamoeba keratitis initially misdiagnosed as herpetic keratitis in 47.6% of instances, bacterial keratitis in 25.2%, and fungal keratitis in 3.9% [42]. Herpetic keratitis represents the most frequent diagnostic confusion, particularly disciform variants presenting with clinical characteristics of corneal irregularities, ring-shaped infiltrate, and opacity. Herpetic keratitis characteristically presents unilaterally with keratic precipitates, pseudoguttata, and elevated intraocular pressure. The key distinguishing feature is Acanthamoeba's severe pain disproportionate to clinical findings, contrasting with HSV keratoneuritis which typically exhibits reduced corneal sensation and pathognomonic dendritic lesions with terminal bulbs [74–77].

Bacterial keratitis warrants consideration in contact lens users presenting with purulent discharge, rapid progression, and anterior chamber inflammation [40, 78]. Fungal keratitis can closely resemble Acanthamoeba keratitis when ring infiltrates develop, occurring in 1–25% of fungal cases compared with about 30% of Acanthamoeba cases. However, fungal keratitis is typically characterized by feathery borders, satellite lesions, dry-textured infiltrates, and color appearance. Given that pooled prevalence of fungal keratitis was reported as 23.64% of clinically suspected cases of microbial keratitis, this diagnosis merits primary consideration during ring infiltrate evaluation [40, 48, 78, 79].

Non-infectious causes of ring infiltrates include rheumatoid arthritis, which produces sterile corneal rings through immune complex deposition; topical anesthetic abuse or nonsteroidal anti-inflammatory drug toxicity, particularly after surface refractive surgery or in patients with preexisting dry eye syndrome; and complications of corneal collagen cross-linking [40, 48].

Polymicrobial involvement affects 55% of Acanthamoeba keratitis, including bacterial co-infection (12.5%), fungal (40%), and triple pathogen scenarios (5%), which can modify characteristic presentations [80, 81]. IVCM, by evidencing double-walled cysts with hyperreflective spots, provides a definitive diagnosis of Acanthamoeba keratitis and shows high sensitivity in detecting co-infections, particularly in atypical presentations [4].

Treatment Strategies

First-Line Treatment

Acanthamoeba keratitis requires prolonged antimicrobial therapy due to significant cystic resistance and organism persistence within ocular tissues. Treatment employs multiple agents, primarily biguanides and diamidines. Initial therapy begins with hourly topical administration, gradually tapering over weeks based on clinical response, with total treatment duration spanning three months to over one year [46].

Biguanide compounds serve as primary therapeutic agents for Acanthamoeba keratitis. Polyhexamethylene biguanide (PHMB) and chlorhexidine represent preferred initial treatments due to their potent anti-Acanthamoeba activity and broad antimicrobial spectrum [1, 46]. These agents bind ostiole mucopolysaccharides, facilitating cellular penetration and phospholipid membrane disruption, resulting in organism death [46]. Diamidine compounds, including propamidine and hexamidine, provide adjunctive therapy when combined with biguanides [82, 83]. These cationic molecules disrupt cellular permeability and denature cytoplasmic proteins, demonstrating activity against both trophozoite and cyst forms [4, 83].

A significant therapeutic advance has been achieved in monotherapy approaches. Dart et al. [84] showed that PHMB 0.08% monotherapy achieves cure rates exceeding 86.7%, equivalent to conventional combination regimens using PHMB 0.02% with propamidine 0.1%. This finding represents a significant therapeutic advancement, offering simplified treatment protocols while maintaining therapeutic efficacy. Clinical dosing protocols utilize variable concentrations based on patient requirements. PHMB formulations span 0.02–0.06% and chlorhexidine preparations 0.02–0.2% [43]. Toxicity profiles remain favorable at 0.02% concentrations, with rare epithelial damage. Prolonged propamidine administration may occasionally induce toxic keratopathy [4].

The therapeutic landscape for Acanthamoeba keratitis has experienced significant advancement with the development of AKANTIOR® (polihexanide 0.8 mg/mL [PHMB 0.08%]), the first licensed monotherapy specifically indicated for this condition [84, 85]. This anti-amoebic polymer proves efficacious against both trophozoites and cysts of Acanthamoeba species, and is formulated as single-dose topical eye drops. The randomized, assessor-masked, active-controlled, multi-center Phase III The Orphan Drug for Acanthamoeba Keratitis (ODAK) trial enrolled 135 patients, demonstrating non-inferiority with a clinical resolution rate of 84.9% for AKANTIOR monotherapy compared to 88.5% for combination therapy of PHMB 0.2 mg/mL plus propamidine 1.0 mg/mL. When adjusted for confounding variables, the AKANTIOR arm achieved a cure rate of 86.7% versus 86.6% in the control group [84].

Comparative analysis with real-world treatment outcomes reveals promising results. In a retrospective study, PHMB 0.08% achieved unweighted and weighted clinical cure rates of 84.8% and 85.1%, respectively, compared with 55.0% and 60.9% for conventional combination therapy with PHMB 0.02% plus diamidine 0.1% [86]. In a comparative trial of PHMB 0.08% monotherapy versus PHMB 0.02% plus propamidine 0.1% for Acanthamoeba keratitis, both treatment arms achieved a median best-corrected visual acuity of 20/20 with approximately similar interquartile ranges. Poor outcomes (≤20/200) occurred in 13.1% (8/61) and 13.6% (9/66) of patients, respectively, while trial failure rates were also comparable (11.5% [7/61] vs. 15.2% [10/66]). The overall therapeutic keratoplasty rate was low (6.3% [8/127]), with no significant difference between groups [84]. These findings support the need to move from variable treatment protocols toward a more standardized therapeutic approach, which may ultimately lead to improved outcomes in the management of Acanthamoeba keratitis [84, 86].

Advanced Treatment Options

When conventional biguanide and diamidine therapies fail to achieve resolution, oral miltefosine serves as an important salvage treatment option, producing encouraging outcomes in refractory cases. However, this anti-amoebic agent frequently triggers intense inflammatory responses, requiring concurrent topical and systemic corticosteroid administration under careful clinical supervision [87, 88].

Azole antifungal agents exhibit potent activity against Acanthamoeba cysts by targeting sterol 14α-demethylase and inhibiting ergosterol biosynthesis. The therapeutic effectiveness against both active and dormant parasite forms stems from 31–35% sequence similarity between Acanthamoeba Cytochrome P450 51 (CYP51) and fungal CYP51 enzymes, making these compounds highly effective throughout the organism's lifecycle [83].

Clinical studies yield variable therapeutic outcomes across different treatment modalities [88–90]. Musayeva et al. [89] observed complete clinical success using triple-drug therapy combining topical voriconazole 1%, PHMB 0.02%, and propamidine 0.1% in 28 patients with Acanthamoeba keratitis, including severe cases. Thulasi et al. [88] reported successful pathogen eradication with miltefosine in treatment-resistant patients, though significant inflammation required corticosteroid management. Conversely, Bagga et al. [90] found discordant results with topical miltefosine monotherapy, demonstrating *in vitro* efficacy but poor clinical response.

Corticosteroid Therapy

Corticosteroid therapy in Acanthamoeba keratitis remains a contentious clinical issue. Although these medications

effectively reduce inflammation and patient symptoms, they present considerable hazards, including disease progression, diagnostic masking, elevated keratoplasty rates, diminished visual prognosis, and prolonged parasite viability [1, 4]. Randag et al. [12] showed in multivariable regression analysis that corticosteroid use prior to diagnosis was positively correlated with treatment failure. Additionally, isolated instances of severe infection deterioration following steroid administration have been documented, warranting prudent use, especially in treatment-resistant cases [91, 92]. Optimal corticosteroid implementation requires confirmed diagnosis and concurrent anti-amoebic therapy [1, 4].

