How Could Contact Lens Wears Be at Risk of Acanthamoeba Infection? A Review
Youhanna W. Ibrahim1, 2, David L. Boase1, and Ian A. Cree1, 2, 3

ABSTRACT
Contact lens wear is highly influential on the incidence of ulcerative keratitis worldwide, particularly in developed countries. The association between Acanthamoeba keratitis and contact lens wear is firmly established; it may account for up to 95% of the reported cases. Before the popularisation of soft contact lens wear, Acanthamoeba keratitis was extremely rare. In 2000 it was estimated that the number of contact lens wearers worldwide was about 80 million, out of whom 33 million were in the United States and 90% of them wore hydrogel soft lenses. Contact lens-related problems depend on many factors, such as lens material, wearing modality, lens hygiene, type of lens-caring solution, the degree of compliance of the lens user with lens wear and care procedures, lens overwear, sleeping in lenses, rate of changing lenses, and lens case hygiene. This paper is a thorough review of the literature aiming to highlight the role of one of the main risk factors of infectious keratitis, contact lens wear, and also to show the responsibility of lens users in aggravating this risk.


KEY WORDS: Acanthamoeba; keratitis; contact lenses; contact lens wearer; lens overwear.

RESUMEN
La utilización de lentes de contacto es un factor que influye sumamente en la incidencia de la queratitis ulcerosa, en particular en los países desarrollados. La asociación entre queratitis por Acanthamoeba y el uso de lentes de contacto está firmemente establecida; podría representar aproximadamente hasta un 95% de los casos registrados. Antes de la popularización del uso de lentes de contacto, la queratitis por Acanthamoeba era muy poco frecuente. En el año 2000 se estimó que, a nivel mundial, había unos 80 millones de usuarios de lentes de contacto, de los cuales 33 millones residían en los Estados Unidos y, de ellos, el 90% utilizaban lentes de contacto blandas de hidrogel. Los problemas derivados del uso de lentes de contacto dependen de otros muchos factores, como el material del que está hecha la lente, la modalidad de uso, las medidas de higiene empleadas, el tipo de solución utilizada para la limpieza y el mantenimiento de la lente, el grado de cumplimiento terapéutico del usuario de las lentes respecto a su utilización y a su limpieza/mantenimiento, el uso de las lentes durante periodos excesivamente prolongados, el dormir con las lentes de contacto puestas, la frecuencia con la que el usuario se cambia de lentes y la limpieza de la funda de las lentes de contacto. Este artículo presenta una revisión minuciosa de la literatura, con el objetivo de resaltar el papel de uno de los principales factores de riesgo de desarrollo de queratitis infecciosa, como es el uso de lentes de contacto, con el fin de ponerte de relieve que el propio usuario de las lentes es, en ocasiones, el responsable de agravar este riesgo.


PALABRAS CLAVE: Acanthamoeba; queratitis; lentes de contacto; usuario de lentes de contacto; uso excesivo de las lentes de contacto.

INTRODUCTION
Acanthamoeba is a ubiquitous pathogen that can be found worldwide with different incidence rates, showing the ability to survive in very harsh environmental circumstances.

Acanthamoeba keratitis is a potentially blinding corneal infection that may aggressively affect both eyes and with the possibility to recur after penetrating keratoplasty.1 Contact lens wear remains the main risk factor in transmitting Acanthamoeba trophozoites and cysts to the cornea.5,6 A 7-year 1997-2003 survey7 showed an increase in the number of hospitalised patients due to contact lens-related corneal ulcers, which correlated with the increase in the number of lens wearers. Acanthamoeba has a great affinity for the attachment to the corneal epithelium8 and to contact lenses.9 The tendency for Acanthamoeba to adhere to surfaces is a key first step in the pathogenesis of Acanthamoeba keratitis, particularly in contact lens wearers. Contact lenses affect corneal epithelium integrity in two different ways: directly, through the associated fitting-related abrasions10 and indirectly, by altering the normal physiological and metabolic cellular activities.11 These later changes render the epithelial cells in a hypoxic status that eventually alters their integrity. Corneal oxygenation is significantly reduced during contact lens overwear, particularly for those who sleep in their lenses overnight.12 However, patient’s compliance and some basic hygienic standards can effectively minimise the risk of Acanthamoeba keratitis.13

