

Recognizing, Treating, and Avoiding Microbial Keratitis In Contact Lens Wear

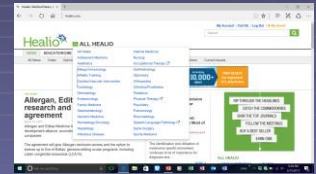
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Michael DePaolis, OD, FAAO FINANCIAL DISCLOSURE STATEMENT

- Associate Professor of Clinical Ophthalmology
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 - Alcon
 - Allergan
 - AMO
 - Bausch & Lomb / Valeant
 - Clerio Vision
 - Cooper Vision
 - Paragon Vision Sciences
 - Shire
 - SynergEyes
 - J&J Vision Care



- Optometric Editor, Primary Care Optometry News
- Professional Editorial Review Board, allaboutvision.com

CONTACT LENS COMPLICATIONS Microbial Keratitis

So, is there a take home here?
Things aren't always as they first appear.



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

November 13, 2014 CDC's Morbidity & Mortality Weekly Report

- In 2010, nearly 1 million Doctor's visits due to keratitis
- Cost to society of \$175 million
- 230,000 involved contact lenses and 25,000 diagnosed as ulcer
- Jennifer Cope, MD, MPH, of the CDC, " ... who wear contact lenses ON are more than 20x more likely to get keratitis." ... not taking care of them properly is the single biggest risk factor for keratitis."

August 20-24, 2015 CDC's Morbidity & Mortality Weekly Report

- Contact Lens Risk Survey – 99% engage in at least one risky behavior
- 82% expired lenses / 55% 'top off' solutions / 50% sleep in their lenses

August 17, 2018 CDC's Morbidity & Mortality Weekly Report

- Six cases of microbial keratitis 2016 – 2018 ... all involved ON wear
- Swimming, delayed care, illegally obtaining lenses additional risks

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case report: LY 65 yof

- Previous hx of contact lens overwear
- Refit into PureVision 2 ou CW x 60-90 days
- Systemic Hx: Breast CA Social Hx: smoker
- C/O redness, discharge, pain, & photophobia OD x 3 day

Dx: Presumed infectious corneal ulcer OD

Tx:

- 5% Homatropine OD in office
- Vigamox OD q30 min x 4 hrs, then q1h
- F/U in 24 hrs



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case report: LY 65 yof 1 Day F/U

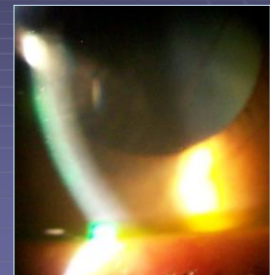
- C/O continued pain, photophobia, & discharge

VA cc 20/50- OD

- SLE: diffuse conjunctival injection, corneal infiltrate w epithelial defect, gr 1+ AC rxn

Tx:

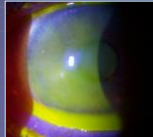
- 5% Homatropine OD
- Vigamox OD q2h
- Polytrim OD q2h
- F/U 24 hrs



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case report: LY 65 yof 4 Day F/U

- Feels much better, still photophobic
- VA cc 20/30- OD
- SLE: minimal conjunctival injection, epithelium intact w infiltrate, AC quiet.



Tx:

- Vigamox OD qid,
- Polytrim OD qid,
- F/U 3 days

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case report: LV 50 yof

- Previous CL wearer commences EWSC x 4 days with expired CL's
- C/O redness, pain, discharge OS x1 day
- Bacterial corneal ulcer diagnosed in ED one day prior
- Blood, chocolate, gram, and acanthamoeba cultures performed
- Ofloxacin OS q2h initiated

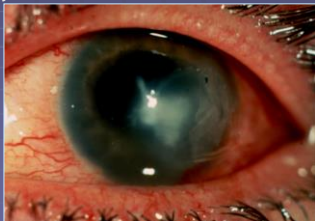
CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case report: LV 50 yof 1 Day F/U

- C/O eye feels worse, using Ofloxacin OS q2h
- VA cc 20/400 (-) Adenopathy
- SLE – Corneal ulcer with hypopyon
- Cultures – no growth

Plan:

- Homatropine 5% bid
- Vigamox q1h
- Tobramycin (1.3%) q1h



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case report: LV 50 yof 3 Day F/U

- C/O eye feels much better, using all meds.
- VA cc 20/200
- SLE - ulcer border well defined, reduced AC reaction, trace hypopyon
- Cultures – still no growth
- Plan: Homatropine 5% qd, Vigamox q2h & Tobramycin q2h

Case report: LV 50 yof 10 Day F/U

- C/O eye feels much better, using all meds.
- VA cc 20/100
- SLE - healing epithelial defect, trace AC reaction, no hypopyon
- Culture – positive for pseudomonas aeruginosa
- Plan: Homatropine 5% qd, Vigamox qid & Tobramycin qid & Pred forte qid
- Ultimate BCVA 20/50

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

TOPICS FOR CONSIDERATION

▪ Epidemiology & risk factors

Is overnight wear the predominant risk factor?