Surgical Interventions

Failed medical therapy necessitates surgical intervention for infection control and visual rehabilitation. Procedures range from epithelial debridement for superficial necrosis to corneal transplantation for advanced disease. Early intervention, within 5.3 months of symptom onset in therapy-resistant Acanthamoeba keratitis, yielded superior visual outcomes compared with delayed surgery [93].

Disease severity determines surgical approach selection. Early infections with endothelial preservation benefit from deep anterior lamellar keratoplasty (DALK), while advanced cases require full-thickness penetrating procedures. Early intervention advocates recommend surgery within 30–60 days from onset of symptoms, concurrent with antimicrobial therapy in poorly responsive cases [94, 95]. Sarnicola et al. [95] achieved successful DALK outcomes in 11 refractory patients in a mean (standard deviation) postoperative follow-up of 24.8 (9.6) months without recurrence or rejection, despite positive deep margins in two cases [95]. Acute presentations with abscess or perforation require therapeutic penetrating keratoplasty [45, 96].

Timing and technique of surgical intervention significantly impact results [45, 93, 95]. A systematic review of 33 studies including 359 eyes with Acanthamoeba keratitis found that, following eradication of infection, optical penetrating keratoplasty achieved the best outcomes, with 94% (82/87) graft clarity, 40% attaining visual acuity of 20/30 or better, and the lowest recurrence rate of 9.5%, outperforming both therapeutic penetrating keratoplasty and therapeutic DALK [97]. Emergency therapeutic penetrating keratoplasty yields poor prognosis, including 56.2% graft failure rates [98] and approximately 20% no-light-perception outcomes in therapeutic cases [99]. Therapeutic keratoplasty is effective for refractory Acanthamoeba keratitis but carries higher risks and poorer vision; whenever feasible, optical keratoplasty after infection resolution should be preferred for superior graft survival and visual outcome [100]. Therapeutic lamellar keratoplasty offers superior visual outcomes compared with therapeutic penetrating keratoplasty while maintaining comparable recurrence rates [101].

Recurrence of Acanthamoeba infection remains problematic, affecting 16.8% of therapeutic and 9.5% of optical penetrating keratoplasties [97, 102]. Cyst reactivation in recipient tissue causes graft colonization, with steroid use and hypopyon representing major risk factors. Prevention requires 1mm healthy margins and prolonged perioperative antimicrobial therapy [43, 46, 103].

Adjunctive Therapies

Corneal cross-linking using photo-activated chromophores (photo-activated chromophore for keratitis–corneal cross-linking, PACK-CXL) has emerged as a promising supplementary approach for treating Acanthamoeba keratitis. This treatment acts through multiple antimicrobial mechanisms: chromophore agents insert between the pathogen's nucleic acids, generate oxygen radicals that damage cell walls, and modify collagen structure to prevent collagenase binding [4].

An *in vitro* study by Atalay [104] demonstrated that PACK-CXL with rose bengal (0.1% and 0.2%) activated by green light (523-nm wavelength) exerted potent anti-amoebic effects against *Acanthamoeba castellanii*, whereas riboflavin (0.1% and 0.25%) activated by UVA (365-nm wavelength) showed no significant amoebicidal activity. Follow-up experiments in a rabbit model of *Acanthamoeba castellanii* keratitis validated that PACK-CXL treatment with rose bengal significantly decreased parasite load and reduced disease severity [105]. Moreover, clinical application of accelerated CXL with 0.1% riboflavin and UVA in six eyes of 5 patients with Acanthamoeba keratitis and progressive corneal melting halted further melting, and none required emergency therapeutic penetrating keratoplasty [106].

Despite promising studies, PACK-CXL treatment requires further investigation due to inconsistent protocols and insufficient data. In a systematic review of 25 studies, including two randomized controlled trials, Papaioannou et al. [107] reported that 10 of 11 eyes with Acanthamoeba keratitis achieved healing with CXL, suggesting potential benefit; however, data remain limited and further controlled studies are needed to confirm CXL efficacy. In a systematic

review of 46 studies, including four randomized controlled trials, Ting et al. [108] reported that adjuvant PACK-CXL accelerated corneal healing in infectious keratitis compared with standard antimicrobial therapy, although evidence quality was low and data on Acanthamoeba keratitis remained insufficient. Among patients treated with PACK-CXL, with or without standard antimicrobial therapy, causative microorganisms included 152 (46.6%) bacteria, 89 (27.3%) fungi, 20 (6.1%) Acanthamoeba, 4 (1.2%) viruses, 20 (6.1%) mixed infections, and 41 (12.6%) culture-negative presumed infectious keratitis.

Amniotic membrane transplantation provides another supportive intervention, utilizing biological membrane placement over infected corneal surfaces to promote healing, alleviate patient discomfort, and control inflammatory responses [109–111].

Clinical Outcomes and Prognostic Factors

Acanthamoeba keratitis prognosis depends on multiple interconnected variables that influence treatment success and visual preservation. A 12-year retrospective study at Moorfields Eye Hospital (UK) analyzed outcomes in 194 patients, identifying factors associated with poor prognosis. Older age, corticosteroid use before antiamoebic therapy, prolonged symptom duration, and severe inflammatory complications—particularly scleritis—were the strongest independent predictors of poor outcomes in patients with Acanthamoeba keratitis [112].

Early identification within fourteen days of symptom development remains the strongest predictor of visual recovery [103, 113]. Diagnostic timing patterns reveal significant disparities across patient populations, with Ross et al. [36] demonstrating that contact lens wearers achieve diagnosis in median duration of 27 days compared to 50 days for non-contact lens users disease. Disease severity also influenced diagnostic timing: patients presenting with advanced signs of Acanthamoeba keratitis had a median time to diagnosis of 35 days, compared with 19 days in those without such signs [36]. Corticosteroid use before definitive diagnosis delays recognition, worsens final vision, and enhances surgical need [1]. Visual outcomes reveal marked heterogeneity, with approximately 39% of patients experiencing significant impairment or complete vision loss. Patients responding to medical therapy alone consistently achieve superior visual outcomes compared to those requiring surgical intervention [1, 114]. The requirement for surgical management, particularly therapeutic penetrating keratoplasty due to extensive damage, indicates poor prognosis [1, 114].

Preventive Measures

Comprehensive public education targeting high-risk populations forms the cornerstone of effective Acanthamoeba keratitis prevention. Water exposure elimination represents the most critical protective strategy, requiring lens removal before swimming, showering, or hot tub use to prevent pathogen exposure [40, 115]. Using daily disposable contact lens systems provides optimal safety through complete contaminant elimination via disposal protocols. Essential hygiene practices constitute the preventive foundation, including thorough hand sanitization before lens handling, exclusive use of recommended disinfection products, and strict replacement schedule adherence to minimize contamination risks. Special populations require individualized preventive approaches. Immunocompromised patients and individuals with occupational water exposure necessitate enhanced counseling and specialized protective protocols [1, 4, 40].

This comprehensive narrative review synthesizes current knowledge from diverse study types, including original research, case series, and clinical trials spanning over two decades (2000–2025), providing clinicians with practical, evidence-based guidance for Acanthamoeba keratitis management. The review addresses all aspects of the disease from pathogenesis to prevention, offering a perspective that is valuable for ophthalmologists. However, as a narrative review this work lacks the systematic methodology and risk of bias assessment inherent to systematic reviews and meta-analyses. The literature search was primarily limited to English-language publications, potentially excluding relevant studies in other languages. Additionally, the heterogeneity of study designs and outcome measures in the included literature limits the ability to draw definitive quantitative conclusions about optimal treatment protocols. The rapidly evolving nature of diagnostic techniques and therapeutic approaches may also result in some information becoming outdated as new evidence emerges.

