THE AMERICAN ACADEMY OF OPTOMETRY
Comments pertaining to contact lens care systems:

Food and Drug Administration (FDA) Ophthalmic Devices Advisory Panel, Center for Devices and Radiological Health Advisory Committee
June 10, 2008

Presented by:
Charlotte Joslin, OD, FAAO
PhD Candidate, Epidemiology, School of Public Health
Assistant Professor, Ophthalmology and Vision Sciences
University of Illinois at Chicago
Disclosures

• No Commercial Disclosures

• Support:
  – Ezell Fellow, American Academy of Optometry
  – Gerhard Cless Foundation
  – Midwest Eye-Banks
  – NIH/NEI K23 15689
  – Prevent Blindness America
  – UIC Campus Research Board
Outbreak History

- Recent reports of an increase in the incidence of *Fusarium* keratitis\(^1,\,2\) and *Acanthamoeba* keratitis\(^3-5\) have resulted in general concern regarding the incidence, severity, and prevention of these conditions, particularly related to multi-purpose solutions (MPS)

- **Fusarium** keratitis
  - Withdrawal of Bausch & Lomb ReNu MoistureLoc®
    - Associated with 94 of 164 (57%) confirmed cases of *Fusarium* keratitis by the Centers for Disease Control and Prevention (CDC)\(^1\)
    - Reduced the incidence of *Fusarium* keratitis\(^6\)

- **Acanthamoeba** keratitis
  - Voluntary recall of Advanced Medical Optics Complete® MoisturePlus™
    - Associated with 21 of 39 (58%) culture-confirmed cases in CDC study\(^4\)
    - *Acanthamoeba* keratitis cases continue
How Did These Problems Occur?

1. Inadequate efficacy of MPS

2. Inadequate lens-related hygiene
1. Inadequate efficacy of Multipurpose Solutions

- *In vitro* studies demonstrate:
  - *Acanthamoeba* are largely resistant to MPS\(^7-16\)
  - Cysts are notably more resistant than trophozoites
  - Some solutions exhibit greater *Acanthamoeba* efficacy
    - Hydrogen peroxide-based lens care systems\(^10, 19\)
    - Rigid gas permeable solutions\(^11\)
1. Inadequate efficacy of Multipurpose Solutions

- Efficacy testing is performed with strains or methods that attenuate organism virulence\textsuperscript{20, 21}
  - i.e., extensive laboratory organism cycling, axenic \textit{Acanthamoeba} culture growth

- May not reflect the virulence of wild type strains that cause infection, as evident with the \textit{Fusarium} keratitis outbreak\textsuperscript{22}

- Stressors which decrease organism virulence may overstate apparent solution efficacy
2. Inadequate lens-related hygiene

- Inadequate lens-related hygiene occurs in both healthy and microbial keratitis patients, ranging >80% in multiple studies\textsuperscript{23-25}

- Inadequate lens-related hygiene was contributory in \textit{Fusarium} and \textit{Acanthamoeba} keratitis outbreaks\textsuperscript{1-3}
  - Failing to remove environmental microbial lens contaminants
  - Reduced biocidal efficacy providing milieu permissive to microbial growth\textsuperscript{22, 26}

- Only two hygiene risk factors identified for contact lens-related microbial keratitis,\textsuperscript{1, 3, 27-29}
  - Overnight lens wear
- Solution reuse

- Yet, concerns exist with common forms of noncompliance\textsuperscript{30, 31}
2. Inadequate lens-related hygiene

- Additional lens-related hygiene issues that increase the relative risk of *Acanthamoeba* keratitis include contact lens exposure to contaminated water
  - Recreational activities such as swimming or hot tub use$^{24, 32, 33}$
  - Exposure to contaminated tap water$^{33-35}$

