# Contact Lens Care - Today and Tomorrow

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The potential for clinically significant interactions to occur between contact lenses and contact lens disinfection solutions has been apparent since the introduction of poly-HEMA based, soft hydrophilic contact lenses almost forty years ago. The advent of new preservatives, such as polyhexanide (PHMB) and POLYQUAD®, specifically selected to reduce absorption into the soft lens matrix due to their molecular size, appeared to have overcome this problem. However, recent research and clinical experience suggests that this may not be the case. Two leading experts, Professor Lyndon Jones from the University of Waterloo School of Optometry, Canada and Dr. Art Epstein, a contact lens and anterior segment disease specialist from New York State and Medical Editor of the e-journal Optometric Physician, recently reviewed current issues surrounding contact lens/solution interactions at a satellite meeting held prior to the opening of the British Contact Lens Association Annual Conference 2006 in Birmingham, England.

## *Silicone Hydrogel Contact Lenses*

Professor Jones questioned why an estimated 30 to 35% of contact lens wearers still stop wearing contact lenses within five years. He stated that discomfort is the prime reason given and asked whether the care solutions used could have an influence. In his view, most contact lens practitioners now tend to accept that all multipurpose solutions are virtually interchangeable and perform adequately. Therefore, although practitioners may take great care over the selection of the best contact lens for their patients, they are generally less concerned about their choice of solution. This attitude towards contact lens care solutions has never been entirely justified and this has become increasingly apparent with the introduction of silicone hydrogel lenses. These lenses were originally developed for continuous wear but have become increasingly popular for daily wear because of their high oxygen transmission and low level of protein deposition. However, Professor Jones warned that silicone hydrogels also have drawbacks. They are generally stiffer than conventional soft lenses and, because of their silicone content, they exhibit reduced wettability and increased lipid deposition. In addition, the relatively small amount of protein deposited on the surface of these lenses tends to be denatured, in contrast to the high levels of largely undenatured protein present on a Group IV, high water content, ionic material such as etafilcon A.

*Professor Lyndon Jones.*

Professor Jones became aware of a potential solution related issue with silicone hydrogel contact lenses when he compared the subjective symptoms and signs observed in a group of fifty soft-lens wearers using either OPTI-FREE® *EXPRESS*® containing POLYQUAD® or polyhexanide-based ReNu MultiPlus* in conjunction with PureVision* lenses for daily wear.[1] He noted that significantly greater levels of relatively asymptomatic corneal staining were present when subjects used ReNu MultiPlus* than when they used OPTI-FREE® *EXPRESS*®. A total of 37% of subjects demonstrated a level of staining consistent with a classical solution-based toxicity reaction when using ReNu MultiPlus* compared to only 2%

when OPTI-FREE® *EXPRESS*® was used.

The corneal staining observed was not associated with lens discomfort or other symptoms and so this clear difference in the clinical performance of these two multipurpose solutions would not have been noted without the use of fluorescein staining. In Professor Jones' experience many contact lens practitioners do not routinely perform this examination and so would have noticed nothing unusual. Professor Jones stressed that fluorescein staining using Cobalt Blue light and a yellow barrier filter is essential if corneal staining is to be reliably detected in practice.

Even if fluorescein is routinely used, Professor Jones indicated that a significant corneal staining response could still be missed. Research has indicated that the time of day at which corneal staining is assessed can be critical. When Jones and co-workers evaluated the corneal staining response to three multipurpose solutions in 20 contact lens wearers using Group II high-water, non-ionic soft lenses, they again found that frequency and severity of staining was highest with polyhexanide based products and could be ranked in the order ReNu MultiPlus* >COMPLETE* >OPTI-FREE® *EXPRESS*®. However, they also found that for the two polyhexanide based products (ReNu MultiPlus* and COMPLETE*) staining was significantly greater at two hours post-lens insertion than at six hours.[2] Professor Jones confirmed that the initial staining response seen after one week of lens wear is generally predictive of the longer-term prognosis, allowing clinical decisions about lens/solution bio-incompatibility to be made quickly.

