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Microbial Keratitis and the Role of Rub and Rinsing

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Recent outbreaks of microbial keratitis in contact lens wearers have involved various pathogens, including *Acanthamoeba* and *Fusarium* species. Specific reasons for the marked increase in microbial keratitis, particularly those involving species typically rarely involved in contact lens infection, remain unknown. Possible contributing factors include inadequacies of various multipurpose solutions against certain pathogens; inadequate lens care hygiene, including elimination of the digital rubbing step; poor contact lens storage case hygiene; and the introduction of new soft contact lens materials that may promote adherence of certain pathogens, particularly when a digital rubbing step is eliminated. Although there is some conflict of opinion in the literature regarding the necessity for a mechanical rub during lens cleaning and disinfection, growing evidence supports the reestablishment of a digital rub component to multipurpose solution lens care systems. This article reviews the literature on whether such a process should be recommended to contact lens wearers.

Key Words: *Acanthamoeba*—Contact lens hygiene—Digital rub—*Fusarium*—Multipurpose solution—Rub and rinse.

Recent outbreaks of microbial keratitis in contact lens wearers have involved *Acanthamoeba* and *Fusarium* species,[1,2] which historically have been involved only rarely in cases of contact lens–associated microbial keratitis.[3,4] These outbreaks may have been associated with the improper use of certain multipurpose solutions,[5] with two multipurpose solutions having been identified as major contributing factors to the risk of microbial keratitis.[2–6] Specific reasons for the increase in microbial keratitis are unknown, but possible contributing factors include inadequacy of the multipurpose solution against certain pathogens, including *Fusarium* and *Acanthamoeba*; inadequate lens care hygiene, including the elimination of the digital rubbing technique; poor contact lens storage case hygiene; and the introduction of new soft contact lens materials that may promote adherence of certain pathogens when a digital rub step is eliminated. This article attempts to address these issues with a comprehensive review of the recent literature on the topic and specifically address the question of whether a digital rub should be reinstated as part of lens care regimens.

Questions arise concerning the effectiveness of various multipurpose solutions against certain pathogens, including *Fusarium* species and *Acanthamoeba* and the possible contribution to the increase of cases of microbial keratitis. The outbreak of *Fusarium* keratitis among patients wearing hydrogel contact lenses was directly linked to the use of one specific multipurpose solution, namely ReNu with MoistureLoc (Bausch & Lomb, Rochester, NY).[2,5] As of June 30, 2006, 115 (70%) of 164 confirmed cases of *Fusarium* keratitis were associated with ReNu with MoistureLoc.[5] Although ReNu with MoistureLoc successfully passed all the requirements of the U.S. Food and Drug Administration for multipurpose solution marketing, this testing did not include evaluating its effectiveness against *Fusarium* species or *Acanthamoeba*. Under stressed conditions, including improper hygiene and improper care of contact lenses, cases, and solution bottles, ReNu with MoistureLoc was actually found to support the growth of certain *Fusarium* strains in a dried crystalline form.[5,7]

Many studies have attempted to evaluate the effectiveness of different multipurpose solutions and hydrogen peroxide solutions against *Acanthamoeba*. Hiti et al.[8] concluded that one-step hydrogen peroxide systems do not have sufficient effects on *Acanthamoeba* cysts because of the rapid hydrogen peroxide neutralization. Hydrogen peroxide systems that involved two steps, in which the soaking time in 3% peroxide was significantly longer, showed much higher efficacy than the one-step hydrogen peroxide solutions.[8] Borazjani and Kilvington[9] found that use of a polyhexamethylene biguanide (PHMB)–preserved system (ReNu MultiPlus Multi-Purpose Solution; Bausch & Lomb), even in the presence of organic soil and when used in a no-rub protocol, effectively reduced the binding capacity of *Acanthamoeba* to contact lenses. However, the digital rubbing step with this study was supplemented by a specific and extensive rinsing technique.[9] Further work by Hiti et al.[10] showed that after exposure to various soft lens solutions, *Acanthamoeba* cysts were still viable in test situations, even after an 8-hour soaking time. The work by Hiti et al.[10] also addressed the efficacy of soft lens and rigid gas-permeable lens multipurpose solutions against cysts of three specific strains of *Acanthamoeba*. Ten solutions were tested, with soaking times of 1 and 8 hours. The rigid gas-permeable lens solution, Boston Advance (0.0005% polyaminopropyl biguanide/0.003% gluconate), showed the greatest amoebicidal efficacy, with all

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evaluated soft contact lens solutions showing weaker amoebicidal effects. ReNu MultiPlus was able to destroy 10^3 cysts, but not 10^4 cysts, after a soaking a time of 8 hours. SOLO-care (CIBA Vision, Duluth, GA), OPTI-FREE Express (Alcon, Forth Worth, TX), and ACTI-MED (Sauflon Pharmaceuticals, London, UK) were also effective against 10^3 cysts. It is clear from these results that adequate exposure time is necessary for proper disinfection. Additionally, these results were achieved under ideal conditions, with suitable and new storage cases and appropriate use of the solutions under test.

