



**Open Public Hearing
Ophthalmic Devices
Panel**

June 10th 2008

Francis S. Mah, M.D.

**Medical Director, Charles T. Campbell
Ophthalmic Microbiology Laboratory**

Director, Clinical Vision Research Center

Department of Ophthalmology

University of Pittsburgh

**American Society of Cataract and
Refractive Surgery - ASCRS**

Disclosure

No financial interest in any of the topics or items discussed.

Have received research support from Alcon Labs, Inc, and Allergan, Inc. for non CTL associated areas.

Impact

- **34 million CTLs wearers in the US**
 - **Annually 30,000 cases of bacterial keratitis**
 - **Compared to non-CTL wearer, 80 fold greater risk to develop microbial keratitis**
 - **Risk of infection varies 1.2 – 25.4 / 10,000**

Wilhelmus KR. Indecision about corticosteroids for bacterial keratitis. An evidence-based update. *Ophthalmology* 2002;109:835-844. Chang et al. Multistate outbreak of *Fusarium* keratitis associated with use of a CTL solution. *JAMA* 296(8), Aug 23/30, 2006. Stapleton et al. The incidence of CTL related microbial keratitis in Australia. *Ophthalmol.* 2008. In press, online.

Impact

- **Up to half of contact lens-related keratitis BCVA 20/60, and a quarter of patients have 20/200 or worse vision.**
- **Corneal opacification and perforation from bacterial keratitis result in ~ 330 corneal transplants a year in North America.**

Fungal Keratitis

➤ Fusarium

- On March 8, 2006, CDC received a report from an ophthalmologist in New Jersey regarding three patients with contact lens--associated Fusarium keratitis during the preceding 3 months.
- Khor et al. *An outbreak of Fusarium keratitis associated with contact lens wear in Singapore.* JAMA. June 2006.



FDA Statement

FOR IMMEDIATE RELEASE

Statement
May 15, 2006

Media Inquiries:

Kristen Neese, 301-827-6242

Consumer Inquiries:

888-INFO-FDA

Bausch & Lomb Global Recall of *ReNu* with *MoistureLoc* Contact Lens Cleaning Solution

On Thursday, May 11, 2006 a team from Bausch & Lomb met with Food & Drug Administration (FDA) officials to share information resulting from the company's internal investigation into cases of *Fusarium* keratitis associated with ReNu with MoistureLoc.

Bausch & Lomb has proposed that unique characteristics of the formulation of the ReNu with MoistureLoc product in certain unusual circumstances can increase the risk of *Fusarium* infection.

Based on this scientific and epidemiological data suggesting that ReNu with MoistureLoc may increase susceptibility to *Fusarium*, Bausch & Lomb has decided to permanently remove the ReNu with MoistureLoc product worldwide. FDA supports this decision. To date, data available do not indicate a problem with ReNu MultiPlus or ReNu Multi-Purpose or generic brands of this contact lens cleaning solution.

While FDA is still concluding its scientific evaluations and expects additional information to be submitted by the sponsor, at this time we recognize that Bausch & Lomb has proposed the formulation as the potential root cause of the increased relative risk of *Fusarium* keratitis associated with use of the ReNu with MoistureLoc product. FDA will continue to review cultures and epidemiological data and if there is new information that adds to or changes our current understanding, we will act on it in a timely and appropriate manner.

As part of the joint Center for Disease Control & Prevention (CDC) and FDA investigation, field officers have been inspecting the Bausch & Lomb plant and facilities in Greenville, SC since March 22, 2006. While the plant inspection is being finalized, there is still some additional testing to be completed. The agency plans to issue observations from the inspections imminently.

ReNu with MoistureLoc contact lens solution, manufactured in the Greenville, SC plant, was voluntarily withdrawn from the market in the United States on April 13, 2006. To date, a majority of the confirmed *Fusarium* cases have been associated with the ReNu with MoistureLoc. Our interest in the MoistureLoc product has been based on the disproportionate number of cases of *Fusarium* keratitis associated with ReNu with Moisture Loc compared to the overall product market share. Based on CDC reports, the number of cases involving various contact lens solutions other than MoistureLoc has remained consistent throughout our investigation, and not disproportionate from the routine incidence of this infection in the population.