The observations reported by Professor Jones have been confirmed and expanded by recent work conducted by Andrasko and co-workers. This group evaluated average corneal staining area in a series of studies involving many current multipurpose solutions combined with silicone hydrogel contact lenses.[3] They found very low levels of corneal staining associated with these lenses in combination with OPTI-FREE® *EXPRESS*® containing POLYQUAD® (averaging below 4% at both 2 and 4 hours across all brands tested). However, the response to polyhexanide based products was unpredictable. While the corneal staining response for most lens/solution combinations was greater than that seen with POLYQUAD®, a particularly high level was noted for PureVision* lenses used with COMPLETE* MoisturePLUS* (38% and 33.7% at 2 and 4 hours respectively) and Focus* AQua*/Solocare Aqua*/ AQuify* (21.3% at 2 hours). In contrast, ReNu* MoistureLoc* containing the disinfectant alexidine, which is structurally related to chlorhexidine, was found to perform acceptably with PureVision* lenses, although subsequent research has demonstrated unacceptable levels of corneal staining with ACUVUE* 2 lenses.[#] Andrasko has proposed a simplified grading system where an incidence of corneal staining <10% is considered acceptable, 10 to 20% is marginal and >20% is unacceptable.This group has developed a corneal staining grid that can serve as a quick reference guide to determine the biocompatibility of various lens/solution combinations (see Figure 1).

The high levels of corneal staining seen with some lens/solution combinations are generally not correlated with significant ocular discomfort.[1,2,4]

| | Unisol 4 Saline | Opti-Free Express* | Opti-Free Replenish* | ReNu ML[I] | Equate[II] | Complete MP[III] | AQuify[IV] |
|---|---|---|---|---|---|---|---|
| ACUVUE* 2 | 1% | TP | 5% | 25% | 1% | 2% | TP |
| PureVision* | 2% | 6% | 7% | 6% | 71% | 48% | 21% |
| OASYS[V] | 2% | 3% | 5% | 10% | 12% | 5% | 1% |
| $O_2$ OPTIX* | 2% | 2% | 5% | 7% | 41% | 18% | 7% |
| Focus N&D[VI] | TP | 4% | TP | 6% | TP | TP | TP |

Acceptable  Marginal  Unacceptable  TP = Testing Planned

[I] ReNu* MoistureLoc*; [II] Formulation identical to ReNu MultiPlus*; [III] COMPLETE* MoisturePLUS*; [IV] Focus* AQuify*; [V] ACUVUE* OASYS*; [VI] Focus* Night & Day*

***Figure 1.*** *Corneal staining grid developed by Andrasko et al.*[3]

[#] Study was conducted prior to Renu* Moisture Loc* being removed from the market.

However, Professor Jones commented that this could be explained by changes in corneal sensitivity. He indicated that in preliminary studies conducted at Waterloo University corneal sensitivity decreased over a 14-day period in contact lens wearers using ReNu MultiPlus*, remained the same in those using COMPLETE* and actually increased when OPTI-FREE® *EXPRESS*® was used. This last finding was presumably due to a depression of corneal sensitivity on enrolment due to the effects of previously used products.

## *The Implications of Corneal Staining*

Dr. Epstein confirmed that in a pilot, cross-over study, the use of OPTI-FREE® *EXPRESS*® was associated with significantly higher corneal sensitivity, compared to ReNu MultiPlus*, both on presentation and after cross-over.[5] He also described a coarse, dense, diffuse superficial punctuate corneal staining that he had observed in a number of previously asymptomatic contact lens wearers fitted with silicone hydrogel lenses when they switched from OPTI-FREE® *EXPRESS*® to ReNu MultiPlus*.[6]

Dr. Epstein indicated that although the patients affected are generally asymptomatic, he believes that corneal staining can be considered as a key element in the genesis of more serious complications. He proposed that the type of corneal staining response observed in the studies outlined by Professor Jones could possibly be a factor in the recent severe problems with fungal keratitis seen in the United States, Singapore and Hong Kong. Reports of contact lens associated *Fusarium* keratitis first started to appear in March this year. Figures reported from the U.S. Center for Disease Control and Prevention (CDC) (www.cdc.gov) on May 12 indicated that the number of reported confirmed cases of *Fusarium* keratitis had reached 122, with 15 "possible" cases and 60 still under investigation.† It was observed that a disproportionately large number of the confirmed cases were associated with use of ReNu* MoistureLoc.* This finding subsequently resulted in the permanent removal of ReNu* MoistureLoc* from the market worldwide and has been linked to certain unique characteristics of the formulation by the manufacturer, Bausch and Lomb.‡

*Dr. Art Epstein.*

Dr. Epstein speculated that there are five elements that may contribute to potentially serious corneal infections observed in soft contact lens wearers.