It is clear from the studies outlined earlier that solution ineffectiveness could potentially contribute to the increased prevalence of *Acanthamoeba* keratitis. Inadequate lens care hygiene may also contribute to the increase in the number of cases of microbial keratitis among contact lens wearers. These behaviors may include topping off of old solutions in the contact lens storage case; improper cleaning, disinfection, or replacement of the contact lens storage case; failure to wash hands before handling lenses and cases; exposure of the lens or lens case to tap water; and elimination of the digital rubbing step when using certain multipurpose solutions.[11] The importance of noncompliance is supported by the recent work of Zhang et al.,[5] who investigated the factors that resulted in the increased prevalence of *Fusarium* keratitis among users of ReNu with MoistureLoc. Their study concluded that under "stressed conditions," films of ReNu with MoistureLoc promoted the "selective and rapid growth and survival" of *Fusarium solani* and *Fusarium oxysporum* on plastic surfaces, particularly contact lens cases containing these stressed ReNu with MoistureLoc films. All the poor hygiene techniques stated earlier can contribute to these stressed conditions. This same study also found that certain components of the multipurpose solution, such as the hydroxymethylcellulose backbone of the polyquaternerium-10 used in ReNu with MoistureLoc as a wetting agent, may combine with water, human epithelial cells, and other forms of organic debris, which may subsequently serve to neutralize the antimicrobial effects of the multipurpose solution and enhance the growth and survival of certain *Fusarium* strains.[5] A related study[7] concluded that the biocidal activity of ReNu with MoistureLoc and other tested solutions were reduced under conditions that simulated the possible impact of solution reuse or misuse. Consistent with these findings was that although ReNu MultiPlus remained effective, even under noncompliant conditions, ReNu with MoistureLoc could be rendered less effective if misuse occurred.[7] Hiti et al.[10] stressed the importance of mechanical cleaning by contact lenses wearers because *Acanthamoeba* cysts and trophozoites are able to adhere to the contact lens surfaces. Their study strongly suggested that eliminating the digital rub may be eliminating a critical preventative technique in managing *Acanthamoeba* keratitis.[10] Cancrini et al.[12] evaluated the amoebicidal activity of five commercially available cleaning and disinfecting products: hydrogen peroxide, chlorhexidine, polyaminopropyl biguanide–poloxamine, thimerosal–polyquaternium, and a combination of thimerosal and chlorhexidine. The cleaning and disinfecting solutions tested were ineffective in removing or in affecting the viability of all *Acanthamoeba* trophozoites or cysts in the 17 hours allotted for the experiment. As a result, the authors strongly emphasized the need for improved hygiene practices for soft and rigid gas-permeable lenses and reiterated the need for a mechanical rubbing of the lenses after their wear.[12]

Poor contact lens storage case hygiene may also be a contributing factor to *Fusarium* keratitis and *Acanthamoeba* keratitis. Joslin et al.[1] reported an increase in the number of diagnosed cases of *Acanthamoeba* keratitis in the Chicago area, with further discussion hypothesizing that this outbreak may be the result of recent action by the Environmental Protection Agency to decrease disinfection byproducts in community water supplies. In an extensive literature review of *Acanthamoeba* keratitis, Awwad et al.[13] emphasized that contact lens wear and exposure to contaminated water sources are still the most important risk factors for *Acanthamoeba* keratitis. Because 85% of American patients with *Acanthamoeba* keratitis are contact lens wearers, prevention of contact lens contamination with *Acanthamoeba* should be a major focus to prevent the condition.[13] This prevention must include improvements in contact lens hygiene and enhancements in the amoebicidal activity of wetting and disinfecting solutions.

