

Biofilms and contact lenses: problems and solutions

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ABSTRACT

Contact lenses provide excellent vision correction for many people worldwide. However, they can become colonised by microorganisms and this can result in infections and inflammatory responses at the surface of the eye during wear. If not quickly and appropriately treated, the infections can lead to loss of vision and even loss of the eye. The microorganisms, most commonly bacteria, that colonise the lenses can form biofilms on the lenses. For the past 25 years, we have been studying the epidemiology of contact lens-related infection and inflammation, the causative organisms, risk factors for developing the conditions, and new ways of reducing biofilm formation. This article provides an overview of this research.

Keywords: antimicrobial devices, biofilms, contact lenses, keratitis, risk factors.

Contact lenses are used by over 150 000 000 people worldwide. In Australia, ~13% of the population wear contact lenses (~3.4 million people). Contact lenses are most commonly used to correct myopia (short sightedness) but can be used to correct hyperopia (long sightedness) and other forms of refractive error. The most commonly worn lenses are soft lenses, accounting for 75% of all lenses worn worldwide.¹ These soft lenses are worn by 48% of wearers on a daily disposable basis (the lens is discarded at the end of the day and a new lens worn the next day) or by 49% of wearers on a daily wear basis (the lens is cleaned and disinfected when not being worn and re-worn each day for 2 or 4 weeks before being discarded).¹ Soft lenses worn on a daily wear basis are disinfected in contact lens cases each night using multipurpose disinfecting solutions by 88% of wearers,¹ with the rest usually using hydrogen peroxide. After removing the lens from the eye (with clean recently washed and dried fingers) and before adding it into the contact lens case for disinfection, manufacturers recommend adding some fresh disinfecting solution to the lenses and rubbing the lens between in the palm of one hand with the fingers of the other to help remove any debris. The lenses should then be rinsed with fresh disinfecting solution and added in to the case with fresh disinfecting solution. All manufacturers have a recommended minimum disinfecting time, which is usually between 4 and 6 h.

Contact lenses and ocular surface infection and inflammation

Unfortunately, wearing contact lenses can be associated with ocular infections and inflammation. When lenses are worn on either a daily disposable or daily wear basis, ocular infections occur at ~2 per 10 000 wearers each year.^{2,3} However, ocular inflammation in the absence of frank infection is much more common, with 2–6 per 100 wearers suffering this each year.²

Contact lens-associated ocular infections, commonly called microbial keratitis, are caused by a wide range of different microorganisms, but *Pseudomonas aeruginosa* is the most common, being isolated from at least 70% of infections worldwide.⁴ These microorganisms can be found in biofilms on contact lenses of people with microbial keratitis (Fig. 1) as well as in their contact lens cases.⁵ Contact lens-associated ocular inflammation is often caused by microorganisms, most commonly bacteria such as various Gram-negative bacteria or *Staphylococcus aureus*, colonising contact lenses during wear.⁶ These bacteria are also isolated from contact lenses cases⁷ where they occur in biofilms (Fig. 2).

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Biofilm-related risk factors associated with contact lens-associated infection and inflammation

Risk factors for developing contact lens-associated infection include poor compliance with hygiene instructions, disinfecting contact lenses with chlorine or heat, infrequent or no disinfection of lenses,² using a particular kind of multipurpose contact lens disinfecting solution that contained only polyhexamethylene biguanide as the disinfectant and was marketed to be used without rubbing contact lenses with the solution,^{8,9} using a disinfecting solution that did not contain a surfactant, and not rubbing and rinsing lenses with a multipurpose disinfecting solution.²

Also, poor lens case hygiene (not air drying lens cases after use) and not replacing lens cases at least every 3 months^{3,8} are associated with greater risk of developing microbial keratitis during daily wear of contact lenses. In one study, 61% of



Fig. 1. Scanning electron micrograph of a biofilm of the posterior surface of a contact lens from a patient with microbial keratitis. *Pseudomonas aeruginosa* was grown from the cornea and from the contact lens. Reproduced from Elder *et al.* (1995)⁵ with permission.

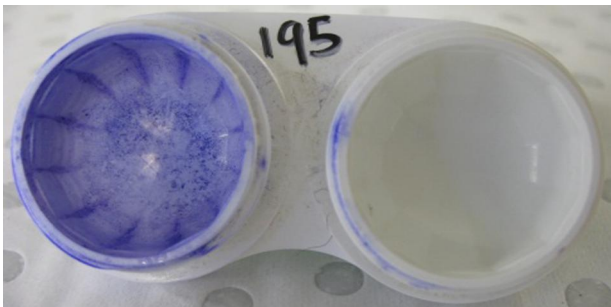


Fig. 2. Biofilm disclosed in one well of a contact lens case after staining with crystal violet.

Table 1. Effect of new compared to manufacturers recommended (rinse lens case with disinfectant, air-dry face down) on numbers of microorganisms isolated from cases.

Guideline	Median numbers of microorganisms (range)	P-value
New: discard old solution in case, fill lens case with new disinfecting solution, rub case with clean fingers for 5 min, discard solution, wipe cases with a clean tissue, air dry face down on clean tissue	12 (0–10 000)	0.004
Manufacturers: discard old solution in case, rinse lens case with disinfecting solution, air dry face down on clean tissue	28 (0–100 000)	

contact lens wearers reported inadequate cleaning of lens storage cases and 13% inadequate cleaning of lenses.¹⁰ A statistical analysis has shown that simply air drying lens cases would reduce the risk of microbial keratitis by 49%, and replacing lens cases at least every 3 months would reduce the risk by 27%.⁸ If people replaced lens storage cases every 3 months and air dried their lens cases they would reduce their risk of keratitis by 62%.⁸ It was perhaps not surprising that people did not understand how to appropriately clean and replace their lens cases when we identified that there were inconsistent instructions and limited recommendations about drying positions, rinsing and rubbing of lens cases.¹¹ Our highlighting of this resulted in disinfectant manufacturers changing their instructions to be more consistent and obvious.