- Higher *Acanthamoeba* keratitis incidence rates in the United Kingdom have been attributed to contaminated tap water and water-storage practices
  - 8 of 27 (30%) of homes sampled in *Acanthamoeba* keratitis patients had *Acanthamoeba*-positive water supplies$^{38}$
  - In 6 of 8 patients, *Acanthamoeba* isolates cultured from tap water were genetically identical to isolates from the cornea$^{38}$
2. Inadequate lens-related hygiene

- MPS base disinfectants are unchanged since introduction, and *in vitro* efficacy against *Acanthamoeba* has always been poor\(^7-16\)
  - MPS have been effective enough to largely prevent *Acanthamoeba* keratitis outbreaks since introduction,\(^39\) despite general lack of efficacy
  - Increase in *Acanthamoeba* keratitis cases has continued
    - Occurring with all solutions following the Complete MoisturePlus recall

- This continuation of cases, together with the general MPS inefficacy, yet a lack of historical *Acanthamoeba* keratitis cases, suggests an overall increase in the organism load

- An increased environmental exposure from *Acanthamoeba* and biofilm overgrowth in water distribution systems has been hypothesized,\(^3,40\) potentially resulting from changes in disinfection practices necessary to meet US Environmental Protection Agency (EPA) disinfection byproduct regulations\(^41\)
2. Inadequate lens-related hygiene

- Inadequate patient compliance does not fully account for recent outbreaks, yet individual hygiene practices are generally constant over time at the population level
  - Breaches in contact lens hygiene decrease solution effectiveness against microbial organisms

- This cannot be overemphasized:
  1) If or when environmental pressures increase microbial load
  2) Ability of *in vitro* efficacy testing to predict effectiveness
Adherence of Microorganisms to Silicone-Hydrogel Lenses

• *In vitro* laboratory studies demonstrate:
  – Increase in *Acanthamoeba* and microbial adherence with first generation silicone hydrogel lenses\(^{43-46}\)
    • Surface treatments increasing wettability\(^{43-45}\)
    • Increased lens oxygen permeability providing superior *in vitro* organism growth\(^{46, 47}\)

• Minimal supportive epidemiologic evidence for
  – *Acanthamoeba* keratitis\(^3\)
  – General microbial keratitis\(^48\)
The Importance of Rubbing and Rinsing

- The importance of a rubbing or cleaning step followed by rinsing with the MPS solution is highlighted by the
  1. Relative lack of efficacy of currently available MPS systems against *Acanthamoeba*
  2. Patient compliance factors decreasing solution effectiveness against all microorganisms

- The rub and rinse step removes bacteria, fungi and *Acanthamoeba* from the lens surface\textsuperscript{49-53}
  - Full rubbing, rinsing, and disinfection regimen results in few surviving microorganisms\textsuperscript{49}
  - Elimination of rubbing and rinsing steps allows microorganism survival on the lens\textsuperscript{49}
  - Rinsing alone is not adequate, as *Fusarium* and other microorganisms remain adherent after rinsing alone\textsuperscript{49, 54}
Recommendation of
The American Academy of Optometry

• MPS systems represent a contributing factor in recent microbial keratitis outbreaks

• The American Academy of Optometry recommends:
  – MPS systems be required to have “rub and rinse” on the label
  – Solutions must demonstrate efficacy against *Acanthamoeba* for FDA approval.
  – Development of on-going surveillance program, as it will provide data useful to:
    • Identify trends in microbial keratitis disease patterns and
    • More rapidly identify microbial keratitis outbreaks and risk factors
References

References


THE AMERICAN ACADEMY OF OPTOMETRY

Comments pertaining to contact lens care systems:

Food and Drug Administration (FDA) Ophthalmic Devices Advisory Panel, Center for Devices and Radiological Health Advisory Committee
June 10, 2008

Presented by:
Charlotte Joslin, OD, FAAO
PhD Candidate, Epidemiology, School of Public Health
Assistant Professor, Ophthalmology and Vision Sciences
University of Illinois at Chicago