What role do silicone hydrogels play in mitigating against risk?

Are certain patients inherently at greater risk?

- Pathophysiology
- Differential diagnosis
- Treatment strategies
- Prevention

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Relative risk of microbial keratitis in contact lens wear?

- Extended wear with conventional lenses
- 1 in 500 patient years (Poggio, et al 1989)
- Daily wear soft lenses
- 1 in 4,000 patient years (Cheng, et al 1999)
- Continuous wear silicone hydrogel lenses
- 1 in 4,000 patient years (Holden, etal 2003)

Morgan, etal Br J Ophth 89(4):2005.

Incidence of severe keratitis: CW SiHy -> 19.8 per 10,000 patient years

Schein, etal Ophthalmology 112(12):2005

▪ Annual Rate of 'Presumed' MK ~ 18 per 10,000 patient years

Stapleton, etal Ophthalmology 115(10):2008

▪ Overnight wear silicone hydrogels – 25.4 per 10,000 patient years

Stapleton, etal PLoS One 12(8): 2017

- MK in daily disposables? ON wear, every day wear, hand hygiene, smoking

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Are certain patients at higher risk ?

Systemic profile

- Immunocompromised
- Metabolic disorders
- Substance abuse **smoking**
- Dermatologic conditions ... atopy & rosacea

Ocular profile

- Ocular surface disease
- Neurotrophic, degenerative, & dystrophic cornea

Kugadas, etal PLoS Pathos 12(9):2016

- **Gut & ocular microbiota** influence susceptibility to *p. aeruginosa* keratitis in mice

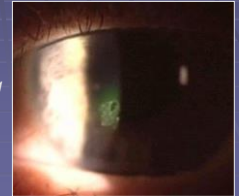
CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS PATHOPHYSIOLOGY

Pathophysiology of microbial keratitis

Landage , etal Invest Oph & Vis Sci 44:1843,2003.

Corneal "homeostasis"

- Limbal stem cells -> migratory basal cells -> wing cells -> surface (squamous) cells
- ON wear diminishes cell shedding
- ON causes paradoxical epithelial thinning



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS PATHOPHYSIOLOGY

Pathophysiology of microbial keratitis

Fleiszig S. Optom Vis Sci 83(12):2006

- *P. aeruginosa* **secretes toxins** to cross basal epithelium / gain access to stroma
- Infected epithelial cells defend by sloughing

Sullivan A. ARVO 2012

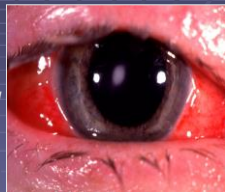
- *P. aeruginosa* **T3SS most virulent**

Wu, etal Oc Surf 15(1):2017

- **Tear fluid increases T3SS** expression in contact lens *P. aeruginosa* biofilms

Subedi, etal Clin Exp Optom 2017

- *P. aeruginosa* **mobile genetic elements** (MGE's) translate resistance



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

What must go wrong in microbial keratitis ?

Breached epithelial barrier function ???

Microbial 'seeding'

Microbial adherence & multiplication

Failure of host immune response

Delayed or insufficient treatment

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS DIAGNOSIS

Is it a sterile or infectious process ?

- Key symptoms?
- Key findings?
- When to culture ?



CONTACT LENS COMPLICATIONS INFILTRATIVE KERATITIS

Infiltrative Keratitis – the great corneal conundrum

- Cellular response – Neutrophils (pmn's), lymphocytes, macrophages
- Originate from tears, limbal vasculature, basal epithelium ?
- Epithelial disruption -> chemotaxis -> infiltration
- Caused by mechanical, toxic, immunogenic, or infectious agents

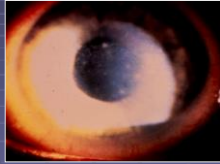
Corneal infiltrate does NOT equal infectious keratitis

CONTACT LENS COMPLICATIONS INFILTRATIVE KERATITIS

What are the relative risks for corneal infiltrative events (CIE's)?

Chalmers (2013)

- Gram (+) bioburden = 3-8x
- Gram (-) bioburden = 5x
- Reusing Daily Disposable = 4x
- ON wear of SiHy = 2-5x
- < 25 yoa or > 50 yoa = 2x
- MPS = 3x



Wilcox (2010), Shovlin (2011), Merchea (2012) & Kivington (2013)

- Increased risk with PQ-1 / Aldox MPS
- Delftia, Stenotrophomonas, Achromobacter, Serratia

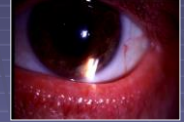
Szczotka-Flynn (2010)

- CIE's statistically more likely in CL bioburden & smoking
- No correlation between corneal staining and CIE's

CONTACT LENS COMPLICATIONS INFILTRATIVE KERATITIS

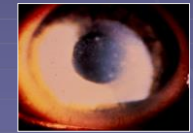
Wilcox, etal Eye & Cont Lens 37(2):2011

- HEMA EW x 6 nights
- Looked at microbial colonization of the lower lid, upper bulbar conjunctiva, and lens surface
- Cultures over 3 yrs -> significant carriers



Carriers of gram (+) organisms on lens

- 3x as likely to have CLPU
- 5x as likely to have Asymptomatic Infiltrates
- Coag (-) s aureus & corynebacterium

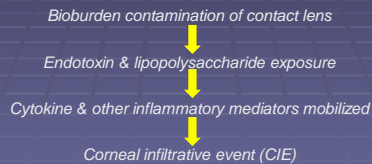


Carriers of gram (-) organisms on lens

- 5x as likely to have CLARE
- Haemophilus

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

What must go wrong in infiltrative keratitis?