Another important factor with *Acanthamoeba* keratitis is that cysts formed by *Acanthamoeba* are highly resistant to temperature, pH levels, and contact lens disinfecting solutions,[10] and this resistance makes contact lens storage cases potential reservoirs for the amoebae. In the instance that the case is also contaminated with bacteria or fungi, the amoebae can use these microbes as a food source, enabling them to multiply to high levels. This increases the potential risk that the amoeba will attach to the surface of the contact lens and then be introduced onto the ocular surface. Hiti et al.[10] also discussed the importance of keeping the contact lens storage case free of all potentially pathogenic microorganisms to prevent the formation of biofilms, which, once formed, act as a protective layer to prevent adequate subsequent disinfection of organisms within the case by the care regimen biocides.[14] Appropriate measures of prevention include frequent case renewal, boiling (>70°C kills amoebic trophozoites) or microwave irradiation (600 W under humid conditions) of the storage case, and mechanical cleansing (i.e., rubbing) to remove any biofilm.[10]

In conjunction with poor contact lens hygiene, there may be a possible link between new silicone hydrogel materials and microbial keratitis, although data generated thus far have not implicated one particular type or design of lens or lens material. Beattie et al.[15] showed that attachment of *Acanthamoeba* to silicone hydrogel materials was greater than that to conventional hydrogel lenses. This increased attachment was thought to be an inherent characteristic of the polymer itself or a side effect of the surface modification procedure that occurs during lens manufacture.[15] More recent work[16] compared *Acanthamoeba* attachment to original, first-generation silicone hydrogel materials and newer, second-generation materials, including consideration of the influence of biofilm and patient wear. Results showed a significantly higher attachment for first-generation silicone hydrogel materials than for second-generation silicone hydrogel lenses or conventional polyhydroxyethylmethacrylate-based hydrogel lenses. Ultimately, if exposed to *Acanthamoeba* while showering or swimming, through noncontinuous wear or through ineffective or improper lens hygiene, including the absence of a manual rub, first-generation silicone hydrogel materials appear to promote a higher risk for *Acanthamoeba* attachment.[16] However, despite the apparent increased level of *Acanthamoeba* attachment to first-generation silicone hydrogel lenses, to date there have been few cases of *Acanthamoeba* keratitis in silicone hydrogel lens wearers.[16] This low rate of infection may be the result of various factors, including the short length of time that silicone hydrogel lenses have been on

the market; poor reporting of cases of *Acanthamoeba* keratitis associated with silicone hydrogel materials; the greater oxygen transmissibility of silicone hydrogel lenses resulting in a healthier corneal surface preventing *Acanthamoeba* keratitis, despite the presence of *Acanthamoeba* on the lens; and possibly the extended-wear nature of many silicone hydrogel lenses eliminating, in some instances, exposure to contaminated contact lens storage cases.

Ahearn et al.[17] recently analyzed the capabilities of *F. solani* and *Ulocladium* species to attach and penetrate hydrogel lenses and silicone hydrogel lenses. Both were found to firmly attach to each family of materials but rarely penetrate them. Their analysis emphasized that "even after vigorous rinsing with multipurpose solution, the fungal attachments were not broken." These results suggest that failing to rub lenses as part of the lens care regimen may lead to higher rates of fungal adherence to lens materials and potentially to explain, at least partially, the increase in fungal keratitis cases found in contact lens wearers.

Rosenthal et al.[18] evaluated the effective contribution of regimen steps on the overall performance of contact lens disinfection processes. Their results clearly suggested that eliminating the rubbing and rinsing steps associated with a multipurpose solution may allow hundreds to thousands of microorganisms to remain on the lens, of which the disinfectant may not be able to kill all. There was a direct correlation between the number of steps in the cleaning regimen and the increased disinfecting efficacy. They reported that in the event of a full rubbing and rinsing regimen, there were essentially no microorganisms on the lenses with any of the multipurpose solutions evaluated. When the digital rubbing step was eliminated but rinsing remained, the efficacy of ReNu MultiPlus was lowered. When all rubbing and rinsing steps were eliminated, all solutions in the study failed to meet the test criteria. The authors recommended a minimum of a 5-second rinse per lens surface to adequately reduce the number of viable microorganisms, in the absence of digitally rubbing the lenses.[18]

In contrast, Borazjani and Kilvington[9] suggested that some multipurpose solution systems, when used as recommended by the manufacturer, are more effective at killing representative strains of *Acanthamoeba* than others, even with the implementation of a no-rub technique. This study reported that ReNu MultiPlus reduced the number of recoverable amoebae by more than 95%, even in the presence of organic soil. These authors reported that no amoeba were recoverable from the contact lens when a 10-mL rinse of ReNu solution was used after a 4-hour storage period. They proposed that this finding indicates the potentially weak binding of *Acanthamoeba* to contact lens surfaces, which can be broken by simply rinsing with multipurpose solution instead of digitally rubbing.[9]