Acanthamoeba Keratitis

- Recent increase in CTL related cases
- May 26th, 2007, the CDC announced an association with AMO Complete MoisturePlus CTL solution



Infectious Disease Task Force



- Eduardo C. Alfonso, MD
- Tat-Keong Chan, MD
- Eric Donnenfeld, MD
- Terry Kim, MD
- Francis S. Mah, MD
- Terrence P. O'Brien, MD

**ASCRS Infectious
Disease Task Force**

Francis S. Mah, MD – Chair

Eduardo Alfonso, MD

Tat-Keong Chan, MD

Eric D. Donnenfeld, MD

Terry Kim, MD

Terrence P. O'Brien, MD

Special Report: Acanthamoeba Keratitis

Keratitis can lead to severe visual disability and requires prompt diagnosis and treatment. Injury to the corneal surface and stroma allows invasion of normal flora as well as organisms harbored by foreign bodies. However, there are a select group of microbial pathogens that can penetrate intact corneal epithelium, *Acanthamoeba* is felt to be in this class of insidious pathogen.

Contact lens wear is an established risk factor for infectious keratitis. All types of contact lenses can cause infection, with extended wear soft lenses conferring greater risk than daily wear hard or soft lenses. Corneal changes from contact lens use include an induced hypoxic and hypercapnic state promoting epithelial cell desquamation and allowing microbial invasion. Contact lenses also induce dry eye and corneal hypesthesia. Overnight rigid gas permeable lens use for orthokeratology has also been associated with bacterial keratitis. Recently, the competition for more comfortable and more consumer friendly contact lens solutions have been identified as playing a key role in the increase in atypical causes of microbial keratitis including *Fusarium* (B&L MoistureLoc) and *Acanthamoeba* (AMO Complete MoisturePlus).

Diagnostic Techniques

Routine culture of corneal infections is not the usual practice in the community. A small peripheral ulcer may be treated empirically, but a large, purulent, central ulcer that extends to the middle to deep stroma should be cultured prior to treatment. In addition, ulcers that are clinically suspicious for fungal, mycobacterial, or amoebic infections or are unresponsive to initial broad spectrum antibiotics warrant cultures. Topical anesthesia with proparacaine hydrochloride is preferred since it has fewer antibacterial properties than other topical anesthetics. A sterile platinum spatula is used to scrape the leading edge as well as the base of the ulcer, while carefully avoiding contamination from the lids and lashes.

In cases of deep stromal suppuration that is not readily accessible or a progressive microbial keratitis unresponsive to therapy, a corneal biopsy may be warranted. A round 2mm to 3mm sterile, disposable skin punch is used to incise

ASCRS Infectious Disease ACA Keratitis RECOMMENDATIONS

- 1. Remove and return any AMO Complete MoisturePlus Solution from offices/places of work.**
- 2. Advise all patients, and especially contact lens wearers, of the association of ACA with the contact lens solution, AMO Complete MoisturePlus Solution so they may dispose of remaining solutions.**

ASCRS Infectious Disease ACA Keratitis RECOMMENDATIONS

- 3. Recommend that all contact lens wearers rub their lenses with an alternate cleaning solution and avoid the 'no rub' technique advocated by manufacturers.**
- 4. Although suspicion should be kept high due to the risk of ACA keratitis, bacterial infectious keratitis is still the most common etiology and should remain on top of the list of differential diagnoses.**

ASCRS Infectious Disease ACA Keratitis RECOMMENDATIONS

- 5.** Be on the lookout for the early signs of ACA keratitis and use vital dyes (fluorescein, lissamine green, rose bengal) to help differentiate these lesions from those caused by herpes simplex keratitis.
- 6.** With cases of acute keratitis, unless it is of an abnormal appearance, larger than 2mm in size, moderate to deep stromal melting, or is central or paracentral, treatment should begin with intensive application of a topical broad spectrum antibiotic(s).

ASCRS Infectious Disease ACA Keratitis RECOMMENDATIONS

- 7.** If the keratitis does not respond, or has any of the above unusual characteristics, corneal scrapings for vital stains (Gram, Geimsa, etc) and cultures should be obtained to identify the pathogen. Confocal microscopy can aid in the diagnosis of ACA.
- 8.** For any contact lens patient with a suspected infection, contact lenses, cases, and cleaning solutions should be collected for culturing.