CONTACT LENS COMPLICATIONS INFILTRATIVE KERATITIS

Contact Lens Peripheral Ulcers (CLPU) ... is it really an ulcer?

Holden, etal Cornea 18(5):1999.

- Histopathology of 3 lesions
- Focal loss of epithelium / underlying pmn's

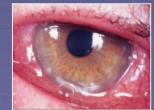


Donshtik, etal Trans Am Ophthal 93:49, 1995.

- N = 52 Patients with CLPU - 85% Single & 15% Multiple
- 50% (8/16) culture positive

CLPU Treatment Staging

- D/C CL's, lubricate, observe
- Steroid / antibiotic gtt ... is Neo/Poly/Dex OK?
- Cycloplegia & antibiotic gtt



CONTACT LENS COMPLICATIONS INFILTRATIVE KERATITIS

What is the best steroid-antibiotic suspension option?

Cost vs compliance (goodrx.com - average cash price)

- Tobramycin / Loteprednol - \$240
- Tobramycin / Dexamethasone - \$108
- Neomycin / Polymyxin / Dexamethasone - \$29



Notivol, etal Clin Ther 26(8):2004.

- Post-op cataract prophylaxis
- Withdrawal for allergic reaction
- Tobra-Dex - 1% (1 out of 104)
- Neo-Poly-Gram - 9% (5 out of 57)
- Neo-Poly-Dex - 0% (0 out of 110)



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Infectious vs sterile infiltrative keratitis

Stein, etal AJO 105(6):632, 1988.

Retrospective analysis of 24 culture (+) and 24 culture (-) cases

Infectious keratitis correlated with

Patient Symptoms

- Dull pain
 - Purulent discharge
- Clinical findings
- Epithelial defect
 - Infiltration
 - Anterior chamber reaction



Aasuri, etal Eye & Con Lens 29 (1S): 2003

Severe pain, lid edema, irregular infiltrate > 2mm, & AC involvement

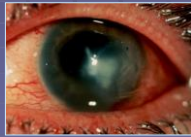
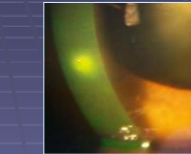
CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

To culture, or not to culture: that is the question

Miller, etal (Bascom Palmer Eye)
ICAAC September 2015 San Diego

- N = 176 cases microbial keratitis
- U of Miami Hospital ER in 2014
- 52% treated without cultures
 - 92% broad spectrum AB's
- 44% those cultured were (+)
- Combination therapy in 27%
 - MRSA and Fusarium

Antimicrobial stewardship?



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

What laboratory tests are indicated ?

- Cytology (scraping)
 - Spatula & calcium alginate swab
 - Microscope, slides, and reagent stains
- Culturing
 - Mini-tip culturettes
 - Spatula, agar plates, thioglycolate media



Which media are indicated ?

- Blood agar – aerobic organisms & saprophytic fungi
- Chocolate agar – neisseria, moraxella, haemophilus
- Lowenstein-Jensen – nocardia & mycobacterium

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

What laboratory tests are indicated ?

- Direct agar plating
- Mini-tip culturettes

Epley, etal Cornea 17(1):1998.
Johns-Hopkins University Hospitals

- Rabbit model keratitis
 - 100% sensitivity & specificity both techniques
- Human model keratitis (n = 12 patients)
 - 58% culture negative both techniques
 - 42% culture positive with both techniques
 - 1 case multiple organisms NOT identified by Mini-tip culturette
- Sensitivity & specificity similar between mini-tip and direct plating techniques

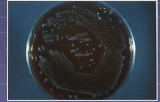


CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Should we look beyond the eye ?

Konda, etal Opt & Vis Sci 11:2013

- Cultured 125 eyes with presumed microbial keratitis
- Cultures (+) in
 - 40% of corneas / 80% of CL cases / 92% of CL's
 - 94% of cornea & CL cultures agreed
 - 77% of cornea & CL case cultures agreed



Martins etal CLAO 28(3):2002.

- 113 ewscI wearers with presumed microbial keratitis
- 29% bandage lenses / 71% cosmetic lenses
- Concordance between corneal and contact lens / case cultures
 - Fungal 100%
 - Amoebic 80%
 - Bacterial 75% (Pseudomonas most common)

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

How important is case hygiene ?

