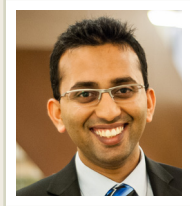
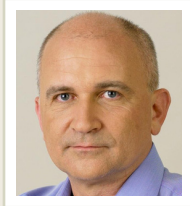


# Contact Lens Update

CLINICAL INSIGHTS BASED IN CURRENT RESEARCH

## Contact lenses and microbes – latest innovations

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**Mark Willcox is Professor at the School of Optometry and Vision Science, University of New South Wales. Mohit Verma is a Banting Postdoctoral Fellow at Harvard University. He recently completed a PhD in Nanotechnology at the University of Waterloo and was an Endeavour Scholar at the University of New South Wales.**

Whilst contact lens wear is generally safe, it can lead to ocular inflammation and infection. During wear, contact lenses can become contaminated by microbes and this contamination has been linked to the development of both microbial keratitis and corneal infiltrates. Several studies have examined the rate of contact lens contamination and the types of microbes that contaminate lenses during wear. The most common microbe to contaminate lenses are the coagulase negative staphylococci, which are commonly found on the skin (including the eyelids) and also isolated from the conjunctiva. Most studies report a contamination rate of 40-50% of lenses,<sup>1-4</sup> with very little difference in the rates reported from different geographical areas (Australia vs. India vs. USA), lens materials (hydrogel vs. silicone hydrogel lenses) or wear schedule (daily disposable vs. daily wear vs. extended wear). In general, these staphylococci are relatively non-pathogenic and infrequently cause complications during lens wear. However, if lenses become colonised by Gram-negative bacteria (such as *Pseudomonas aeruginosa*) or coagulase positive *S. aureus*, there is more risk of initiating ocular inflammation and even infection.

During daily wear of contact lenses it is necessary to store and disinfect the lenses when they are not being worn. However, the contact lens cases in which the lenses are stored are known to be commonly contaminated by microbes. Similarly to lenses, the most common microbes isolated from contact lens cases are the coagulase negative staphylococci, but lens cases can be contaminated by more diverse types of microbes and more commonly than lenses; up to 92% contact lenses cases can be contaminated.<sup>5</sup> Again, case contamination does not seem to be affected by geography or lens polymer type. Colonisation of contact lens cases by Gram-negative bacteria has been correlated to the production of corneal infiltrates during daily lens wear.<sup>6</sup>

Over the past 15 years, several groups have been developing antimicrobial contact lenses, contact lens cases, or ways of detecting microbial contamination so that users can dispose of lenses or cases when they become contaminated.

### Development of antimicrobial contact lenses and lens cases

Several groups in industry and academia have been developing antimicrobial contact lenses, although they are not currently for sale anywhere in the world. There are several antimicrobial lens cases for sale, which are based on release of silver to kill microbes. For lenses, the main antimicrobials being examined in research laboratories include silver, cationic peptides and small molecules that inhibit microbial communication.

#### *Silver lens cases:*

Silver has effects on many microbial factors, including perturbing microbial membranes and interacting with microbial DNA.<sup>7</sup> Silver lens cases have been shown to be effective against a range of bacteria in laboratory studies, including *S. aureus*, and several genera/species of Gram negative bacteria such as *P. aeruginosa* and

*Serratia marcescens*.<sup>8,9</sup> They are also effective at reducing microbial colonisation of contact lens cases when used in clinical trials.<sup>9,10</sup> However, no studies have been reported to date that demonstrate that the reductions in microbial colonisation of cases by silver results in reducing the rate of corneal infiltrates.

*Contact lenses coated with melimine:*

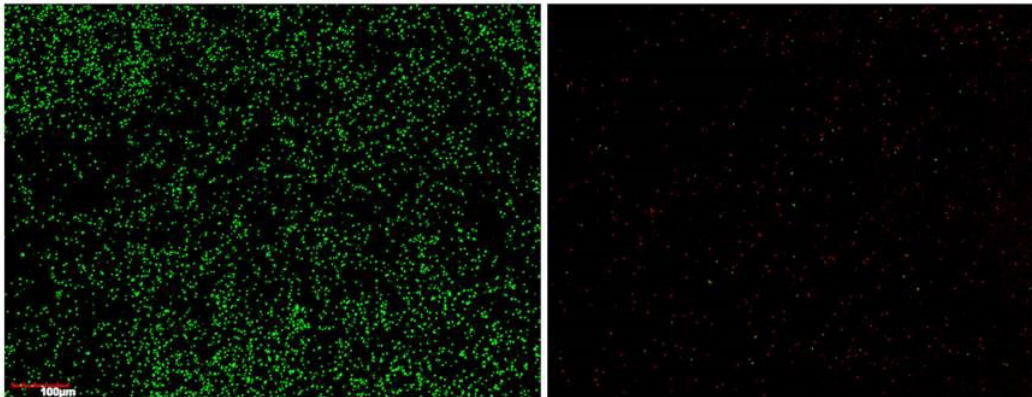
We have shown that contact lenses coated with the antimicrobial cationic peptide melimine can significantly reduce the number of microbes that colonise lenses in laboratory studies,<sup>11,12</sup> and can be worn safely by volunteers in a small one day clinical trial.<sup>13</sup>

