World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-47 June 2025
ISSN: 2749-3644

PATHOGENESIS OF MICROBIAL KERATITIS (LITERATURE REVIEW)

Bekmurodova Orzigul Kamolovna
Senior Lecturer of the Department of Ophthalmology, Bukhara State Medical Institute named after Abu Ali Ibn Sino
bekmurodovaorzigul@bsmi.uz
ORCID: https://orcid.org/0009-0000-9931-973X

Article history:

Received: April 24th 2025
Accepted: May 20th 2025

Abstract:

Microbial keratitis is a sight-threatening eye infection caused by bacteria, fungi, and protists. Defects and damage to the epithelium are key predisposing factors that make the eye susceptible to corneal pathogens. Among bacterial pathogens, the most common causative agents of keratitis are Staphylococcus aureus, Pseudomonas aeruginosa, Streptococcus pneumoniae and Serratia species. Fungal causative agents of corneal infections include both filamentous and yeast fungi, including Fusarium, Aspergillus, Phaeohyphomycetes, Curvularia, Paecilomyces, Scedosporium, and Candida, and among protists, Acanthamoeba spp. are responsible for ocular disease. Clinical signs include redness, pain, lacrimation, blurred vision, and inflammation, but symptoms vary depending on the causative agent.

Keywords: keratitis, Staphylococcus aureus, Pseudomonas aeruginosa, Streptococcus pneumoniae, Serratia species

INTRODUCTION

The unique structure of the human eye, as well as its exposure to environmental influences, makes it susceptible to a number of agents that can cause infection. Injuries and epithelial defects disrupt protective mechanisms, and exposure to pathogenic microbes can lead to corneal inflammation or keratitis. An intact ocular surface prevents most microorganisms, but once the anatomical barriers are breached, the host's defense mechanisms against pathogens are insufficient to prevent infection, which can eventually lead to vision loss. Microbial or infectious keratitis is a potentially dangerous eye disease caused by bacteria, fungi, protists, etc. This is an inflammation of the cornea caused by pathogenic microbes that eventually penetrate the corneal stroma, causing inflammation and, ultimately, destruction of these structures [1,2]. The most common factors predisposing to the development of infectious keratitis are the use of contact lenses, especially nighttime or prolonged wear, inadequate disinfectant solutions, trauma, eye surgery, especially corneal surgery, chronic diseases of the ocular surface such as diabetes mellitus and/or prolonged use of topical corticosteroids [2,3]. Patients usually complain of redness, lacrimation, rapid onset of pain and blurred vision.

The clinical picture may vary depending on the causative agent that caused keratitis. This condition should be treated as a medical emergency, and adequate treatment should be initiated immediately [4,5,6].

If appropriate antimicrobial treatment is postponed, only 50% of the eyes will gain good visual acuity [8]. Appropriate management and timely initiation of treatment can reduce the incidence of severe vision loss by limiting corneal damage. Here we present a brief overview of bacterial, fungal, and protistic keratitis. Numerous microorganisms can infect the eye through both direct and indirect contact with the eye. The most common clinically important microorganisms that cause eye infections are considered in this article about the anatomical part of the eye involved in the disease, and the pathogenic mechanisms and treatment of the disease are discussed [7,8,9,10].

Pathogenesis

Adhesion

The first step in the pathogenesis of Acanthamoeba keratitis is the ability of amoebae to bind to the corneal epithelium, which determines the degree of pathogenicity of various isolates. The pathogenic cascade begins through the binding of amoebae to mannose glycoproteins on the surface of the cornea through an adhesive expressed on the membrane of trophozoites and called mannose-binding protein (MBP) [10, 11].

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This adhesion is an essential prerequisite for the development of infection. A mild corneal injury or abrasion is required to develop an infection in the cornea. An abrasion or injury leads to an increase in the expression of mannose glycoproteins on the corneal epithelium and, consequently, increases the adhesion of amoebae to the damaged cornea, compared with a healthy cornea [12]. In addition to serving as a vector for the introduction of trophozoites onto the surface of the cornea, contact lenses also increase the level of mannose glycoproteins on the corneal epithelium.