CONTACT LENS-RELATED PROBLEMS
Contact Lens-Induced Trauma

Direct Traumatic Effect of Lenses. The corneal epithelium, with its tight junctions, creates an important barrier against Acanthamoeba invasion to the underlying corneal structures. Corneal epithelial cells are more resistant to the cytopathic effect of Acanthamoeba trophozoites than keratoctyes.14 Contact lens wear cause minor corneal abrasions, which is the key initial step for Acanthamoeba infection. Martinez et al.10 suggested that corneal trauma was the crucial factor for Acanthamoeba infection, rather than immunosuppression. The adherence of the Acanthamoeba protozoon to an intact corneal epithelium without trauma did not lead, in animal models,
to the development of keratitis. Corneal abrasion was absolutely essential for the induction of *Acanthamoeba* keratitis in hamsters infected with contaminated contact lenses.\(^\text{35}\)

Corneal epithelial defects make it possible for the *Acanthamoeba* protozoon to attach to the epithelium and to subsequently invade the rest of the underlying stromal layers. Corneal injury exposes protein sites known as mannose glycoproteins on the surface of injured corneas. The adhesion of the *Acanthamoeba* to the corneal epithelial cells is the result of a unique interaction between corresponding mannose-binding glycoproteins on the adjacent surface membranes.\(^\text{8,16,17}\) Sugar inhibition assays\(^\text{8,18}\) revealed how *Acanthamoeba* can selectively bind with high affinity to mannose saccharides and not to non-mannosylated neoglycoproteins, such as galactose, fucose, galactosamine or lactose. The corneal surface mannose receptors stimulate *Acanthamoeba* to secrete pathogenic proteases\(^\text{16}\) which, in turn, induce epithelium apoptosis\(^\text{19}\) and facilitate amoeba invasion to the underlying stroma. Alizadeh et al.\(^\text{20}\) showed that contact lens wear exacerbated *Acanthamoeba* keratitis through the secretion of mannose-induced protease 133. In addition, the attachment of *Acanthamoeba* to corneal epithelial cells helps the phagocytosis and digestion of bacteria\(^\text{21}\) that provide an important nutrition source for *Acanthamoeba*. However, Sharma et al.\(^\text{22}\) found no difference between the adherence ability of *Acanthamoeba* to corneal epithelial cells of normal non-lens wearers and that of asymptomatic contact lens wearers.

**Indirect Traumatic Effect of Lenses.** Contact lens wear is usually associated with corneal epithelial hypoxia and hypercapnia, particularly when sleeping in lenses or when using lenses having low oxygen transmissibility.\(^\text{11}\) Carbon dioxide accumulation alters the normal metabolic pathways, which leads to a series of micro-structural changes affecting all corneal layers, such as epithelial microcysts, depletion of epithelial glycogen storage, lactic acid accumulation, corneal acidosis, epithelial oedema,\(^\text{11}\) decreased mitotic rate, increased central corneal thinning,\(^\text{23}\) corneal hypoxia,\(^\text{24}\) compromised junctional integrity, increased epithelial cells permeability,\(^\text{25}\) increased cellular epithelial fragility, epithelial punctation, microscopic abrasion, sloughing of the epithelium and, eventually, corneal ulceration. In addition, changes in tear film thickness and stability\(^\text{26}\) and alteration of the normal profile of conjunctival commensals\(^\text{27}\) have been recognised. All these changes collectively breach the natural extra ocular protective mechanisms, rendering the cornea an easy target to a wide array of pathogens, including the *Acanthamoeba*.

**Attachment of Acanthamoeba to Contact Lenses**

Contact lenses serve as a vehicle for the harbouring, transmission and delivery of microorganisms to the eye. *Acanthamoeba* has a high affinity for contact lens surfaces, a property that plays an important role in the pathogenesis of *Acanthamoeba* keratitis and creates an actual threat to contact lens wearers.\(^\text{28}\) The adherence of *Acanthamoeba* trophozoites and cysts to contact lenses can be detected and quantified using different methods and techniques.\(^\text{8,29-31}\) The ability of *Acanthamoeba* to attach to contact lenses is influenced by several factors:

**Contact Lens Material, Ionicity, and Water Content.** The manufacturing material affects contact lens ability as a mechanical host allowing attachment and transfer of *Acanthamoeba* trophozoites or cysts onto the corneal surface. The incidence of *Acanthamoeba* is much lower with rigid lenses, as compared with the soft type. The lower incidence of *Acanthamoeba* keratitis found in the Netherlands\(^\text{32}\) was attributed to the greater proportion of Dutch contact lens wearers that used rigid gas-permeable lenses. Rigid gas-permeable lenses were recommended to hospital staff members wearing lenses, with the aim of minimising the risk of infectious keratitis, due to the easy removal of the attached *Acanthamoeba* trophozoites and cysts from the surface of this type of contact lenses.\(^\text{33}\)

Kilvington et al.\(^\text{14}\) showed that cyst attachment occurred only for soft lenses, but not for gas-permeable ones. However, a significant adherence of trophozoites was detected in the case of rigid gas-permeable lenses, as compared with soft contact ones\(^\text{35}\), with greater affinity for the silicone acrylate material of rigid lenses than for the fluoropolymer material of those same lenses.\(^\text{36}\)

The greater affinity of *Acanthamoeba* trophozoites for silicone hydrogel lenses, as compared with conventional hydrogel lenses (\(P<0.001\)) was attributed to the attachment characteristics of the polymer of silicone type.\(^\text{57,58}\) The attachment of *Acanthamoeba* trophozoites to different soft contact lens materials, such as polymacon, etafilcon A, lidofilon A, and bufilcon A varied significantly, with the greatest adherence being observed for lidofilon A and the least for the etafilcon A lenses.\(^\text{29}\) Adherence of cysts and trophozoites was found to be higher for the non-ionic than for the ionic disposable lenses.\(^\text{38}\) Simmons et al.\(^\text{39}\) suggested that the attachment of *Acanthamoeba* was highly dependant on the ionic nature and the water content of soft contact lenses. Collectively, these reasons could explain why *Acanthamoeba* adherence is higher for disposable and extended-wear soft lenses than for the conventional soft daily and rigid lenses.

**Duration of Exposure and Protozoon Concentration.** Both cysts and trophozoites showed an immediate adherence to contact lenses, which was observed to happen within 10 seconds after exposure.\(^\text{36}\) *Acanthamoeba* adherence to lens surface increased significantly for longer exposure durations and for higher concentrations of inoculum.\(^\text{39,40}\) The higher water content of disposable soft contact lenses allows longer time of lens wear and, in turn, gives enough time of exposure for the lenses to be loaded with *Acanthamoeba*. This could add to the reasons why disposable soft contact lenses wearers are at greater risk of suffering from *Acanthamoeba* keratitis than those wearers of other types of contact lenses. However, Sharma et al.\(^\text{22}\) found no difference in *Acanthamoeba* adherence to different contact lenses with increasing exposure time.

**Acanthamoeba-Life Stage.** *Acanthamoeba* trophozoite shows a greater tendency to adhere to contact lenses, as compared with the cystic form.\(^\text{39,36,40-42}\) In contrast to the cystic form, Sharma et al.\(^\text{36}\) noticed more adherence of trophozoites to rigid gas-permeable lenses than to soft ones. Similarly, Kelly et al.\(^\text{29}\) observed more preference of trophozoites to adhere...
Contact Lens Disinfecting Solutions. The use of ineffective contact lens disinfecting solutions is strongly linked to the threat of *Acanthamoeba* infection in contact lens wearers. A 10-year survey (1994-2004) showed that *Acanthamoeba* was isolated in contact lenses and contact lens disinfecting solutions in all cases of *Acanthamoeba* keratitis. The one-step 3% hydrogen peroxide and multipurpose solutions were found to be ineffective in killing *Acanthamoeba* cysts and trophozoites, as well as bacteria and fungi. However, in addition to the broad antimicrobial activity of multipurpose solutions, they were found to be capable of reducing the adherence capability of *Acanthamoeba* to contact lenses. Opti-Free express multipurpose solution significantly reduced the adherence of trophozoites and cysts when used to clean, rinse, and soak soft contact lenses. Complete Easy Rub multipurpose solution was effective in removing bacteria, fungi and *Acanthamoeba* from silicone hydrogel lenses.