Vijay, etal Eye & Con Lens 41(2): 2015

- Innoculated contact lens cases with *s. aureus* (7.1 log CFU) or *p. aeruginosa* (8.4 log CFU) to establish adequate biofilm
- Assess combinations of rinsing, wiping, and/or air drying of cases
- Only MPS rinse, clean wipe, and air drying (6hr) effective
 - 0.9 log survival of *p. aeruginosa*
 - 3.4 log survival of *s. aureus*



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Does culturing impact outcomes ?

Bhadange, etal Br J Ophth 10:2014

- N = 60 cases of microbial keratitis at LV Prasad Eye Institute
- Retrospectively compared culture negative with culture positive
 - Size of infiltrate or history of trauma had no association with culture result
 - Prior topical antibiotic use with culture negative
 - Longer duration of symptoms and treatment with culture negative
 - More major surgery in culture positive
- Outcomes ...
 - Treatment success in 90% of culture (+) and 83% of culture (-)
 - Final VA 1.8 logMar in culture (+) and 2.3 logMar in culture (-)

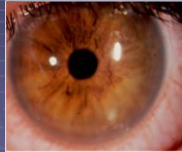
CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

When should we culture ?

- Ulcer > 2mm from limbus and ...
- Epithelial defect > 2mm and...
- Ulcer depth > 20% corneal thickness and...
- AC reaction > grade 2

Additional considerations ...

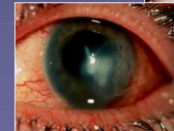
- History of vegetative trauma
- Hospital exposure
- Immunocompromised
- Non responsive to first line therapy



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Are all ulcers created equal ?

- Microbe virulence
- Host defense
- Time to treatment
- Appropriate treatment



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

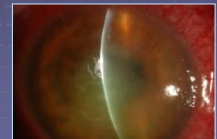
Case report: MR 33 yof

- Daily wear SCL / Variable MPS qhs
- C/O red, pain, tearing, blurry OD x 2 days
- Saw PCP yesterday and on gentamycin OD qid
- Systemic Hx: excellent. No meds. NKDA.
- Social Hx: Prior substance abuse
- Work Hx: Social coordinator at long term health care facility

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case report: MR 33 yof

- VA OD cc HM @ 1 ft
- + vesicular lesion on upper lip
- No preauricular adenopathy
- Decreased corneal sensation OD
- SLE – central corneal ulcer, peripheral satellite lesions, & AC rxn



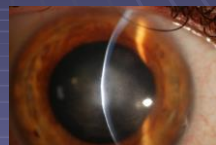
Impression: Corneal ulcer OD – bacterial vs herpetic

- Plan: 1) Labs for bacteria, fungal, viral, and acanthamoeba
2) Atropine OD qd, Vigamox OD qh, Valtrex 1000mg tid 3) F/U 24h

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case Report: MR 33 yof - 14 Day f/u

- VA OD cc 20/80
- No culture growth
- Vigamox OD q3h, Pred Forte OD qid
- Valtrex 1000mg tid
- SLE – ulcer re-epithelialized, stromal scar, AC deep & quiet

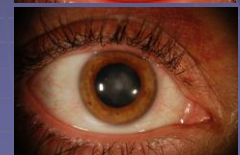
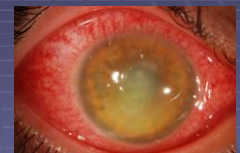


Plan: 1) Vigamox OD qid, Pred Forte OD qid, Valtrex 1000mg qd, f/u in 1 week.

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case report: MR 33 yof

- Would you have done anything differently during the work-up?
Culture nasal passages
- What do you think was the offending microorganism?
HSV vs bacterial vs multi-organism
- How would you treat it differently today ?
Zirgan Ophthalmic gel q3h x 7d



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

HSV Clinical Pearls ...

- Oral acyclovir alone as effective as topical antivirals in treating HSV epithelial keratitis (Cochrane Data Base 2010)
- Valacyclovir 1 gm tid 7-10 days (no lactose!)
- Antiviral induced crystalline nephrotoxicity?
 - Creatine clearance normal at 100ml / minute
 - Lower? Valacyclovir 500mg bid to tid
 - Or ... Zirgan 5x daily for 7 days

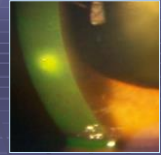


Valacyclovir + HIV (+) ... thrombotic thrombocytopenic purpura ?

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

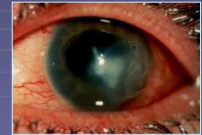
To treat or refer?

- Is monotherapy acceptable?
- What resistant microbes are of concern?
- What additional therapeutic agents are indicated?



If you elect to treat ...

- Early recognition
- Do not pressure patch
- Strong cycloplegia - 5% H or 1% A
- NSAIDS not indicated
- ANTIBIOTICS – broad spectrum approach
- DAMAGE CONTROL – steroids, azithromycin, or oral doxycycline



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

What does today's microbial keratitis look like ?