The second important element involved in adhesion is the number of acanthopodia on the surface of the amoeba. Pathogenic amoebas have more than 100 acanthopodia per cell compared to non-pathogenic amoebas. Therefore, non-pathogenic amoebas have a very low level of binding to host cells compared to pathogenic amoebas [10,12,13]. This leads to an increase in the number of trophozoites binding to the cornea conditioned by contact lenses compared to the normal cornea, as a result of which it was found that more than 80% of cases of Acanthamoeba keratitis are associated with the use of CL [5]. Therefore, it is believed that the number of acanthopodia is also closely related to the rate of their attachment to the surface of the cornea. After attachment, intracellular signaling processes trigger a pathogenic cascade involved in the pathogenesis of acanthamoebic keratitis.

Mycotic keratitis

Mycotic keratitis is a fungal infection of the cornea caused by filamentous and/or yeast—like fungi. They can be more than

50% of all culturally positive microbial keratitis, especially in tropical and subtropical countries [14,15]. It is reported that there is a strong geographical correlation between the occurrence of different types of keratomycosis. For example, the proportion of keratitis caused by yeast-like fungi tends to increase in temperate countries, while corneal ulcers caused by filamentous fungi are more common in tropical latitudes [16].

Filamentous fungi such as Fusarium, Aspergillus, Phaeohyphomycetes, Curvularia, Paecilomyces, and Scedosporium apiospermum are most often associated with keratitis caused by filamentous fungi [17,18]. However, Candida albicans and other Candida species are the most common yeast-like fungi that cause keratitis. Keratitis is reportedly caused by eye injury, which is usually the most important predisposing factor in healthy young men engaged in agriculture or other outdoor activities [19]. These fungi do not penetrate the intact cornea, and penetration occurs only when the epithelium is damaged. Traumatic agents of animal origin or plant substances, soil or dust particles, or directly implant fungal conidia onto the abrasive epithelium of the cornea for fungal invasion [18,20].

Bacterial keratitis

The main bacterial pathogens of infectious keratitis include Staphylococcus aureus, Pseudomonas aeruginosa, and pneumococcal streptococcus.

and Serratia species [21,22]. Community-acquired cases of bacterial keratitis are usually resolved with empirical treatment, however, if no measures are taken, this can lead to perforation, endophthalmitis, and vision loss [23]. Clinical manifestations of bacterial keratitis include acute pain, redness, photophobia, and corneal ulceration [24].

Pseudomonas aeruginosa ulcers are more severe than other bacterial ulcers and are often difficult to treat, resulting in a worse visual result than other bacterial ulcers [20,22]. Bacterial keratitis accounts for approximately 90% of all cases of microbial keratitis [25], the most common causative agent of which is P. aeruginosa

all over the world [20]. Infection of the cornea with Pseudomonas aeruginosa is most often associated with the use of contact lenses. Before the advent of contact lenses, it was rarely reported as a problem [26,27]. The resistance of Pseudomonas aeruginosa to disinfectants, combined with its adhesive ability to plastic, facilitates its entry into the eye, where it can react with defective corneal epithelium, penetrating into the corneal stroma. On the other hand, pneumonia is the primary cause of corneal ulcers in developing countries; however, some reports emphasize that streptococci occur most often after P. aeruginosa and/or eye infections caused by S. aureus [24,25]. Unlike P. aeruginosa, pneumococcal keratitis is usually not associated with contact lens use and predisposing factors include eye injury or surgery [28,29].

Adhesion

Bacteria initiate infection by interacting with receptors on the surface of the host cell using various adhesives that bind bacteria to corneal epithelial cells. Microbial adhesives are not only involved in the attachment of bacteria to the surface of epithelial cells, but can also play an active role in subsequent interactions and the infectious process.

They can act as toxins that initiate microbial invasion and contribute to the subsequent pathogenic cascade. Bacteria secrete several adhesives on the surface of epithelial cells. Their surface, such as pili or fimbriae, recognizes specific carbohydrates or proteins on the surface of the host cell. The adhesion of P. aeruginosa, S. pneumonia, and S. aureus to the damaged corneal epithelium is significantly higher than that of other bacteria, which explains their frequent release in cases of keratitis.