In terms of future research directions, effective management of Acanthamoeba keratitis requires advances in diagnostics, treatment, and prevention. Machine-learning technologies show diagnostic promise but must demonstrate superiority over current methods while addressing cost-effectiveness and deployment challenges [70–

72]. The greatest need is therapies targeting cyst-resistant forms, whose protective walls and survival abilities limit treatment success. Progress may come from novel antimicrobials, improved delivery methods, or targeting virulence factors such as protease mannose-induced protein (MIP)-133 [32, 116]. Understanding how mannose-binding proteins aid attachment and how contact lenses increase mannosylated proteins on the corneal surface may open up preventive strategies [116]. Prevention research is critical as global contact lens use expands, particularly in developing regions with poor water safety and weak public health infrastructure [1, 4, 9]. Additional priorities include standardized treatment protocols, early diagnostic markers, and long-term outcomes. Integrating novel therapies with artificial intelligence-driven diagnostics may ultimately improve patient care worldwide.

CONCLUSIONS

Acanthamoeba keratitis represents one of the most challenging corneal infections in contemporary ophthalmology, demanding immediate recognition and aggressive treatment to prevent devastating visual consequences. The dramatic increase in global incidence, primarily driven by expanding contact lens usage, underscores the urgent need for enhanced awareness among both clinicians and patients. The evolution of diagnostic technologies, particularly IVCM and molecular techniques, has revolutionized our ability to achieve rapid and accurate identification. These advances have shifted the diagnostic paradigm from reliance on traditional culture methods with their inherent limitations to sophisticated imaging and genetic detection systems that enable timely therapeutic intervention. Treatment approaches have similarly evolved, with recent evidence supporting simplified monotherapy regimens using higher-concentration biguanides while maintaining awareness of advanced therapeutic options for refractory cases. The critical importance of early diagnosis cannot be overstated, as it constitutes the most powerful predictor of visual preservation. Preventive strategies centered on proper contact lens hygiene and water exposure avoidance continue to represent the most effective approach to reducing disease burden. As contact lens usage expands globally, particularly in developing regions, comprehensive education programs and improved water infrastructure become increasingly vital. Successful management of Acanthamoeba keratitis requires high clinical suspicion, rapid diagnosis, appropriate treatment, and effective prevention strategies. Continued research, education, and technological innovation are essential to reduce vision loss from this devastating infection and improve patient outcomes globally.

ETHICAL DECLARATIONS

Ethical approval: This was a narrative review and no ethical approval was required.All figures included were sourced from the patient documentation archives of our unit, and informed consent was obtained from every patient prior to their inclusion in the review.

Conflict of interest: None.

FUNDING

None.

ACKNOWLEDGMENTS

None.

REFERENCES

1. Garg D, Daigavane S. A Comprehensive Review on Acanthamoeba Keratitis: An Overview of Epidemiology, Risk Factors, and Therapeutic Strategies. Cureus. 2024 Aug 26;16(8):e67803. doi: 10.7759/cureus.67803. PMID: 39328676; PMCID: PMC11424229.
2. Nunes TE, Brazil NT, Fuentefria AM, Rott MB. Acanthamoeba and Fusarium interactions: A possible problem in keratitis. Acta Trop. 2016 May;157:102-7. doi: 10.1016/j.actatropica.2016.02.001. Epub 2016 Feb 3. PMID: 26851515.
3. Varacalli G, Di Zazzo A, Mori T, Dohlman TH, Spelta S, Coassin M, Bonini S. Challenges in Acanthamoeba Keratitis: A Review. J Clin Med. 2021 Mar 1;10(5):942. doi: 10.3390/jcm10050942. PMID: 33804353; PMCID: PMC7957573.
4. Raghavan A, Rammohan R. Acanthamoeba keratitis - A review. Indian J Ophthalmol. 2024 Apr 1;72(4):473-482. doi: 10.4103/IJO.IJO_2627_23. Epub 2024 Mar 8. PMID: 38454853; PMCID: PMC11149514.
5. McKelvie J, Alshiakhi M, Ziaei M, Patel DV, McGhee CN. The rising tide of Acanthamoeba keratitis in Auckland, New Zealand: a 7-year review of presentation, diagnosis and outcomes (2009-2016). Clin Exp Ophthalmol. 2018 Aug;46(6):600-607. doi: 10.1111/ceo.13166. Epub 2018 Mar 5. PMID: 29412494.
6. Cabrera-Aguas M, Khoo P, Watson SL. Infectious keratitis: A review. Clin Exp Ophthalmol. 2022 Jul;50(5):543-562. doi: 10.1111/ceo.14113. Epub 2022 Jun 3. PMID: 35610943; PMCID: PMC9542356.