Problems Caused by Contact Lens Wearers

Contact Lens Overwear

Corneal overwear-related problems could develop in the long term for any type of contact lenses, including those designed for extended wear. The overwear problems were influenced by the rate of oxygen transmission and permeability through the lens material, lens thickness, lens type, wearing modalities, replacement schedule, repeated wear of disposable lenses, and overnight sleep in lenses. A lower incidence of microbial keratitis was reported for silicone hydrogel lenses with high oxygen permeability than for other soft lenses having low oxygen permeability used with an extended
wear scheme. However, occasional pathophysiological problems, such as diffuse corneal infiltration, development of mucin balls, superior epithelial arcuate lesions, contact lens papillary conjunctivitis, corneal erosions, corneal dryness and discomfort, central corneal thinning, and thickened conjunctival epithelium due to increased metaplasia were reported with the overnight use of silicone hydrogel lenses with high oxygen permeability. A significantly higher risk of bacterial keratitis and a greater incidence of complications, such as limbal neovascularisation and corneal oedema, were reported in wearers whose daily wear time was higher than 12 hours.

**Overnight Sleep in Different Types of Contact Lenses**

The cornea gets its oxygen supply directly from the air when the eye is opened and from the surrounding blood vessels when it is closed. The new versions of rigid and soft contact lenses were designed to allow oxygen delivery to the cornea at an almost similar level under either opened or closed-eye conditions. However, corneal hypoxia, subepithelial infiltrations, immune ring formation, changes in corneal curvature, central corneal thinning, alteration in the number of polymorphonuclear leukocytes, and variations in the level of different inflammatory mediators in the tear film were reported upon wearing contact lenses for multiple sleep cycles. The results of various surveys suggested that the overnight wear of contact lenses was the main cause of microbial keratitis, with a greater concern for the immunocompromised patients, where the risk of unusual infections was very high.

The overnight wear-related corneal changes and the risk of ulcerative keratitis was found to be significantly dependent on the lens type. Overnight wear of rigid gas-permeable contact lenses was associated with higher levels of corneal hypoxia and epithelial oedema, as compared with soft lenses. However, Graham et al. stated that the severity of corneal swelling with rigid gas-permeable lenses was not a reliable predictor of ocular complications. No significant difference was recognised in the bacterial binding ability to reliable predictor of ocular complications. No significant difference was recognised in the bacterial binding ability to

**Corneal Hypoxic Changes**

Corneal hypoxic changes, such as epithelial oedema and microcysts were not recognised among the overnight wearers of extended wear lenses, with no significant difference in limbal redness between them and the non-lens users. Kenyon et al. suggested that neither the level of overnight corneal swelling nor the period between removals could influence the incidence or the severity of corneal problems of extended wear lenses.

**Non-Compliant Contact Lens Users**

The compliance of contact lens wearers with the recommended lens care hygiene procedures is crucial to reduce the risk of serious infections. D’Aversa et al. reviewed the medical records of 12 patients and found that substandard lens-care methods were used in 13 out of 14 (92.9%) eyes infected with *Acanthamoeba*. The use of tap water for the care of contact lenses was widely accepted as the main risk factor in *Acanthamoeba* infection.

In the United Kingdom, 91% of the soft contact lens wearers and 94% of the rigid lens wearers avoided the disease by the complete avoidance of water and the use of powerful lens disinfecting solutions. In the USA, the withdrawal of salt tablets from the market was responsible for the decrease in the incidence of *Acanthamoeba* keratitis in the mid 80s. A recent study showed that the Chicago-area tap water contained a highly virulent *Acanthamoeba* strain that was contributing to the increased incidence rate of *Acanthamoeba* keratitis in this area. Swimming, diving, showering or washing the face while wearing contact lenses was reported to cause *Acanthamoeba* keratitis. The 50-fold increase in the risk of *Acanthamoeba* keratitis among disposable contact lens users was largely attributable to repeated wear of lenses, lack of disinfection, and use of saline and chlorine-based solutions.