Quick fixes for reducing biofilms in lens cases

We examined contact lens cases and how contact lens wearers could best care for them so that they could minimise microbial colonisation and biofilms. All lens cases become contaminated by a range of microorganisms, most commonly bacteria, during use, but the level of contamination and types of microorganisms is associated with use of different multipurpose disinfecting solutions.⁷ These microorganisms can coaggregate and cohere to form multispecies biofilms.¹² We also showed that it was important to use the contact lens case supplied (commonly for free) with the disinfecting solution being used, as mismatching lens cases with disinfecting solutions was a risk factor for lens case contamination.¹³ In a laboratory study, after growing biofilms of either *P. aeruginosa* or *S. aureus* in contact lens storage cases, simply rinsing these in either disinfecting solution or hot water did not affect biofilms of *S. aureus* and resulted in only partial removal of biofilms of *P. aeruginosa*.¹⁴ Rinsing cases with multipurpose disinfecting solutions, using a clean tissue to wipe cases, and then air-drying cases face down resulted in significant reductions in the biofilms of both bacterial types.^{14–17} Our clinical trial comparing manufacturers’ guidelines (rinse lens case with disinfectant, air-dry face down) with the new guidelines that incorporated wiping cases with a clean tissue as well as rubbing and rinsing cases and air drying face down, resulted a halving of the median number of bacteria in lens cases (Table 1).¹⁸

Antimicrobial lens cases to reduce microbial biofilms

Along with recommendations to standardise and change contact lens case cleaning instructions, several manufacturers have developed silver-containing contact lens cases. We have

tested these in laboratory and clinical trials. Our laboratory tests showed that silver-containing lens cases could reduce the numbers of live *P. aeruginosa* and other bacteria that adhered to their surfaces, especially in combination with multipurpose disinfecting solutions.^{15,19,20} However, this did not translate to the results from our clinical studies. Neither of the clinical trials we have conducted showed reductions in the frequency of contamination of lens cases.^{21,22} Although one trial found reductions in the numbers of bacteria that colonised silver cases,²² the other study found that this might be related to the types of contact lenses being worn,²¹ and as each study used different silver-containing cases, this might also have affected the results.

Thus, it appears that silver may have a small effect on microbial colonisation of lens cases. As we have shown, a more effective way to control colonisation and biofilm formation was to rub, rinse, tissue wipe and air-dry cases.

Development of antimicrobial contact lenses

The same microorganisms can be found in lens cases, on contact lenses and in ulcers on the eye of patients with microbial keratitis.²³ This indicates that there is a likely transfer of microorganisms from cases, to lenses and then onto the eye to cause infections. However, not all cases of microbial keratitis occur during daily wear of lenses.^{2,3,9} Furthermore, we have shown a correlation between contamination of contact lenses by microorganisms and contamination of the domestic water supply.^{24,25} Thus, we, and others, have been working on developing antimicrobial lenses.

We have tested antimicrobial contact lenses produced using silver (M. D. P. Willcox, unpubl. data), quorum sensing inhibitors²⁶ and cationic peptides²⁷ in laboratory studies and clinical trials. The development of our cationic peptide-coated contact lenses has progressed the furthest and been reviewed previously.²⁷

Since that review, we have tested the cationic peptide-coated contact lenses in a Phase III clinical trial. This trial examined whether wearing our cationic peptide-coated contact lenses could reduce the incidence of bacterially driven ocular surface inflammation during lens wear. The participants of the study wore the antimicrobial lens in one eye and a normal lens in the other for 3 months, replacing lenses every 2 weeks. The study was powered to show a 65% reduction in the incidence of ocular inflammation. The study was successful and showed that the lenses produced a 69% reduction in ocular inflammation.²⁸ We also showed that they did not alter the normal microorganisms that colonise the eyelids or conjunctiva²⁹ and that they were safe and comfortable to wear.³⁰ However, we did show that the lenses slowly lost activity during wear most probably due to proteolysis,³¹ which may have been the reason they did not show any greater reduction in incidence of inflammation. We have now developed antimicrobial cationic peptide mimics^{32–34} and tested peptoids,³⁵ which are proteolytically stable and some of which we have recently shown to be able to reduce microbial colonisation, to a greater degree than our cationic peptide, when bound to contact lenses. We are now setting up to test these in pre-clinical tests before embarking on clinical trials.

Conclusions

Biofilms are associated with contact lens-associated ocular infection and inflammation. Our studies have shown that wiping lens cases with a clean tissue or using silver-containing contact lens cases with appropriate disinfectants can reduce the frequency or amount of microorganisms in the cases. We are the first in the world to show that antimicrobial contact lenses can reduce the incidence of bacterially driven contact lens-associated ocular inflammation. Although we need to refine our antimicrobial contact lenses for optimum activity, we remain confident that these, combined with good hygiene practices, are likely to reduce the incidence of potentially blinding infection and inflammation with contact lenses.

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Data availability. Data sharing is not applicable as no new data were generated or analysed during this study.

Conflicts of interest. The authors hold patents on peptide mimics US-2019-0256466-A1. The authors declare that they have no other conflicts of interest.

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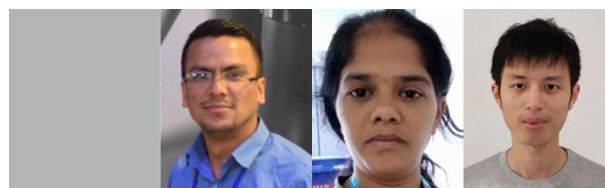
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