7. Rayamajhee B, Willcox MDP, Henriquez FL, Petsoglou C, Subedi D, Carnt N. Acanthamoeba, an environmental phagocyte enhancing survival and transmission of human pathogens. Trends Parasitol. 2022 Nov;38(11):975-990. doi: 10.1016/j.pt.2022.08.007. Epub 2022 Sep 12. PMID: 36109313.
8. Ilyas M, Stapleton F, Willcox MDP, Henriquez F, Peguda HK, Rayamajhee B, Zahid T, Petsoglou C, Carnt NA. Epidemiology of and Genetic Factors Associated with Acanthamoeba Keratitis. Pathogens. 2024 Feb 4;13(2):142. doi: 10.3390/pathogens13020142. PMID: 38392880; PMCID: PMC10892102.
9. Zhang Y, Xu X, Wei Z, Cao K, Zhang Z, Liang Q. The global epidemiology and clinical diagnosis of Acanthamoeba keratitis. J Infect Public Health. 2023 Jun;16(6):841-852. doi: 10.1016/j.jiph.2023.03.020. Epub 2023 Mar 23. PMID: 37030037.
10. Verani JR, Lorick SA, Yoder JS, Beach MJ, Braden CR, Roberts JM, Conover CS, Chen S, McConnell KA, Chang DC, Park BJ, Jones DB, Visvesvara GS, Roy SL; AcanthamoebaKeratitis Investigation Team. National outbreak of Acanthamoeba keratitis associated with use of a contact lens solution, United States. Emerg Infect Dis. 2009 Aug;15(8):1236-42. doi: 10.3201/eid1508.090225. PMID: 19751585; PMCID: PMC2815976.
11. Arnaiz-Camacho A, Goterris Bonet L, Bisbe Lopez L, Martín Nalda S, Puig Galy J, García-Hidalgo S, Pablos-Jiménez T, Pairó-Salvador A. Acanthamoeba keratitis in the last decade. What have we learned? Arch Soc Esp Oftalmol (Engl Ed). 2025 Jan;100(1):28-36. doi: 10.1016/j.oftale.2024.11.001. Epub 2024 Nov 19. PMID: 39566599.
12. Randag AC, van Rooij J, van Goor AT, Verkerk S, Wisse RPL, Saelens IEY, Stoutenbeek R, van Dooren BTH, Cheng YYY, Eggink CA. The rising incidence of Acanthamoeba keratitis: A 7-year nationwide survey and clinical assessment of risk factors and functional outcomes. PLoS One. 2019 Sep 6;14(9):e0222092. doi: 10.1371/journal.pone.0222092. PMID: 31491000.
13. Stellwagen A, MacGregor C, Kung R, Konstantopoulos A, Hossain P. Personal hygiene risk factors for contact lens-related microbial keratitis. BMJ Open Ophthalmol. 2020 Sep 8;5(1):e000476. doi: 10.1136/bmjophth-2020-000476. PMID: 32953996; PMCID: PMC7481083.
14. Tanhehco T, Colby K. The clinical experience of Acanthamoeba keratitis at a tertiary care eye hospital. Cornea. 2010 Sep;29(9):1005-10. doi: 10.1097/ICO.0b013e3181cf9949. PMID: 20539211.
15. Carnt N, Stapleton F. Strategies for the prevention of contact lens-related Acanthamoeba keratitis: a review. Ophthalmic Physiol Opt. 2016 Mar;36(2):77-92. doi: 10.1111/opo.12271. Epub 2015 Dec 21. PMID: 26691018.
16. Kim CK, Karslioglu MZ, Zhao SH, Lee OL. Infectious Keratitis in Patients Over 65: A Review on Treatment and Preserving Eyesight. Clin Interv Aging. 2024 Jul 31;19:1393-1405. doi: 10.2147/CIA.S467262. PMID: 39099749; PMCID: PMC11298191.
17. Bharathi JM, Srinivasan M, Ramakrishnan R, Meenakshi R, Padmavathy S, Lalitha PN. A study of the spectrum of Acanthamoeba keratitis: a three-year study at a tertiary eye care referral center in South India. Indian J Ophthalmol. 2007 Jan-Feb;55(1):37-42. doi: 10.4103/0301-4738.29493. PMID: 17189885.
18. Messina M, Tucci D, Mocini S, Marruso V, Crotti S, Said D, Dua HS, Cagini C. Increasing incidence of contact-lens-related Acanthamoeba keratitis in a tertiary ophthalmology department in an Italian population. Eur J Ophthalmol. 2024 Nov;34(6):1875-1883. doi: 10.1177/11206721241242165. Epub 2024 Mar 20. PMID: 38509758.
19. Dirim Erdogan D, Aykur M, Selvi Gunel N, Palamar M, Barut Selver O, Ozel B, Yagci A, Gunduz C, Dagci H. The Risk Factors and Clinical Features of Acanthamoeba Keratitis: First Time Detection of Acanthamoeba T5 Genotype from Keratitis Patients in Turkey. Acta Parasitol. 2022 Sep;67(3):1384-1392. doi: 10.1007/s11686-022-00596-4. Epub 2022 Jul 21. PMID: 35864410.
20. Lalitha P, Lin CC, Srinivasan M, Mascarenhas J, Prajna NV, Keenan JD, McLeod SD, Acharya NR, Lietman TM, Porco TC. Acanthamoeba keratitis in South India: a longitudinal analysis of epidemics. Ophthalmic Epidemiol. 2012 Apr;19(2):111-5. doi: 10.3109/09286586.2011.645990. Epub 2012 Feb 24. PMID: 22364672; PMCID: PMC3830554.
21. Vingataramin Y, Delumeau A, Quétel I, Gros O, Vedy S, Marcelino I. Characterization of the natural bacterial microbiota of pathogenic free-living amoebae (Acanthamoeba spp. and Naegleria fowleri) isolated from rivers and tap water in Guadeloupe. Sci Total Environ. 2025 May 1;975:179204. doi: 10.1016/j.scitotenv.2025.179204. Epub 2025 Apr 5. PMID: 40187337.
22. Chomicz L, Szaflik JP, Kuligowska A, Conn DB, Baltaza W, Szostakowska B, Zawadzki PJ, Dybicz M, Machalińska A, Perkowski K, Bajer A, Szaflik J. Concomitant Potentially Contagious Factors Detected in Poland and Regarding Acanthamoeba Strains, Etiological Agents of Keratitis in Humans. Microorganisms. 2024 Nov 28;12(12):2445. doi: 10.3390/microorganisms12122445. PMID: 39770648; PMCID: PMC11676076.
23. Siddiqui R, Khan NA. Biology and pathogenesis of Acanthamoeba. Parasit Vectors. 2012 Jan 10;5:6. doi: 10.1186/1756-3305-5-6. PMID: 22229971; PMCID: PMC3284432.
24. Betanzos A, Bañuelos C, Orozco E. Host Invasion by Pathogenic Amoebae: Epithelial Disruption by Parasite Proteins. Genes (Basel). 2019 Aug 14;10(8):618. doi: 10.3390/genes10080618. PMID: 31416298; PMCID: PMC6723116.
25. Takaoka-Sugihara N, Yamagami S, Yokoo S, Matsubara M, Yagita K. Cytopathic effect of Acanthamoeba on human corneal fibroblasts. Mol Vis. 2012;18:2221-8. Epub 2012 Aug 9. PMID: 22933834; PMCID: PMC3429359.

26. Choaji M, Samba-Louaka A, Fechtali-Moute Z, Aucher W, Pomel S. Encystment and Excystment Processes in Acanthamoeba castellanii: An Emphasis on Cellulose Involvement. Pathogens. 2025 Mar 10;14(3):268. doi: 10.3390/pathogens14030268. PMID: 40137753; PMCID: PMC11945136.
27. Guimaraes AJ, Gomes KX, Cortines JR, Peralta JM, Peralta RH. Acanthamoeba spp. as a universal host for pathogenic microorganisms: One bridge from environment to host virulence. Microbiol Res. 2016 Dec;193:30-38. doi: 10.1016/j.micres.2016.08.001. Epub 2016 Aug 2. PMID: 27825484.
28. Hamid MWA, Bin Abd Majid R, Victor Ernest VFK, Mohamed Shakrin NNS, Mohamad Hamzah F, Haque M. A Narrative Review of Acanthamoeba Isolates in Malaysia: Challenges in Infection Management and Natural Therapeutic Advancements. Cureus. 2024 Nov 1;16(11):e72851. doi: 10.7759/cureus.72851. PMID: 39493340; PMCID: PMC11530292.
29. Sharma C, Khurana S, Megha K, Thakur A, Bhatia A, Gupta A. Assessment of pathogenic potential of Acanthamoeba isolates by in vitro and in vivo tests. Parasitol Res. 2023 Sep;122(9):2109-2118. doi: 10.1007/s00436-023-07910-7. Epub 2023 Jul 7. PMID: 37418019.
30. Duarte JL, Furst C, Klisiowicz DR, Klassen G, Costa AO. Morphological, genotypic, and physiological characterization of Acanthamoeba isolates from keratitis patients and the domestic environment in Vitoria, Espírito Santo, Brazil. Exp Parasitol. 2013 Sep;135(1):9-14. doi: 10.1016/j.exppara.2013.05.013. Epub 2013 Jun 6. PMID: 23748160.
31. Wang Y, Jiang L, Zhao Y, Ju X, Wang L, Jin L, Fine RD, Li M. Biological characteristics and pathogenicity of Acanthamoeba. Front Microbiol. 2023 Apr 5;14:1147077. doi: 10.3389/fmicb.2023.1147077. PMID: 37089530; PMCID: PMC10113681.
32. Panjwani N. Pathogenesis of acanthamoeba keratitis. Ocul Surf. 2010 Apr;8(2):70-9. doi: 10.1016/s1542-0124(12)70071-x. PMID: 20427010; PMCID: PMC3072032.
33. Lorenzo-Morales J, Khan NA, Walochnik J. An update on Acanthamoeba keratitis: diagnosis, pathogenesis and treatment. Parasite. 2015;22:10. doi: 10.1051/parasite/2015010. Epub 2015 Feb 18. PMID: 25687209; PMCID: PMC4330640.
34. Marciano-Cabral F, Cabral G. Acanthamoeba spp. as agents of disease in humans. Clin Microbiol Rev. 2003 Apr;16(2):273-307. doi: 10.1128/CMR.16.2.273-307.2003. PMID: 12692099; PMCID: PMC153146.
35. Waghmare SV, Jeria S. A Review of Contact Lens-Related Risk Factors and Complications. Cureus. 2022 Oct 10;14(10):e30118. doi: 10.7759/cureus.30118. PMID: 36381898; PMCID: PMC9644230.
36. Ross J, Roy SL, Mathers WD, Ritterband DC, Yoder JS, Ayers T, Shah RD, Samper ME, Shih CY, Schmitz A, Brown AC. Clinical characteristics of Acanthamoeba keratitis infections in 28 states, 2008 to 2011. Cornea. 2014 Feb;33(2):161-8. doi: 10.1097/ICO.0000000000000014. PMID: 24322804.
37. Kilvington S, Gray T, Dart J, Morlet N, Beeching JR, Frazer DG, Matheson M. Acanthamoeba keratitis: the role of domestic tap water contamination in the United Kingdom. Invest Ophthalmol Vis Sci. 2004 Jan;45(1):165-9. doi: 10.1167/iovs.03-0559. PMID: 14691169.
38. Carnt NA, Subedi D, Connor S, Kilvington S. The relationship between environmental sources and the susceptibility of Acanthamoeba keratitis in the United Kingdom. PLoS One. 2020 Mar 11;15(3):e0229681. doi: 10.1371/journal.pone.0229681. PMID: 32160218; PMCID: PMC7065798.
39. Bao M, Bao H, Wang S, Zhou H. The pathogenesis, risk factors, diagnosis and treatment of Acanthamoeba keratitis. Front Med (Lausanne). 2025 Jul 24;12:1559224. doi: 10.3389/fmed.2025.1559224. PMID: 40776920; PMCID: PMC12328393.
40. Somani SN, Ronquillo Y, Moshirfar M. Acanthamoeba Keratitis. 2023 Nov 23. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 31751053.
41. Höllhumer R, Keay L, Watson SL. Acanthamoeba keratitis in Australia: demographics, associated factors, presentation and outcomes: a 15-year case review. Eye (Lond). 2020 Apr;34(4):725-732. doi: 10.1038/s41433-019-0589-6. Epub 2019 Sep 25. PMID: 31554948; PMCID: PMC7093427.
42. Daas L, Szentmáry N, Eppig T, Langenbucher A, Hasenfus A, Roth M, Saeger M, Nölle B, Lippmann B, Böhringer D, Reinhard T, Kelbsch C, Messmer E, Pleyer U, Roters S, Zhivov A, Engelmann K, Schrecker J, Zumhagen L, Thieme H, Darawsha R, Meyer-Ter-Vehn T, Dick B, Görsch I, Hermel M, Kohlhaas M, Seitz B. Das Deutsche Akanthamöbenkeratitis-Register : Erste Ergebnisse einer multizentrischen Erhebung [The German Acanthamoeba keratitis register: Initial results of a multicenter study]. Ophthalmologe. 2015 Sep;112(9):752-63. German. doi: 10.1007/s00347-014-3225-7. Erratum in: Ophthalmologe. 2015 Nov;112(11):942. doi: 10.1007/s00347-015-0144-1. PMID: 25833754.
43. Dart JK, Saw VP, Kilvington S. Acanthamoeba keratitis: diagnosis and treatment update 2009. Am J Ophthalmol. 2009 Oct;148(4):487-499.e2. doi: 10.1016/j.ajo.2009.06.009. Epub 2009 Aug 5. PMID: 19660733.
44. Tu EY, Joslin CE, Sugar J, Shoff ME, Booton GC. Prognostic factors affecting visual outcome in Acanthamoeba keratitis. Ophthalmology. 2008 Nov;115(11):1998-2003. doi: 10.1016/j.ophtha.2008.04.038. Epub 2008 Jun 24. PMID: 18571729; PMCID: PMC3816554.