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Volume-47 June 2025
ISSN: 2749-3644

Studies have shown that purified peels successfully compete with cold-causing bacteria for binding to the surface of the eye and are used to protect against keratitis caused by P. aeruginosa. Corneal epithelial glycoproteins act as surface receptors providing pilus and amino acid binding activity. Sugar sialic acid was able to completely inhibit pilus binding.

with mouse corneal epithelial cells [28,29,30]. On the other hand, bacterial flagella are filamentous organelles responsible for bacterial motility and, therefore, also responsible for the spread of infection. More than 95% of clinical isolates of P. aeruginosa are flagellate, and mutants with a deficiency of flagella were found to be non-virulent [8]. In addition, anti-flagellar antibodies homologous to the infecting strain protect mice from Pseudomonas corneal infection [16,14]. In addition, glycocalyx can also play an important role in bacterial adhesion by producing mucosal aggregates resistant to phagocytosis, which allows them to attach to cells [12].

S. aureus surface adhesives, known collectively as MSCRAMMS (microbial surface components that recognize adhesive matrix molecules), have also been recognized as mediating bacterial adhesion to host extracellular matrix components, collagen, fibronectin, fibrinogen, laminin, and elastin [20,16]; the role of MSCRAMMC (collagen-binding adhesive) in S. aureus keratitis has been studied and It was concluded that collagen-binding adhesive is a virulence factor in S. aureus keratitis and is involved in the early stages of pathogenesis.

S. aureus corneal infections. Similarly, [30] studied the role of S. aureus fibronectin-binding protein as an adhesive/invasive protein of epithelial and/or endothelial cells. Their data showed that FnBPs is a surface ligand for human corneal cells and plays a key role in host-parasite interaction. It serves as an important adhesive and triggers invasion of ulcerative keratitis caused by S. aureus.

Similarly, streptococci colonize various parts of the human body, expressing a variety of adhesins, and, consequently, their attachment to human tissues is mediated by a diverse group of bacterial surface proteins, MSCRAMMS [27, 28, 29]. Plasmin and fibronectin binding protein A (PfbA), MSCRAMMS, is known to promote bacterial adhesion and penetration into human epithelial cells by recognizing fibronectin-like molecules. In addition, pneumococcal surface adhesin A (PsaA), pneumococcal surface protein A (PspA), pneumolysin (ply), pneumococcal adhesion and virulence factor A (PavA), choline-binding protein A (CbpA/PcpA), putative protease maturation protein A (PpmA), IgAI protease (IgAIp) and Streptococcal lipoprotein rotamase A (SIsA) has been shown to be associated with pneumococcal adhesion and virulence [23]. The surface of streptococcal cells may contain fibrillar structures such as pills and fibrils, which can also promote attachment to the cell surface and initiate infection. Pneumococcal surface protein C (PspC) promotes the adhesion and absorption of pneumococci by nasopharyngeal epithelial cells (Hammerschmidt et al., 2000). In addition, antibodies against PsaA, which encode pneumococcal surface adhesin A (PsaA), lead to a decrease in adhesion to nasopharyngeal epithelial cells [31]. Therefore, these adhesives are likely involved in the initial stages of pneumococcal infection.

CONCLUSIONS

Microbial keratitis is a complex disease, the treatment of which must take into account many factors. This is a serious public health problem, especially in developing countries where access to medical care is limited and economic barriers are huge, and where it can be a major cause of vision loss among the young population. As with all corneal infections, proper identification of the pathogen, followed by appropriate targeted therapy, can reduce the risk of complications. A better understanding of the pathogenetic cascade will undoubtedly lead to improved clinical treatment. However, the emergence of drug-resistant strains, along with recurrent infections, highlights the need for more effective treatment methods. In addition, it is also important to identify the genetic basis of the virulence factors responsible for the disease, since the pathogenicity of keratitis is a combination of multiple events occurring simultaneously in time and space, successful transmission of the pathogen to a susceptible organism, overcoming its physiological barriers and, ultimately, the development of the disease. Subsequently, a complete understanding of the pathogenesis of a particular organism will undoubtedly lead to the identification of potential therapeutic interventions.