Cationic peptides act by disrupting microbial cell membranes, which are more negatively charged than mammalian cell membranes. Similarly, we have demonstrated that covalently attaching a small molecule (variously called furanones, fimbrolides or dihydropyrrolones – differences largely due to substitution of carbon for nitrogen in the molecules to improve stability whilst maintaining antimicrobial activity) to contact lenses results in lenses that have reduced colonisation of various microbes in the laboratory and can be worn safely for one continuous 24-hour period.<sup>14</sup>

**Biofilm formation by *Staphylococcus aureus***

Control surface

Melimine coated surface



**Green cells = live cells, Red cells = dead cells.** Note the smaller number of green (*S. aureus*) cells on the control surface and higher number of red (dead) cells on the melimine-coated surface.

The melimine-coated and furanone-coated lenses are being tested in longer term daily and continuous wear clinical trials over the next 12-18 months to determine whether they can reduce the incidence of corneal infiltrates caused by microbial colonisation of lenses.

**Detecting microbial contamination in contact lens cases**

Non-compliance of contact lens wearers is the prime culprit for microbial contamination of lens cases.<sup>15</sup> Currently, patient education and behaviour modification are being promoted as key methods for improving compliance.<sup>16</sup> A recent study demonstrated that the use of written instructions in addition to oral ones led to an improvement in compliance of contact lens wearers, yet microbial contamination of lens cases was still prevalent at 79%.<sup>17</sup> The pathogens present on the lens cases can be transmitted to contact lenses and lead to microbial keratitis. Novel technologies are necessary to complement the education and prescription provided by the practitioner.

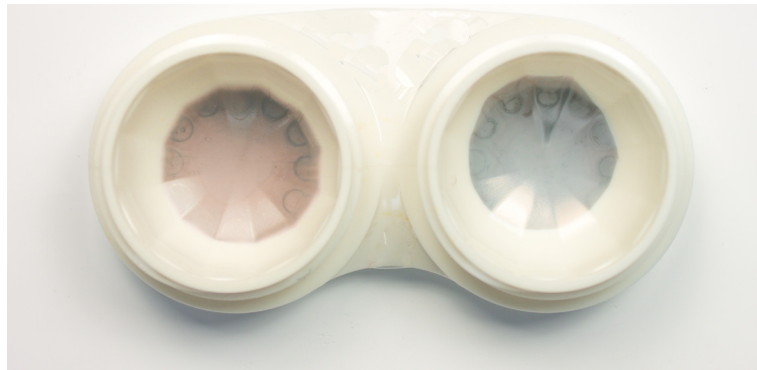
Specialized contact lens cases such as Count-it™ and LensAlert® are available to assist the wearer in following replacement schedules, but these do not depend on whether the lens case is contaminated or not.<sup>18</sup>

### Gold nanoparticles:

Other technologies are being developed to detect bacterial contamination in the lens case by providing a color change and thereby alerting the user. A color change is possible by the use of gold nanoparticles, because these nanoparticles exhibit environment-dependent optical properties.<sup>19</sup> In solution, the presence of bacteria leads to aggregation of gold nanoparticles due to electrostatic interactions, which in turn causes the nanoparticles to absorb light at longer wavelengths and hence present a different color.

The color of gold nanoparticles and their response can be tuned using different shapes of particles such as nanospheres, nanostars, nanocubes and nanorods.<sup>20</sup> The use of gold nanoparticles can provide a set of unique responses for different bacteria, leading to a “chemical nose” biosensor because it functions in a manner similar to the human nose where each odour molecule binds to a set of receptors leading to the recognition of the smell. Such a “chemical nose” has been used to detect and distinguish between ocular pathogens.<sup>21</sup>

Gold nanoparticles have also been immobilized on contact lens cases to facilitate the detection of biofilms.<sup>22</sup> Here, the formation of biofilm leads to a change of refractive index on the surface of the lens case, which causes gold nanoparticles to absorb light strongly at shorter wavelengths and hence a color change. Whether gold nanoparticles are used in solution or on the surface, they may manage to provide a visual color change to the lens wearer and act as a warning system to discontinue the use of a contaminated lens case. Such a color change may provide an active method of assessing the microbial status of the contact lens case and holds potential to improve compliance in contact lens wearers.



Contact lens case enhanced with gold nanoparticles. Red (left) indicates the presence of a *Staphylococcus aureus* biofilm, and blue (right) indicates a clean surface (saline control). (Photo courtesy of Sarah LeBlanc)

### Conclusion

Several antimicrobial strategies are being developed for contact lenses and lens cases. However, clinical trials are needed to demonstrate safety and efficacy, especially in reducing corneal infiltrative events caused by microbial contamination of lenses. For the various methods that help people determine whether their contact lens cases are contaminated, after further development there needs to be clinical trials conducted to assess acceptance of these and the robustness of the approaches.

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