45. Szentmáry N, Daas L, Shi L, Laurik KL, Lepper S, Milioti G, Seitz B. Acanthamoeba keratitis - Clinical signs, differential diagnosis and treatment. J Curr Ophthalmol. 2018 Oct 19;31(1):16-23. doi: 10.1016/j.joco.2018.09.008. PMID: 30899841; PMCID: PMC6407156.
46. Fu L, Wasielica-Poslednik J, Geerling G, Robbie S, D'Esposito F, Musa M, Tognetto D, Giglio R, Gagliano C, Zeppieri M. Navigating the Challenges of Acanthamoeba Keratitis: Current Trends and Future Directions. Life (Basel). 2025 Jun 10;15(6):933. doi: 10.3390/life15060933. PMID: 40566585; PMCID: PMC12194555.
47. Korkmaz I, Barut Selver O, Simsek C, Palamar M. Negative Corneal Fluorescein Staining as an Exceptionally Early Sign of Acanthamoeba Keratitis: A Case Report. Eye Contact Lens. 2021 Nov 1;47(11):622-624. doi: 10.1097/ICL.0000000000000825. PMID: 34348354.
48. Przybek-Skrzypecka J, Skrzypecki J, Suh L, Szaflik JP. Corneal ring infiltrate- far more than Acanthamoeba keratitis: review of pathophysiology, morphology, differential diagnosis and management. J Ophthalmic Inflamm Infect. 2023 Dec 19;13(1):55. doi: 10.1186/s12348-023-00379-6. PMID: 38112842; PMCID: PMC10730498.
49. Garg P, Kalra P, Joseph J. Non-contact lens related Acanthamoeba keratitis. Indian J Ophthalmol. 2017 Nov;65(11):1079-1086. doi: 10.4103/ijo.IJO_826_17. PMID: 29133630; PMCID: PMC5700572.
50. Hoffman JJ, Dart JKG, De SK, Carnt N, Cleary G, Hau S. Comparison of culture, confocal microscopy and PCR in routine hospital use for microbial keratitis diagnosis. Eye (Lond). 2022 Nov;36(11):2172-2178. doi: 10.1038/s41433-021-01812-7. Epub 2021 Nov 5. PMID: 34741122; PMCID: PMC9581916.
51. Ung L, Bispo PJM, Shanbhag SS, Gilmore MS, Chodosh J. The persistent dilemma of microbial keratitis: Global burden, diagnosis, and antimicrobial resistance. Surv Ophthalmol. 2019 May-Jun;64(3):255-271. doi: 10.1016/j.survophthal.2018.12.003. Epub 2018 Dec 24. PMID: 30590103; PMCID: PMC7021355.
52. El-Sayed NM, Hikal WM. Several staining techniques to enhance the visibility of Acanthamoeba cysts. Parasitol Res. 2015 Mar;114(3):823-30. doi: 10.1007/s00436-014-4190-4. Epub 2014 Oct 28. PMID: 25346196.
53. Bharathi MJ, Ramakrishnan R, Meenakshi R, Mittal S, Shivakumar C, Srinivasan M. Microbiological diagnosis of infective keratitis: comparative evaluation of direct microscopy and culture results. Br J Ophthalmol. 2006 Oct;90(10):1271-6. doi: 10.1136/bjo.2006.096230. Epub 2006 Jul 12. PMID: 16837544; PMCID: PMC1857439.
54. Kaufman AR, Tu EY. Advances in the management of Acanthamoeba keratitis: A review of the literature and synthesized algorithmic approach. Ocul Surf. 2022 Jul;25:26-36. doi: 10.1016/j.jtos.2022.04.003. Epub 2022 Apr 22. PMID: 35462076.
55. Goh JWY, Harrison R, Hau S, Alexander CL, Tole DM, Avadhanam VS. Comparison of In Vivo Confocal Microscopy, PCR and Culture of Corneal Scrapes in the Diagnosis of Acanthamoeba Keratitis. Cornea. 2018 Apr;37(4):480-485. doi: 10.1097/ICO.0000000000001497. PMID: 29256983.
56. Yera H, Ok V, Lee Koy Kuet F, Dahane N, Ariey F, Hasseine L, Delaunay P, Martiano D, Marty P, Bourges JL. PCR and culture for diagnosis of Acanthamoeba keratitis. Br J Ophthalmol. 2021 Sep;105(9):1302-1306. doi: 10.1136/bjophthalmol-2020-316730. Epub 2020 Oct 24. PMID: 33099504.
57. Shareef O, Shareef S, Saeed HN. New Frontiers in Acanthamoeba Keratitis Diagnosis and Management. Biology (Basel). 2023 Dec 5;12(12):1489. doi: 10.3390/biology12121489. PMID: 38132315; PMCID: PMC10740828.
58. Liu HY, Hopping GC, Vaidyanathan U, Ronquillo YC, Hoopes PC, Moshirfar M. Polymerase Chain Reaction and Its Application in the Diagnosis of Infectious Keratitis. Med Hypothesis Discov Innov Ophthalmol. 2019 Fall;8(3):152-155. PMID: 31598517; PMCID: PMC6778471.
59. Hadziavdic K, Lekang K, Lanzen A, Jonassen I, Thompson EM, Troedsson C. Characterization of the 18S rRNA gene for designing universal eukaryote specific primers. PLoS One. 2014 Feb 7;9(2):e87624. doi: 10.1371/journal.pone.0087624. PMID: 24516555; PMCID: PMC3917833.
60. Yera H, Zamfir O, Bourcier T, Ancelle T, Batellier L, Dupouy-Camet J, Chaumeil C. Comparison of PCR, microscopic examination and culture for the early diagnosis and characterization of Acanthamoeba isolates from ocular infections. Eur J Clin Microbiol Infect Dis. 2007 Mar;26(3):221-4. doi: 10.1007/s10096-007-0268-6. PMID: 17393203.
61. Schroeder JM, Booton GC, Hay J, Niszl IA, Seal DV, Markus MB, Fuerst PA, Byers TJ. Use of subgenic 18S ribosomal DNA PCR and sequencing for genus and genotype identification of acanthamoebae from humans with keratitis and from sewage sludge. J Clin Microbiol. 2001 May;39(5):1903-11. doi: 10.1128/JCM.39.5.1903-1911.2001. PMID: 11326011; PMCID: PMC88046.
62. Zemba M, Dumitrescu OM, Dimirache AE, Branisteanu DC, Balta F, Burcea M, Moraru AD, Gradinaru S. Diagnostic methods for the etiological assessment of infectious corneal pathology (Review). Exp Ther Med. 2022 Feb;23(2):137. doi: 10.3892/etm.2021.11060. Epub 2021 Dec 13. PMID: 35069818; PMCID: PMC8756399.
63. Li S, Bian J, Wang Y, Wang S, Wang X, Shi W. Clinical features and serial changes of Acanthamoeba keratitis: an in vivo confocal microscopy study. Eye (Lond). 2020 Feb;34(2):327-334. doi: 10.1038/s41433-019-0482-3. Epub 2019 Jul 10. PMID: 31292523; PMCID: PMC7002551.