REFERENCES

1. H. Alizadeh, M.S. Podgerni, J.P. McCully, J.Y. Niederkorn, Apoptosis as a mechanism of cytolysis of tumor cells by a pathogenic free-living amoeba, Infect. The immune system. 62 (1994b) 1298-1303.
2. H. Alizadeh, S. Neelam, M. Hurt, J.J. Niederkorn, The role of contact lens wear, bacterial flora, and mannose-induced pathogenic protease in the pathogenesis of amoebic keratitis, Infect. Immunization. 73 (2005) 1061-1068.
3. L.G. Alionte, B.M. Cannon, K.D. White, A.R. Caballero, R.J. O'Callaghan, J.A. Hobden, Pseudomonas aeruginosa LasA protease and corneal infections, Curr. Eye Res. 22 (2001) 266-271.

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-47 June 2025
ISSN: 2749-3644

4. Z. Ansari, D. Miller, A. Galor, Modern views on fungal keratitis: diagnosis and treatment, current course. Fungal infection. Article 7 (2013) 209-218.
5. R.A. Ansorg, M.E. Knohe, A.F. Spice, K.J. Kraus, Differentiation of the main flagellated antigens of Pseudomonas aeruginosa by slide coagglutination, J. Clin. Microbiol. 20 (1984) 84-88.
6. Y. Akil, R. Siddiqui, A. Anwar, M.R. Shah, S. Khoja, N.A. Khan, Photochemotherapeutic strategy for combating acanthamoebic infections, antimicrobials. Agents of chemotherapy. 59 (2015) 3031-3041.
7. P.A. Asbell, D.F. Sam, M. Shaw, D.S. Draghi, N.P. Brown, An increase in the prevalence of methicillin resistance in serious eye infections caused by staphylococcus aureus in the United States: from 2000 to 2005, J. Cataract. Refractory surgery. 34 (2008) 814-818.
8. S. Bang, E. Edell, A.O. Egrari, J.D. Gotch, Voriconazole treatment of 3 eyes with resistant acanthamoebic keratitis, Am. J. Ophthalmol. 149 (2010) 66–69.
9. J.P. Barletta, G. Angella, K.S. Balch, H.G. Dimova, G.A. Stern, M.T. Moser, G.B. van Setten, G.S. Schultz, Inhibition of pseudomonas corneal ulceration in rabbits with a synthetic matrix metalloproteinase inhibitor, Invest. Ophthalmol.Vis. science. 37 (1996) 20-28.
10. M.B. Berman, Regulation of MMP-1 collagenase secretion by corneal fibroblasts using plasmin, Cornea 12 (1993), 420-432.
11. M.J. Bharati, R. Ramakrishnan, S. Shivakumar, R. Meenakshi, D. Lionalraj, Etiology and structure of sensitivity to antibacterial drugs in community-acquired bacterial eye infections in a top-level ophthalmological hospital in South India, Indian J. Ophthalmol. 58 (2010) 497-507.
12. J.M. Blondeau, Fluoroquinolones: mechanism of action, classification and development of resistance, An overview. Ophthalmol. No. 49 (Supplement 2) (2004) S73–S78.
13. J.P. Bouchard, G. Tronchin, V. Anne, R. Robert, J.M. Senet, Laminin receptors in Candida albicans microbial tubes, Infection. Immunity. 58 (1990) 48-54.
14. J.P. Bouchard, M. Sanchez, A. Chevaye, A. Marot-Leblond, J.S. Lisitsky, G. Tronchin, D. Chabasse, Recognition of laminin and fibrinogen of Aspergillus fumigatus conidia, dependent on sialic acid, Infect. Immunization. 65 (1997) 2717–2724.