- Sand, etal Ophth 122(5): 2015
- All cultured cases of microbial keratitis from Doheny Eye (DEI) and LA County USC Medical Center (LAC-USC) from 2008-2012.
 - N = 290 cases from DEI -> 63% culture positive
 - N = 186 cases from LAC-USC -> 82% culture positive
 - Gram (+) 69% Coag (-) staph most common
 - P. aeruginosa most common gram (-)
 - Ciprofloxacin effective against 73% of all isolates
 - 44% of isolates ORSA

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

What does today's microbial keratitis look like ?

- Ni, etal Cornea 34(3):2015
- N = 323 infectious keratitis cases at Will's Eye Hospital (2009-2012)
 - Contact lens wearers – p. aeruginosa and fusarium
 - Non-lens related – s. aureus and candida
 - Most cases in spring and fewest in winter
 - p. aeruginosa and MSSA susceptible to fluoroquinolones
 - 38% CNSA & all MRSA resistant to moxifloxacin and gatifloxacin
 - Good susceptibility to tobramycin, gentamycin, and vancomycin
 - Voriconazole effective against all fungi

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Is monotherapy acceptable? In mild to moderate cases, yes!

- Ciprofloxacin study group Eifferman, etal Ophth 103(11):1996
- Ofloxacin study group O'Brien, etal Ophth 104(11):1997

But, then ... staph aureus resistance occurs

- Alexandrakis, etal Ophth 107(8):2000
- % of s. aureus isolates resistant to fluoroquinolones: 11% -> 28%
- Goldstein, etal Ophth 106(7):1999.
- Gram (-) : Gram (+) Ratio - 82%:18% in 1993 to 51%:49% in 1997

Jhanji, etal Cat & Ref Surg 33(8):2007

- Coag (-) S. epidermidis failed treatment with cefazolin (5%) & gatifloxacin (0.3%)
- Success with vancomycin (5%) and tobramycin (1.3%)

Moshifar, etal Cat & Ref Surg 32(3):2006

- P aeruginosa s/p PRK despite moxifloxacin prophylaxis
- MRSA keratitis s/p LASIK despite gatifloxacin prophylaxis
- Successfully treated with fortified aminoglycosides

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Is empirical treatment still acceptable ?

Steger, etal Ophthalmologie 111(7):2014

- Medical University of Innsbruck
- 123 cases of microbial keratitis 2010 – 2012
- Cultures positive in 56% of cases
- 59% gram (+) and 51% gram (-) and 7% fungal
- 30% mixed !!
- Combination of aminoglycoside and 2nd generation fluoroquinolone best initial treatment ... 88% effective
- Fluoroquinolone alone less effective

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Which 'resistant' microbes should we be concerned about?

- MRSA contains an enzyme that breaks B-lactam ring of antibiotics – increasing resistance to penicillin, methicillin, cephalosporins, and **many fluoroquinolones**
- ARMOR Surveillance: 38% S aureus & 30% CoNS are MRSA (Asbell 2016)
- 2% general population & 20% health care workers harbor MRSA
- **8%-13% of contact sports athletes harbor MRSA (Karaniika 2016)**
- In eye care MRSA occurs most frequently as post-op complication
- Athletes, dialysis, immunocompromised, & nursing home residents

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

How do we best treat MRSA?

- Oral – Bactrim (trimethoprim 160mg / sulfamethoxazole 800mg) bid x 10d
- Topical – Bactroban (mupirocin)
- Ocular Polytrim, Besivance, and vancomycin

Ocular TRUST found 3rd & 4th generation FQ's effective against ~ 30% of MRSA isolates, while **Polytrim effective against 95% of MRSA isolates**

McDonald & Blondeau Cat & Ref Surg 36(9):2010

- Up to 85% MRSA strains resistant to moxifloxacin & gatifloxacin
- **Besifloxacin greater efficacy against multi-drug resistant S aureus**

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Which 'resistant' microbes should we be concerned about?

Pseudomonas remains a viable threat

- **Fluoroquinolone resistant *Pseudomonas aeruginosa* (biofilm)** (Zegans 2001)
- **Effectively treated with fortified aminoglycosides or cephalosporins** (Kowalski 2001)
- ***Pseudomonas* still prominent organism in contact lens related microbial keratitis – 80% in Iranian study** (Hedayati 2015)
- ***Pseudomonas* mobile genetic elements facilitates transfer of resistance to antibiotics** (Subedi 2017)

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

What therapeutic strategies are indicated ?

- Should you treat or refer?
- When in doubt ... culture
- Prescribe aggressively
 - Moxifloxacin, gatifloxacin, or besifloxacin
 - Loading dose with frequent dosing
- Consider adjunct agents
 - **Fortified tobramycin** or amikacin (gram-)
 - **Polytrim** or vancomycin (gram +)
- Minimize collateral tissue damage
 - Oral doxycycline Ollivier, etal Am J Vet Res 64(9): 2003
 - Topical azithromycin
 - Topical corticosteroids

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

When does topical steroid use make sense?

Wilhemus Ophthal 109(5):2002.