64. De Craene S, Knoeri J, Georgeon C, Kestelyn P, Borderie VM. Assessment of Confocal Microscopy for the Diagnosis of Polymerase Chain Reaction-Positive Acanthamoeba Keratitis: A Case-Control Study. Ophthalmology. 2018 Feb;125(2):161-168. doi: 10.1016/j.ophtha.2017.08.037. Epub 2017 Sep 29. PMID: 28965660.
65. Chidambaram JD, Prajna NV, Larke NL, Palepu S, Lanjewar S, Shah M, Elakkiya S, Lalitha P, Carnt N, Vesaluoma MH, Mason M, Hau S, Burton MJ. Prospective Study of the Diagnostic Accuracy of the In Vivo Laser Scanning Confocal Microscope for Severe Microbial Keratitis. Ophthalmology. 2016 Nov;123(11):2285-2293. doi: 10.1016/j.ophtha.2016.07.009. Epub 2016 Aug 15. PMID: 27538797; PMCID: PMC5081072.
66. Lee HJ, Alipour F, Cruzat A, Posarelli M, Zheng L, Hamrah P. Utility of In Vivo Confocal Microscopy in Diagnosis of Acanthamoeba Keratitis: A Comparison of Patient Outcomes. Cornea. 2023 Feb 1;42(2):135-140. doi: 10.1097/ICO.0000000000003184. Epub 2022 Nov 21. PMID: 36582032; PMCID: PMC9811484.
67. Recchioni A, Barua A, Dominguez-Vicent A. Enhancing Clinical Decision-Making in Complex Corneal Disorders: The Role of In-Vivo Confocal Microscopy. Life (Basel). 2023 Mar 2;13(3):679. doi: 10.3390/life13030679. PMID: 36983835; PMCID: PMC10059758.
68. Alsoudi AF, Golen JR, Seitzman GD, Lietman TM, Keenan JD. Comparison of two confocal microscopes for diagnosis of acanthamoeba keratitis. Eye (Lond). 2021 Jul;35(7):2061-2063. doi: 10.1038/s41433-020-1117-4. Epub 2020 Aug 5. PMID: 32760010; PMCID: PMC8225617.
69. Agarwal M, Asokan R, Therese KL, Lakshmipathy M. Bilateral Acanthamoeba keratitis with radial keratoneuritis - utility of AS-OCT in management and treatment. Clin Exp Optom. 2021 Nov;104(8):871-873. doi: 10.1080/08164622.2021.1878857. Epub 2021 Feb 28. PMID: 33689643.
70. Zhang Z, Wang H, Wang S, Wei Z, Zhang Y, Wang Z, Chen K, Ou Z, Liang Q. Deep learning-based classification of infectious keratitis on slit-lamp images. Ther Adv Chronic Dis. 2022 Nov 14;13:20406223221136071. doi: 10.1177/20406223221136071. PMID: 36407021; PMCID: PMC9666706.
71. Essalat M, Abolhosseini M, Le TH, Moshtaghion SM, Kanavi MR. Interpretable deep learning for diagnosis of fungal and acanthamoeba keratitis using in vivo confocal microscopy images. Sci Rep. 2023 Jun 2;13(1):8953. doi: 10.1038/s41598-023-35085-9. PMID: 37268665; PMCID: PMC10238502.
72. Shareef O, Soleimani M, Tu E, Jacobs DS, Ciolino JB, Rahdar A, Cheraqpour K, Ashraf M, Habib NB, Greenfield J, Yousefi S, Djalilian AR, Saeed HN. A novel artificial intelligence model for diagnosing Acanthamoeba keratitis through confocal microscopy. Ocul Surf. 2024 Oct;34:159-164. doi: 10.1016/j.jtos.2024.07.010. Epub 2024 Jul 29. PMID: 39084255.
73. Koyama A, Miyazaki D, Nakagawa Y, Ayatsuka Y, Miyake H, Ehara F, Sasaki SI, Shimizu Y, Inoue Y. Determination of probability of causative pathogen in infectious keratitis using deep learning algorithm of slit-lamp images. Sci Rep. 2021 Nov 22;11(1):22642. doi: 10.1038/s41598-021-02138-w. PMID: 34811468; PMCID: PMC8608802.
74. Wróbel-Dudzińska D, Ziaja-Sołtys M, Rymgayłło-Jankowska B, Derda M, Klepacz R, Zalewski D, Żarnowski T, Bogucka-Kocka A. Complicated Diagnosis and Treatment of Rare Painless Acanthamoeba Keratitis. J Clin Med. 2025 Jul 5;14(13):4763. doi: 10.3390/jcm14134763. PMID: 40649137; PMCID: PMC12251361.
75. Ward MS, Hastings JP, Shmunes KM, Ronquillo Y, Hoopes PC, Moshirfar M. Atypical presentation of acanthamoeba keratitis resembling central toxic keratopathy. Am J Ophthalmol Case Rep. 2021 Dec 16;25:101243. doi: 10.1016/j.ajoc.2021.101243. PMID: 35028488; PMCID: PMC8715135.
76. Alreshidi SO, Vargas JM, Ahmad K, Alothman AY, Albalawi ED, Almulhim A, Alenezi SH, ALBalawi HB, Alali NM, Hashem F, Aljindan M. Differentiation of acanthamoeba keratitis from other non-acanthamoeba keratitis: Risk factors and clinical features. PLoS One. 2024 Mar 12;19(3):e0299492. doi: 10.1371/journal.pone.0299492. PMID: 38470877; PMCID: PMC10931457.
77. Singh RB, Batta P. Herpes simplex virus keratitis mimicking Acanthamoeba keratitis: a clinicopathological correlation. BMJ Case Rep. 2018 Sep 19;2018:bcr2018226100. doi: 10.1136/bcr-2018-226100. PMID: 30232207; PMCID: PMC6150157.
78. Mascarenhas J, Lalitha P, Prajna NV, Srinivasan M, Das M, D'Silva SS, Oldenburg CE, Borkar DS, Esterberg EJ, Lietman TM, Keenan JD. Acanthamoeba, fungal, and bacterial keratitis: a comparison of risk factors and clinical features. Am J Ophthalmol. 2014 Jan;157(1):56-62. doi: 10.1016/j.ajo.2013.08.032. Epub 2013 Nov 5. PMID: 24200232; PMCID: PMC3865075.
79. Ahmadikia K, Aghaei Gharehbolagh S, Fallah B, Naeimi Eshkaleti M, Malekifar P, Rahsepar S, Getso MI, Sharma S, Mahmoudi S. Distribution, Prevalence, and Causative Agents of Fungal Keratitis: A Systematic Review and Meta-Analysis (1990 to 2020). Front Cell Infect Microbiol. 2021 Aug 26;11:698780. doi: 10.3389/fcimb.2021.698780. PMID: 34513726; PMCID: PMC8428535.
80. Raghavan A, Baidwal S, Venkatapathy N, Rammohan R. The Acanthamoeba-Fungal Keratitis Study. Am J Ophthalmol. 2019 May;201:31-36. doi: 10.1016/j.ajo.2019.01.024. Epub 2019 Feb 2. PMID: 30721687.