On reviewing all the available data, it would appear that failing to rub lenses as part of the cleaning process, with the concurrent absence of adequate rinsing, does not seem to be prudent behavior. A lens care system may show adequate efficacy when used correctly as described in the labeling process, but may not show adequate efficacy in the uncontrollable real world, where patients are free to do as they choose and noncompliant behaviors will inevitably occur. In the face of potentially sight-threatening complications, such as fungal and *Acanthamoeba* keratitis, do practitioners place sufficient emphasis on proper care regimen practices? Although minimizing the steps in the care regimen of contact lenses is attractive from a convenience perspective, this convenience appears to have some negative consequences, namely a greater level of microbial adherence to lenses.

Although there is some conflict of opinion in the literature regarding the need for a mechanical rub during lens care procedures, the burden of evidence weighs in favor of reestablishing a digital rub component to multipurpose solution lens care system regimens.

REFERENCES

1. Joslin CE, Tu EY, McMahon TT, et al. Epidemiological characteristics of a Chicago area *Acanthamoeba* keratitis outbreak. *Am J Ophthalmol* 2006;142:212–217.
2. Chang DC, Grant GB, O'Donnell K, et al. Multistate outbreak of *Fusarium* keratitis associated with use of a contact lens solution. *JAMA* 2006;296:953–963.
3. Schein OD, Ormerod LD, Barraquer E, et al. Microbiology of contact lens–related keratitis. *Cornea* 1989;8:281–285.
4. Wilhelmus KR, Robinson NM, Font RA, et al. Fungal keratitis in contact lens wearers. *Am J Ophthalmol* 1988;106:708–714.
5. Zhang S, Ahearn DG, Noble-Wang JA, et al. Growth and survival of *Fusarium solani–F. oxysporum* complex on stressed multipurpose contact lens care solution films on plastic surfaces in situ and in vitro. *Cornea* 2006;25:1210–1216.
6. Joslin CE, Tu EY, Shoff ME, et al. The association of contact lens solution use and *Acanthamoeba* keratitis. *Am J. Ophthalmol* 2007; 144(2):169–180.
7. Levy B, Heiler D, Norton S. Report on testing from an investigation of *Fusarium* keratitis in contact lens wearers. *Eye Contact Lens* 2006;32: 256–261.
8. Hiti K, Walochnik J, Faschinger C, et al. One- and two-step hydrogen peroxide contact lens disinfection solutions against *Acanthamoeba*: How effective are they? *Eye* 2005;19:1301–1305.
9. Borazjani RN, Kilvington S. Effect of a multipurpose contact lens solution on the survival and binding of *Acanthamoeba* species on contact lenses examined with a no-rub regimen. *Eye Contact Lens* 2005;31:39–45.
10. Hiti K, Walochnik J, Maria Haller-Schober E, et al. Efficacy of contact lens storage solutions against different *Acanthamoeba* strains. *Cornea* 2006;25:423–427.
11. Claydon BE, Efron N. Non-compliance in contact lens wear. *Ophthalmic Physiol Opt* 1994;14:356–364.
12. Cancrini G, Iori A, Mancino R. *Acanthamoeba* adherence to contact lenses, removal by rinsing procedures, and survival to some ophthalmic products. *Parassitologia* 1998;40:275–278.
13. Awwad ST, Petroll WM, McCulley JP, et al. Updates in *Acanthamoeba* keratitis. *Eye Contact Lens* 2007;33:1–8.
14. Elder MJ, Stapleton F, Evans E, et al. Biofilm-related infections in ophthalmology. *Eye* 1995;9(part 1):102–109.
15. Beattie TK, Tomlinson A, McFadyen AK, et al. Enhanced attachment of *Acanthamoeba* to extended-wear silicone hydrogel contact lenses: A new risk factor for infection? *Ophthalmology* 2003;110:765–771.
16. Beattie TK, Tomlinson A, McFadyen AK. Attachment of *Acanthamoeba* to first- and second-generation silicone hydrogel contact lenses. *Ophthalmology* 2006;113:117–125.
17. Ahearn DG, Simmons RB, Zhang S, et al. Attachment to and penetration of conventional and silicone hydrogel contact lenses by *Fusarium solani* and *Ulocladium* sp. in vitro. *Cornea*, in press.
18. Rosenthal RA, Henry CL, Schlech BA. Contribution of regimen steps to disinfection of hydrophilic contact lenses. *Contact Lens Anterior Eye* 2004;27:149–156.