- 50 yr literature review – Avoid steroid use in microbial keratitis Carmichael 1990
- 40 bacterial corneal ulcers tx w AB's x 24 hrs, then steroid or placebo
- No difference in complications, healing rates, or VA outcome Srinivasan Arch Ophth 2011
- 442 bacterial corneal ulcers treated with moxi-saline vs moxi-dex
- No difference in perforation, scarring or BCVA between groups
- **Benefits? Severe keratitis and earlier intervention (win 2-3 days)**
- Blair, etal Can J Ophth 46(1):2011
- N = 30 ulcers treated with Zymar / Placebo vs Zymar / Dexameth
- **No difference in healing, though smaller residual ulcer size in steroid tx**

Who should NOT get steroids? Suspected fungal, acanthamoeba, nocardia

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

New treatment paradigms?

Tam, etal J Clin Invest 10:2012

- Synthesized **keratins** from cytokeratin 6A (skin, hair, nails, cornea)
- Bacteriocidal against S pyogenes, E coli, S aureus, & P aeruginosa
- Possible non-toxic, biocompatible, and inexpensive anti-infective

Dutta, etal AAOpt Seattle 10/2013

- Peptide **melimine** bacteriocidal against P aeruginosa & S aureus
- No cytotoxicity in rabbit models

Kolar, etal Cell Mol Life Sci 8-14-2014 epub

- **Esculatrin** (frog skin antimicrobial peptide)
- Bacteriocidal against pseudomonas aeruginosa without cytotoxicity
- Effective at tid dosing in murine microbial keratitis model

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

What about non-pharmaceutical treatment strategies?

Randleman, et al OSN 30(13):2012

- N = 16 culture positive bacterial keratitis
- Single tx with CCXL and .01% riboflavin
- 12/14 eyes successfully treated

Said, et al Ophthalmol 2014

PACK (PhotoActivated Chromophore for Keratitis) – CCXL

- Corneal collagen cross-linking for infectious keratitis
- Biomicroscope mounted cross-linking instrument & photosensitizing agent
- Works by liberating reactive oxygen species for disinfection as well as increasing collagen resistance to proteolytic enzymes
- **Effective against a variety of bacterial, fungal, and amoebic species, but NOT viral species**

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

What about non-pharmaceutical treatment strategies?

Mohammadpour & Sabet J Ophth Vis Res 11(1):2016

- N = 6 eyes with infectious keratitis and descemetocoele
- Non responsive to antibiotic therapy
- **Amniotic Membrane Therapy for 3 months**
- All eyes recovered BCVA of 20/30 – 20/50

Tabatabaei, et al Oc Surf 15(2): 2017

- N = 49 eyes AB gtt / AM vs 50 eyes AB gtt alone
- AB/AM group better VA and smaller residual scar

- Cryopreserved – Prokera
- Dehydrated – AmbioDisc, BioDOptix, Blythe Aril, VisiDisc, AlphaVision, ReNovaAT, Amnio Tek-C



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Patient consideration in prevention

- Compatible ocular surface
- Wear and care compliance
 - Dumbleton, et al Cont Lens & Ant Eye 2011
- Responsible behavior and reporting – contact lenses w/o prescription
 - Land, et al J Forensic Sci 2017

Contact lens considerations in prevention

- Optimize oxygen transmission & mobility
- Surface characteristics
 - Lakkis, et al (AAO Boston 2011)
 - Silver salt infused Acuvue Advance lenses well tolerated
 - Dutta, et al Invest Ophth 2016
 - Melimine coated contact lenses reduced incidence of p. aeruginosa induced MK in rabbits

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

While clinical data supports the claims of safety and efficacy of silicone hydrogels, patient selection remains key -

Avoid continuous wear in ...

- Smokers
- History of CLARE
- Pre-existing ocular surface disease
- Young males (?)
- History of poor compliance
- Swimmers (and other water exposure)
 - Choo, et al Optom & Vis Sci 82(2):2005.

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case report - ES 21 yof

Hx: OD painful, red, photophobic, discharge x 2 days

Wears: B&L SofLens toric OU qd x 12 hr

Contact Lens Care: Variable

Systemic Hx: Mononucleosis 2 months prior

No medications: NKDA

Family Hx: Maternal keratoconus & Paternal BRVO

BUT

Current contact lenses 3 months old

Wearing EW x 1 week

Water skiing & swimming yesterday

Still wearing lenses !!

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case report – ES 21 yof

OD pupil miotic, no APD, No ipsilateral adenopathy

VA cc OD 20/30 & OS 20/30+

SLE OD - Gr 1 lid edema, gr 2 conjunctival injection, 1mm epithelial defect, NO infiltrate, gr 1 AC reaction.

Impression: Corneal abrasion OD

PLAN:

- D/C contact lenses
- Homatropine OD
- Vigamox OD q2h (Ciprofloxacin)
- F/U 48 hr or asap if sx intensify



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case report - ES 21 yof 4 Day F/U

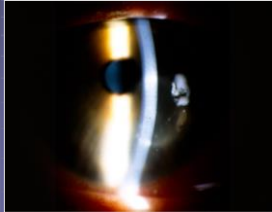
CC: 'Eye feels much better' VA cc OD 20/30 & OS 20/25+

SLE OD – Lids flat, trace conjunctival injection, 4mm ring infiltrate, no endothelial precipitates, AC d&q.