The compliance of contact lens users with the recommended care procedures is ineffective if these solutions do not manage to kill *Acanthamoeba*. To avoid the persistent use of non-sterile solutions by non-compliant lens wearers, Moore recommended heat disinfection of lenses—between 70 and 80°C for 10 minutes—and the use of 3% hydrogen peroxide for 2-3 hours, 0.001% thimerosal with edetate for 4 hours, 0.005% benzalkonium chloride with edetate for 4 hours, 0.001% chlorhexidine for 4 hours or 0.004% chlorhexidine for 1 hour. Better compliance of contact lens wearers was achieved with the introduction of multipurpose solutions. The multipurpose solutions replaced the need for additional rinsing solution, offering a single solution for lens care procedures is ineffective if these solutions do not manage to kill *Acanthamoeba*. To avoid the persistent use of non-sterile solutions by non-compliant lens wearers, Moore recommended heat disinfection of lenses—between 70 and 80°C for 10 minutes—and the use of 3% hydrogen peroxide for 2-3 hours, 0.001% thimerosal with edetate for 4 hours, 0.005% benzalkonium chloride with edetate for 4 hours, 0.001% chlorhexidine for 4 hours or 0.004% chlorhexidine for 1 hour. Better compliance of contact lens wearers was achieved with the introduction of multipurpose solutions. The multipurpose solutions provided potent antimicrobial protection with less toxic and less allergenic effects.

The non-compliance of contact lens users could occur in the case of deliberate reuse of daily disposable contact lenses, when wearing expired lenses without replacement or if using cheap contact lenses purchased from unlicensed vendors. Old contact lenses could colonise more microorganisms due to the increased lens surface tear and wear-related scratches or to the accumulated deposits. The relationship between repeated use of daily disposable lenses
and risk of \textit{Acanthamoeba}\textsuperscript{12,113} and microbial keratitis\textsuperscript{93,114} is well established. Daily disposable lenses were designed for single use only, where a new sterile set should be opened every morning and discarded in the evening. This wear modality aimed to provide a greater hygienic advantage, by avoiding the necessity and the cost of disinfecting solutions and storage cases. For hygiene purposes, daily disposable lenses were recommended for those lens wearers having jobs entailing a great potential risk of infection, such as hospital staff members.\textsuperscript{13} Dart et al.\textsuperscript{13} reported that vision loss was less likely to occur for daily disposable than for reusable soft lens wearers, though no significant reduction in the risk of microbial keratitis was found for users of daily disposable and silicone hydrogel lenses. However, the assumed lens wearers’ compliance could sometimes divert the attention of professionals from considering \textit{Acanthamoeba} infection in daily disposable contact lens wearers. A delay of 17 days before starting the anti-\textit{Acanthamoeba} treatment was reported.\textsuperscript{116}

Radford et al.\textsuperscript{73} stated that the low care philosophy of daily disposable lens use has resulted in an absolute absence of care, and emphasised the importance of warning patients against the increased risk of infection upon reuse of daily disposable contact lenses. The non-compliance of contact lens users has been attributed to the convenience of using multipurpose or one-step solutions instead of using two-step hydrogen peroxide solutions. Financial savings achieved by reusing daily disposable contact lenses is another factor.\textsuperscript{117}

**CONCLUSION**

Contact lens wear is the main cause of ulcerative keratitis, which could get seriously complicated with corneal scarring and lead to permanent vision loss. The association between \textit{Acanthamoeba} keratitis and contact lens wear is firmly established. Contact lenses have a great impact on corneal epithelium and risk of \textit{Acanthamoeba} infection, such as hospital staff members. A delay of 17 days before starting the anti-\textit{Acanthamoeba} treatment was reported. A low care philosophy of daily disposable lens use has resulted in an absolute absence of care, and emphasised the importance of warning patients against the increased risk of infection upon reuse of daily disposable contact lenses. The non-compliance of contact lens users has been attributed to the convenience of using multipurpose or one-step solutions instead of using two-step hydrogen peroxide solutions. Financial savings achieved by reusing daily disposable contact lenses is another factor.

**REFERENCES**

38. Beattie TK, Tomlinson A, Seal, DV. Surface treatment or material characteristic: the reason for the high level of Acanthamoeba attachment to silicone hydrogel contact lenses. Eye Contact Lenses. 2003;29:540-543; discussion S57-S59, S192-S194.
51. Beattie TK, Tomlinson A, Seal DV, Surface treatment or material characteristic: the reason for the high level of Acanthamoeba attachment to silicone hydrogel contact lenses. Eye Contact Lenses. 2003;29:540-543; discussion S57-S59, S192-S194.
64. Rapkpin JS. The effect of daily vs. extended wear on contact lens complications. CLAO J. 1988;14:139-142.