15. S.D. Boveland, P.A. Moore, J. Mysore, T.M. Krunkoski, W.M. Dietrich, K. Jarrett, K. Page Carmichael, Immunohistochemical study of matrix metalloproteinases-2 and -9, macrophage inflammatory protein-2 and tissue inhibitors of matrix metalloproteinases-1 and -2 in normal, purulent-necrotic and fungal infection. horse cornea, veterinarian. Ophthalmol. 13 (2010) 81-90.
16. I.M. Bromley, K. Donaldson, Binding of Aspergillus fumigatus spores to lung epithelial cells and basement membrane proteins: significance for asthmatic lungs, Thorax 51 (1996) 1203-1209.
17. M. Busin, M. Shpitsnas, Supportive release of gentamicin by contact lenses with a pre-soaked therapeutic dressing, Ophthalmol 95 (1988), 796-798.
18. A.R. Caballero, S.S. McCormick, A. Tan, R.J. O'Callaghan, Isolation and characterization of a new protease of Staphylococcus aureus, Invest. Ophthalmol. Vis. Science. 49 (2008) 5514.
19. A.R. Caballero, T.J. Foster, I.R. Monk, A. Tan, K.L. Balzli, R.J. O'Callaghan, Ocular pathology of a staphylococcus aureus mutant lacking a newly discovered virulence factor, Invest. Ophthalmology. Vis. Sci. 51 (2010) 3891.
20. M.S. Callegan, L.S. Engel, J.M. Hill, R.J. O'Callaghan, Staphylococcus aureus virulence in the cornea: the role of alpha-toxin and protein A in pathogenesis, Infect. The immune system. 62 (1994) 2478-2482.
21. Z. Kao, D.M. Jefferson, N. Panjwani, The role of carbohydrate-mediated adhesion in cytopathogenic mechanisms of acanthamoeba, J. Biol. Chemistry. 273 (1998) 15838-15845.
22. D. W. Clarke, H. Alizadeh, J. Y. Niederkorn, Inability of Acanthamoeba castellanii to cause intraocular infections, Invest. Ophthalmology. Fish. Sci. 46 (2005)72–2478.
23. C. B. 1 Kosar, E. J. Cohen, S. J. Rapuano, P. R. Laibson, Infection of the corneal wound surface after phacoemulsification, Arch. Ophthalmol. 119 (2001) 1755-1759.
24. D. J. Koster, P. R. Badenoch, Host, microbial and pharmacological factors influencing the outcome of purulent keratitis, Br. J. Ophthalmol. 71 (1987)96-101.
25. J. W. Kosterton, Pseudomonas aeruginosa in nature and diseases, in: L. D.
26. Sabat (ed.), Pseudomonas aeruginosa: organisms, diseases caused by it and their treatment, Hans Huber, Bern, 1980. 1980.
27. P. Coulot, J. P. Bouchara, G. Renier, V. Annaix, C. Planchenault, G. Tronchin, D. Chabasse, specific interaction of Aspergillus fumigatus with fibrinogen and its role in cell adhesion, infections. Immune. 62 (1994) 2169-2177.
28. J. J. Dykes, M. S. Austin, G. D. Slup, J. M. Moreau, E. B. Hume, H. V. Thompson, F. M. McAleese, T. J.

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-47 June 2025
ISSN: 2749-3644

Foster, R. J. O'Callaghan, Corneal pathogenesis or Strain of Staphylococcus aureus Newman, Invest. Ophthalmology. Fish. Sci. 43 (2002)1109–1115.

29. J. K. Dart, V. P. Sou, S. Kilvington, Acanthamoebic keratitis: an update on diagnosis and treatment for 2009, Am. J. Ophthalmol. 148 (2009) 487-499.
30. J. F. De Jonkheer, Ecology of acanthamoeba, section "Infection". Dis. 13 (Supplement 5) (1991) pp. 385-387.
31. J. Hamilton, L. Jeevons, S. Yangchim, N. Vanittanakom, R.J. Hay, Sialic acid-dependent recognition of laminin by conidia Penicillium marneffei, Infection. Immune. 66 (1998) 6024–6026.