1. *Poorer than expected antimicrobial performance of contact lens solutions in the presence of contact lenses.*
2. *Formulation components, particularly cellulose derivatives, that under certain circumstances can provide a nutritive source for contaminating microorganisms.*
3. *Resistance of microorganisms to the biocide in question, particularly if the activity of the biocide is lowered by lens uptake.*
4. *Chemical trauma due to the uptake and release of biocide by the lens, which manifests as corneal staining.*
5. *Blocking of the normal inflammatory response due to the presence of a soft contact lens on the eye.*

## *Lens Care Product Evaluation*

Additional comments were provided by Dr. Leslie Napier, Associate Director of Consumer Products, Clinical Research and Development from Alcon Research Limited, Fort Worth, Texas. She indicated that current lens care product standards detailed in FDA guidelines still only require controlled clinical studies on 60 patients fitted with Group I and Group IV soft contact lenses. Since most literature reports of significant corneal staining have involved Group II or silicone hydrogel lenses, these problems might only

† Quoted from the American Academy of Ophthalmology website, May 15 2006.

‡ Quoted from the U.S. Food and Drug Administration website, May 15 2006.

be detected if more extensive clinical studies are conducted. Dr. Napier also pointed out that current disinfection test requirements do not take into account the effect of lenses on the biocide activity. Studies have shown that the presence of soft contact lenses can significantly reduce the activity of polyhexanide containing solutions while having little effect on the activity of OPTI-FREE® *EXPRESS*®.[7,8]

Dr. Napier said that this observation could be partly explained by variations in the absorption of the biocides into the matrix of soft contact lenses due to differing molecular sizes. A large molecule, such as POLYQUAD®, is absorbed to a lesser extent than a much smaller molecule, such as chlorhexidine, leaving more of the disinfectant available in solution to kill contaminating microorganisms. In addition, biocides can also be adsorbed onto the lens surface, but this effect can be reduced by careful formulation. Absorbed disinfectant can be released as a bolus, when the lens is placed on the eye, producing a high local concentration that can cause an ocular reaction, typically exhibited by corneal staining. Adsorbed disinfectant can also be gradually released and this may be implicated in red eye reactions and tarsal plate changes seen with some solution/ lens combinations. Dr. Napier claimed that the disinfectant alexidine, included in the formulation of ReNu* MoistureLoc*, has a similar molecular weight to chlorhexidine and would be expected to be absorbed into soft contact lenses in a similar fashion.

Dr. Napier confirmed that differences in biocide uptake and release have been demonstrated with silicone hydrogel lenses. She presented data to show that when PureVision* lenses were soaked for 24 hours in multipurpose solutions containing either polyhexanide (PHMB) or POLYQUAD® and then placed in saline for a further 24 hours, an average of 2.7 micrograms/lens of polyhexanide was released from the lenses compared to less than 0.5 micrograms/lens of POLYQUAD®, even though the starting concentration of POLYQUAD® was several times that of polyhexanide in the respective formulations.

## *Conclusions*

The three expert speakers presenting at this meeting were in agreement that unacceptable levels of asymptomatic corneal staining, seen with certain combinations of multi-purpose solutions and soft contact lenses, could have serious clinical implications. The staining patterns seen are an indication of the uptake and release of biocide by the lens. This has implications both for the disinfecting performance of the solution and the disruption of the normal physiological barriers. Such events could easily be associated with avoidable incidents of contact lens related complications.[9]

Current testing requirements for lens care products do not take into account the lens/solution interactions described here. Practitioners were advised to monitor patients using fluorescein staining viewed under Cobalt blue light with a suitable yellow barrier filter and to take note of the corneal staining grid prepared by Andrasko and co-workers when selecting lens/ solution combinations. Practitioners were also recommended to inform patients of the potential down-sides of switching solutions, particularly to store brand solutions where the exact composition may not be known or may change without notice and where appropriate data on lens/solution interactions may not be readily available.

## *References.*

**1.**Jones L et al. Optom Vis Sci. 2002; 79: 753-61. **2.** Jones LW et al. ARVO 2005, # 917. **3.** Andrasko GJ et al. ARVO 2006, # 2392. **4.**Garofalo RJ et al. Eye Contact Lens. 2005; 31: 166-74. **5.**Epstein AB. Eye Contact Lens. 2005; 31: 1-1. **6.**Epstein AB. Contact Lens Spectrum. 2002; 17: 30. **7.**Rosenthal RA et al. Poster BCLA 2001. **8.**Miller MJ et al. CLAO J. 2001; 27: 16-22. **9.**Jalbert I et al. ARVO 2006, #2412.