ASCRS Infectious Disease ACA Keratitis RECOMMENDATIONS

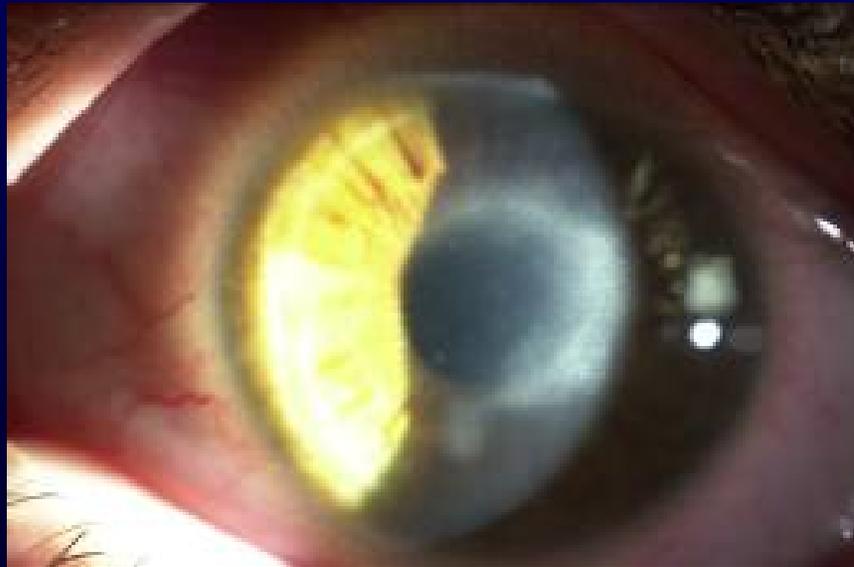
9. Steroids should be used with caution in the above concerning situations, and preferably only if the organism has been identified, and the patient is clinically responding to the treatment.
10. Early diagnosis is the key to improved outcomes so consider earlier referral to a specialist than usual.

ASCRS Infectious Disease ACA Keratitis RECOMMENDATIONS

- 11.** Treatment involves extended and frequent dosing of at least one of the cystocidal biguanides (PHMB 0.02% and/or chlorhexidine 0.02%), and at least one other agent – neomycin, propamidine, and/or clotrimazole, for weeks to months. In addition, the treating clinician may consider judicious use of oral itraconazole as an adjunct to topical therapy.

Acanthamoeba Keratitis Issues

1. Bring together federal (FDA, CDC, EPA, etc), clinical, research and industry leaders to determine scope and direction
2. Approve or allow appropriate treatment – propamidine, chlorhexidine, &/or PHMB



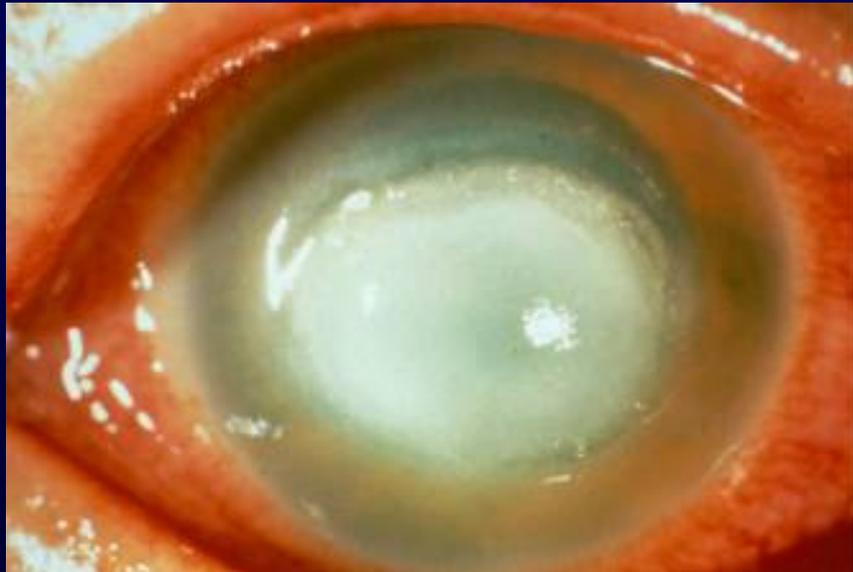
Acanthamoeba Keratitis Issues

3. Mandate teaching of better hygiene including forbidding tap water rinse, showering, bathing, swimming with CTLs – by clinicians and industry
4. Recognize confocal as a valuable tool in diagnosis



Acanthamoeba Keratitis Issues

5. Establish adequate standards for amoebic disinfection of CTL care solutions
6. Research should be done to combine efforts in CTL material technology and solution advances such that optimal combinations can be determined





Thank You.