Impression: Corneal ring infiltrate OD

PLAN:

- Homatropine OD
- Pred Forte OD q2h
- Ciloxan OD q2h
- F/U 48 hr or asap if symptoms
- R/O Acanthamoeba



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case report - ES 21 yof 6 Day F/U

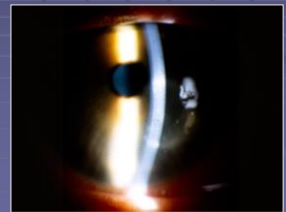
CC: 'Eye feels better, but slightly cloudy' VA cc OD 20/30

SLE OD – No change.

Impression: Corneal Ring Infiltrate

Plan:

- Telephone corneal consult
- Vancomycin OD q2h
- Pred Forte OD q2h
- Ciloxan OD q2h
- F/U 48 hr or asap if symptoms intensify



CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Case report – ES 21 yof 8 Day F/U

CC: 'Eye feels much better' VA cc OD 20/30

SLE OD – Lids flat, trace conjunctival injection, ring infiltrate fading with intact epithelium, AC d&q.

Impression: Resolving ring infiltrate OD

PLAN: Vancomycin OD qid, Pred Forte OD qid, & Ciloxan OD qid

Case report – ES 21 yof 14 Day F/U

CC: 'Eye feels 100%, drops burn' VA cc OD 20/20

SLE OD – Lids flat, conjunctiva white, cornea gr 1 diffuse spk.

Plan: Discontinue all medications. Resume CL wear in 1 week.

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

ES 21 yof – Questions for consideration

- Should we have cultured? (*hindsight always 20/20*)
- What are the differential diagnoses of a corneal ring infiltrate (*PATH*)?
- Was this infectious or was it a sterile immune response? (*yes ...?*)
- How would you treat it today? (*Ciprofloxacin & Tobramycin?*)

CONTACT LENS COMPLICATIONS MICROBIAL KERATITIS

Acanthamoeba Keratitis

▪ Species with ocular morbidity

▪ Risk factors & pathogenesis

▪ Diagnosis

▪ Treatment

▪ Prevention



CONTACT LENS COMPLICATIONS ACANTHAMOEBA KERATITIS

Protozoan

- Ubiquitous in water sources
- Trophozoite or cystic forms
- Ocular morbidity: *A. castellani*, *A. polyphaga*, & *A. hatchetti*

RISK FACTORS

- Antecedent trauma
- Sources of contamination (water, soil, sewage)
- Contact lenses (poor hygiene)

ANNUALIZED INCIDENCE

- 1-2 per 1,000,000 wearers

Seals, etal Eye 17 (893): 2003

- 1: 30,000 contact lens wearing years
- 88% Hydrogel wearers / 12% GPCL wearers
- Higher prevalence in Scotland and South Korea

CONTACT LENS COMPLICATIONS ACANTHAMOEBA KERATITIS

Joslin, etal AJO 142(2):2006.

- 40 cases of AK in Chicago between 2003 & 2005
- Diagnosis made by confocal microscopy, histology, or culture (+)
- 95% wore contact lenses
- Uneven RR between Cook and surrounding counties**
- Current AK rates > historical rates (RR 6.67)**

Joslin, etal AJO 143 (2):2007.

- Retrospective review of 39 AK cases @ UIC / 100 controls
- 92% of AK cases wore soft contact lenses
- Exclusive use of AMO Complete Moisture Plus with AK (OR 16.67)
- 38% of AK cases never used AMO Complete Moisture Plus
- Pattern of risk with ...
 - Showering with lenses
 - Reusing solutions
 - Lack of rubbing

CONTACT LENS COMPLICATIONS ACANTHAMOEBA KERATITIS

What about orthokeratology / vision shaping therapy?

Chan, etal Am J Ophth 158(6):2014

- N = 23 cases of MK in orthokeratology wearers in Hong Kong
- 3 cases AK from corneal scrapings & 5 cases AK from CLs and case
- Mean treatment 31 days. No emergency surgery. BCVA 20/28
- Early diagnosis of MK in orthokeratology patients critical**

Cope, etal Ophth 123(7):2016.