81. Tu EY, Joslin CE, Nijm LM, Feder RS, Jain S, Shoff ME. Polymicrobial keratitis: Acanthamoeba and infectious crystalline keratopathy. Am J Ophthalmol. 2009 Jul;148(1):13-9.e2. doi: 10.1016/j.ajo.2009.01.020. Epub 2009 Mar 27. PMID: 19327742; PMCID: PMC2830559.
82. Papa V, Rama P, Radford C, Minassian DC, Dart JKG. Acanthamoeba keratitis therapy: time to cure and visual outcome analysis for different antiamoebic therapies in 227 cases. Br J Ophthalmol. 2020 Apr;104(4):575-581. doi: 10.1136/bjophthalmol-2019-314485. Epub 2019 Aug 10. PMID: 31401556.
83. Shing B, Balen M, McKerrow JH, Debnath A. Acanthamoeba Keratitis: an update on amebicidal and cysticidal drug screening methodologies and potential treatment with azole drugs. Expert Rev Anti Infect Ther. 2021 Nov;19(11):1427-1441. doi: 10.1080/14787210.2021.1924673. Epub 2021 May 19. PMID: 33929276; PMCID: PMC8551003.
84. Dart JKG, Papa V, Rama P, Knutsson KA, Ahmad S, Hau S, Sanchez S, Franch A, Birattari F, Leon P, Fasolo A, Kominek EM, Jadczyk-Sorek K, Carley F, Hossain P, Minassian DC. The Orphan Drug for Acanthamoeba Keratitis (ODAK) Trial: PHMB 0.08% (Polihexanide) and Placebo versus PHMB 0.02% and Propamidine 0.1. Ophthalmology. 2024 Mar;131(3):277-287. doi: 10.1016/j.ophtha.2023.09.031. Epub 2023 Oct 5. PMID: 37802392.
85. Dart JKG, Papa V, Rama P, Knutsson KA, Ahmad S, Hau S, Sanchez S, Franch A, Birattari F, Leon P, Fasolo A, Mrukwa-Kominek E, Jadczyk-Sorek K, Carley F, Parwez H, Minassian DC. Acanthamoeba keratitis treatment outcomes compared for drug delivery by protocol versus physician's individualised treatment. Ocul Surf. 2025 Apr 7;38:132-141. doi: 10.1016/j.jtos.2025.03.008. Epub ahead of print. PMID: 40204130.
86. Papa V, Galeone C, De Francesco M, Bodicoat DH, Alves R, Spaepen E, Dart JKG, Arteaga C. Polihexanide (PHMB) 0.08% versus currently used treatments for Acanthamoeba keratitis: indirect treatment comparisons. BMJ Open Ophthalmol. 2025 Jul 13;10(1):e002082. doi: 10.1136/bmjophth-2024-002082. PMID: 40659372; PMCID: PMC12258341.
87. Avdagic E, Chew HF, Veldman P, Tu EY, Jafri M, Doshi R, Boggild AK, Reidy JJ, Farooq AV. Resolution of Acanthamoeba Keratitis with Adjunctive Use of Oral Miltefosine. Ocul Immunol Inflamm. 2021 Feb 17;29(2):278-281. doi: 10.1080/09273948.2019.1695853. Epub 2019 Dec 12. PMID: 31829774.
88. Thulasi P, Saeed HN, Rapuano CJ, Hou JH, Appenheimer AB, Chodosh J, Kang JJ, Morrill AM, Vyas N, Zegans ME, Zuckerman R, Tu EY. Oral Miltefosine as Salvage Therapy for Refractory Acanthamoeba Keratitis. Am J Ophthalmol. 2021 Mar;223:75-82. doi: 10.1016/j.ajo.2020.09.048. Epub 2020 Oct 10. PMID: 33045218.
89. Musayeva A, Riedl JC, Schuster AK, Wasielica-Poslednik J, Pfeiffer N, Gericke A. Topical Voriconazole as Supplemental Treatment for Acanthamoeba Keratitis. Cornea. 2020 Aug;39(8):986-990. doi: 10.1097/ICO.0000000000002315. PMID: 32243421.
90. Bagga B, Joseph J, Garg P, Chandran K, Jayabhasker P, Manjulatha K, Sharma S. Efficacy of Topical Miltefosine in Patients with Acanthamoeba Keratitis: A Pilot Study. Ophthalmology. 2019 May;126(5):768-770. doi: 10.1016/j.ophtha.2018.12.028. Epub 2018 Dec 17. PMID: 30572075.
91. Bataillie S, Van Ginderdeuren R, Van Calster J, Foets B, Delbeke H. How a Devastating Case of Acanthamoeba Sclerokeratitis Ended up with Serious Systemic Sequelae. Case Rep Ophthalmol. 2020 Jul 14;11(2):348-355. doi: 10.1159/000508326. PMID: 32884549; PMCID: PMC7443666.
92. Rammohan R, Hajib Naraharirao M, Veerappan S, Vijayaraghavan P, Rajaraman R, Manayath GJ, Dsouza P, Radhakrishnan S, Venkatapathy N, Lakshmipathi D, Madhuravasal Krishnan J, Raghavan A. Cluster of Post-Operative Endophthalmitis Caused by Acanthamoeba T10 Genotype - A First Report. Cornea. 2021 Feb 1;40(2):232-241. doi: 10.1097/ICO.0000000000002603. PMID: 33201060.
93. Laurik KL, Szentmáry N, Daas L, Langenbucher A, Seitz B. Early Penetrating Keratoplasty À Chaud May Improve Outcome in Therapy-Resistant Acanthamoeba Keratitis. Adv Ther. 2019 Sep;36(9):2528-2540. doi: 10.1007/s12325-019-01031-3. Epub 2019 Jul 17. PMID: 31317392.
94. Di Zazzo A, Kheirkhah A, Abud TB, Goyal S, Dana R. Management of high-risk corneal transplantation. Surv Ophthalmol. 2017 Nov-Dec;62(6):816-827. doi: 10.1016/j.survophthal.2016.12.010. Epub 2016 Dec 22. PMID: 28012874; PMCID: PMC5479764.
95. Sarnicola E, Sarnicola C, Sabatino F, Tosi GM, Perri P, Sarnicola V. Early Deep Anterior Lamellar Keratoplasty (DALK) for Acanthamoeba Keratitis Poorly Responsive to Medical Treatment. Cornea. 2016 Jan;35(1):1-5. doi: 10.1097/ICO.0000000000000681. PMID: 26562819.
96. Alfonso-Muñoz EA, Roig-Revert MJ, Fernández-López E, Hernández-Díaz M, Araujo-Miranda R, Peris-Martínez C. A report of 10 patients with Acanthamoeba keratitis. Arch Soc Esp Oftalmol (Engl Ed). 2018 Oct;93(10):497-502. English, Spanish. doi: 10.1016/j.oftal.2018.04.009. Epub 2018 Jun 6. PMID: 29885816.
97. Di Zazzo A, Varacalli G, De Gregorio C, Coassin M, Bonini S. Therapeutic Corneal Transplantation in Acanthamoeba Keratitis: Penetrating Versus Lamellar Keratoplasty. Cornea. 2022 Mar 1;41(3):396-401. doi: 10.1097/ICO.0000000000002880. PMID: 34690262.