- N = 37 AK cases in GPCLs from 2 investigations (2007, 2011) in US
- 24% in orthokeratology
- Significant risk factors for AK ...
 - Orthokeratology
 - Sleeping with GPCL's
 - Storing GPCL's in tap water
 - Topping off contact lens solutions

CONTACT LENS COMPLICATIONS ACANTHAMOEBA KERATITIS

Diagnosis

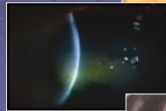
- History of contact lens wear with poor compliance
- Coexisting trauma (abrasion)
- Exposure to contamination
- Pain disproportionate to findings**
- Non-responsive to treatment (MK and HSV)

External examination

- Ipsilateral adenopathy
- Reactive ptosis

Biomicroscopy

- "Patchy" Epithelopathy
- Non-suppurative stromal keratitis
- Radial keratoneuritis**



CONTACT LENS COMPLICATIONS ACANTHAMOEBA KERATITIS

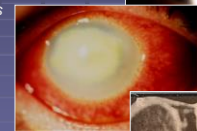
Biomicroscopy

- Ring infiltrate not an early finding**
- Pseudoguttata
- Hypopyon -> Iritis -> Scleritis

Tu, etal Ophth 115(11):2008.

- 72 cases of AK
- 66% bcva 20/25+
- 33% bcva < 20/25

- Deep stromal involvement or the presence of a ring infiltrate independently associated with a poorer visual outcome**



CONTACT LENS COMPLICATIONS ACANTHAMOEBA KERATITIS

Laboratory Testing

Corneal scrapings & biopsy

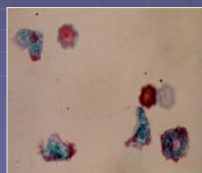
- Non-nutrient agar (e-coli overlay)
- Giemsa or trichrome stain
- Immunofluorescent studies

Confocal microscopy

Polymerase chain reaction (pcr)

Scheid Exp Parasitol 2017

AK genotype 4 escaped PCR detection!



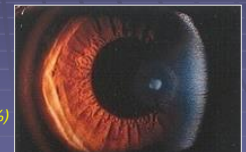
CONTACT LENS COMPLICATIONS ACANTHAMOEBA KERATITIS

Mathers, etal Arch Ophthal 118(2):2000.

- AK diagnosis with **polymerase chain reaction**
- 31 patients with suspected AK
- 77% pcr positive** (91% A. castellani)
- Majority no contact lens history

Tu, etal Cornea 27(7):2008.

- Confocal microscopy both sensitive (91%) and specific (100%) for AK**
- AK culture sensitivity 53%
- AK smears and scrapings sensitivity 83%



CONTACT LENS COMPLICATIONS ACANTHAMOEBA KERATITIS

Treatment Strategies – Do we have an optimal in-vitro test?

Lim, et al. *Clin Exp Opth* 28(2):2000.

- In vitro susceptibility of 19 strains of acanthamoeba
- **Minimum [drug] to inhibit excystation**
- Propamidine & Polyhexamethylene best activity

Wysenbeek, et al. *Cornea* 19(4):2000.

- In-vitro susceptibility of acanthamoeba trophozoites & cysts
- **Reculture technique up to 48 hours**
- Chlorhexidine only agent effective against trophozoites & cysts

CONTACT LENS COMPLICATIONS ACANTHAMOEBA KERATITIS

Contemporary Treatment Protocols

Aminoglycosides

- Neomycin

Cationic antiseptics (Biguanides)

- Chlorhexidine
- Polyhexamethylene biguanides

Aromatic Diamidines

- Propamidine isethionate

Imidazole Antifungals

- Miconazole
- Clotrimazole

CONTACT LENS COMPLICATIONS ACANTHAMOEBA KERATITIS

Contemporary clinical treatment outcomes

- Propamidine & neomycin -> 47% (Meisler, et al)
- Propamidine & PHMB -> 80% (McCulley, et al)
- Propamidine & PHMB: -> 96% (Wilhelmus, et al)
- Propamidine & chlorhexidine -> 96% (Seals, et al)

Dart, et al. *AJO* 148: 2009

Diamidines & biguanides appear to be synergistic and are the best current therapeutic approach

Lim, et al. *AJO* 2008

Neither chlorhexidine or PHMB monotherapy effective

Impavido (miltefosine)

Achieved **FDA orphan drug** status in 2016

Oral antimicrobial used to treat mucosal leishmaniasis

Antimicrobial alters membrane structure of FLA

CONTACT LENS COMPLICATIONS ACANTHAMOEBA KERATITIS

'Adjunct' treatment protocols

- Topical corticosteroids - Not During Active Infection
- Cryotherapy - Results Have Been Unsatisfactory
- Conjunctival flaps - Not During Active Infection
- Penetrating keratoplasty - Early In The Event Of Impending Perforation & Late For Visual Restoration
- Corneal **collagen cross-linking?** (Randleman ASCRS 2012)

How persistent can acanthamoeba be?

Yang, et al. *Br J Opth* 85(3):2001.

Cysts persist up to **31 months** post-treatment

Gooi, et al. *Cornea* 27(2):2008

Cysts & trophozoites isolated in cornea **52 weeks** after treatment

CONTACT LENS COMPLICATIONS ACANTHAMOEBA KERATITIS

Basic tenets of lens care

- Hand hygiene essential
- "Rub and rinse" recommended
- Always use fresh solutions nightly
- Always store solutions in a sealed fashion
- Attention to lens case hygiene is imperative
- No water exposure!



Thank you for attending!
Michael DePaolis, OD, FAO