98. Kashiwabuchi RT, de Freitas D, Alvarenga LS, Vieira L, Contarini P, Sato E, Foronda A, Hofling-Lima AL. Corneal graft survival after therapeutic keratoplasty for Acanthamoeba keratitis. Acta Ophthalmol. 2008 Sep;86(6):666-9. doi: 10.1111/j.1600-0420.2007.01086.x. PMID: 18752517.
99. Robaei D, Carnt N, Minassian DC, Dart JK. Therapeutic and optical keratoplasty in the management of Acanthamoeba keratitis: risk factors, outcomes, and summary of the literature. Ophthalmology. 2015 Jan;122(1):17-24. doi: 10.1016/j.ophtha.2014.07.052. Epub 2014 Sep 26. PMID: 25262318.
100. Kitzmann AS, Goins KM, Sutphin JE, Wagoner MD. Keratoplasty for treatment of Acanthamoeba keratitis. Ophthalmology. 2009 May;116(5):864-9. doi: 10.1016/j.ophtha.2008.12.029. PMID: 19410943.
101. Zhang T, Xie L, Dong Y, Cheng J. Therapeutic keratoplasty for severe Acanthamoeba keratitis: risk factors, clinical features, and outcomes of postoperative recurrence. Graefes Arch Clin Exp Ophthalmol. 2023 May;261(5):1299-1309. doi: 10.1007/s00417-022-05883-4. Epub 2022 Nov 11. PMID: 36367557.
102. Rama P, Matuska S, Viganò M, Spinelli A, Paganoni G, Brancato R. Bilateral Acanthamoeba keratitis with late recurrence of the infection in a corneal graft: a case report. Eur J Ophthalmol. 2003 Apr;13(3):311-4. doi: 10.1177/112067210301300312. PMID: 12747654.
103. Petrillo F, Tortori A, Vallino V, Galdiero M, Fea AM, De Sanctis U, Reibaldi M. Understanding Acanthamoeba Keratitis: An In-Depth Review of a Sight-Threatening Eye Infection. Microorganisms. 2024 Apr 9;12(4):758. doi: 10.3390/microorganisms12040758. PMID: 38674702; PMCID: PMC11052265.
104. Atalay HT, Dogruman-Al F, Sarzhanov F, Özmen MC, Tefon AB, Arıbaş YK, Bilgihan K. Effect of Riboflavin/Rose Bengal-Mediated PACK-CXL on Acanthamoeba Trophozoites and Cysts in Vitro. Curr Eye Res. 2018 Nov;43(11):1322-1325. doi: 10.1080/02713683.2018.1501074. Epub 2018 Aug 7. PMID: 30021467.
105. Atalay HT, Uysal BS, Sarzhanov F, Usluca S, Yeşilırmak N, Özmen MC, Erganiş S, Tefon AB, Dogruman-Al F, Bilgihan K. Rose Bengal-Mediated Photodynamic Antimicrobial Treatment of Acanthamoeba Keratitis. Curr Eye Res. 2020 Oct;45(10):1205-1210. doi: 10.1080/02713683.2020.1731830. Epub 2020 Feb 27. PMID: 32065854.
106. Cristian C, Marco CDV, Arturo K, Claudio P, Miguel S, Rolf R, Remigio L, Leonidas T. Accelerated collagen cross-linking in the management of advanced Acanthamoeba keratitis. Arq Bras Oftalmol. 2019 Mar-Apr;82(2):103-106. doi: 10.5935/0004-2749.20190018. Epub 2019 Jan 10. PMID: 30726402.
107. Papaioannou L, Miligkos M, Papathanassiou M. Corneal Collagen Cross-Linking for Infectious Keratitis: A Systematic Review and Meta-Analysis. Cornea. 2016 Jan;35(1):62-71. doi: 10.1097/ICO.0000000000000644. PMID: 26509768.
108. Ting DSJ, Henein C, Said DG, Dua HS. Photoactivated chromophore for infectious keratitis - Corneal cross-linking (PACK-CXL): A systematic review and meta-analysis. Ocul Surf. 2019 Oct;17(4):624-634. doi: 10.1016/j.jtos.2019.08.006. Epub 2019 Aug 8. PMID: 31401338.
109. Ting DSJ, Henein C, Said DG, Dua HS. Amniotic membrane transplantation for infectious keratitis: a systematic review and meta-analysis. Sci Rep. 2021 Jun 21;11(1):13007. doi: 10.1038/s41598-021-92366-x. PMID: 34155280.
110. Müller-Morales CA, Vera-Duarte GR, Oliva-Bienzobas V, Ramirez-Miranda A, Navas A, Graue-Hernandez EO. Use of Amniotic Membrane Transplant and Deep Anterior Keratoplasty in a Patient with Bilateral Acanthamoeba Infectious Keratitis: A Case Report. Case Rep Ophthalmol. 2023 Oct 20;14(1):568-575. doi: 10.1159/000533988. PMID: 37901622; PMCID: PMC10601850.
111. Bourcier T, Patteau F, Borderie V, Baudrimont M, Rondeau N, Bonnel S, Chaumeil C, Laroche L. Intérêt de la greffe de membrane amniotique dans le traitement des kératites amibiennes sévères [Amniotic membrane transplantation for the treatment severe acanthamoeba keratitis]. Can J Ophthalmol. 2004 Oct;39(6):621-31. French. PMID: 15559648.
112. Carnt N, Robaei D, Minassian DC, Dart JKG. Acanthamoeba keratitis in 194 patients: risk factors for bad outcomes and severe inflammatory complications. Br J Ophthalmol. 2018 Oct;102(10):1431-1435. doi: 10.1136/bjophthalmol-2017-310806. Epub 2018 Jan 3. PMID: 29298778.
113. Vilares-Morgado R, Ferreira AM, Marques-Couto P, Madeira C, Moreira R, Torrão L, Neves-Cardoso P, Cunha AM, Rebelo S, Pinheiro-Costa J. Clinical outcomes and prognostic factors in Acanthamoeba keratitis. Cont Lens Anterior Eye. 2024 Apr;47(2):102119. doi: 10.1016/j.clae.2023.102119. Epub 2024 Jan 13. PMID: 38220498.
114. 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 Jan 27;25:101372. doi: 10.1016/j.ajoc.2022.101372. PMID: 35198803; PMCID: PMC8842025.
115. Karaca I, Barut Selver O, Palamar M, Egrilmez S, Aydemir S, Yagci A. Contact Lens-Associated Microbial Keratitis in a Tertiary Eye Care Center in Turkey. Eye Contact Lens. 2020 Mar;46(2):110-115. doi: 10.1097/ICL.0000000000000617. PMID: 31045617.
116. Niederkorn JY. The biology of Acanthamoeba keratitis. Exp Eye Res. 2021 Jan;202:108365. doi: 10.1016/j.exer.2020.108365. Epub 2020 Nov 19. PMID: 33221372; PMCID: PMC7856181.