What is the most common symptom for an emergency visit for CL patients?

Red eyes because they don’t look so good.

Our goal today is to determine how to differentiate the bad red eye from the really bad red eye.... And make it better!

CLARE: Subjective
Contact Lens Acute Red Eye

- Rxn
  - Cornea
  - Conjunctiva

- Occurs primarily with EW

- Wakes up with:
  - Redness
  - Tearing
  - Photophobia
  - Irritation to moderate pain

CLARE: Objective Signs

- Bulbar Hyperemia
  - Moderate to severe
  - Circumferential or sectoral

- Rarely Bilateral
- No A/C reaction
- Lid edema uncommon

- Infiltration
  - Peripheral to mid-peri
  - Diffuse
  - Focal - low to moderate number

- No epithelial involvement
  - No significant staining

- None to mild VA reduction

CLARE

**ETIOLOGY**

- Inflammatory rxn
- Gram (-) endotoxins on CL surface
- Tight lens induced hypoxia

**TREATMENT**

- D/C CL Wear
- Lubricants & Cycloplege
- Steroids?
  - Severe symptoms
  - Significant infiltration
- Re-establish successful DW first
- Recurrence possible
Differential diagnosis is critical


DIFFERENTIAL DIAGNOSIS

<table>
<thead>
<tr>
<th>STERILE</th>
<th>INFECTIOUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>None-irritation-mild pain</td>
<td>Moderate to severe pain</td>
</tr>
<tr>
<td>Small</td>
<td>Large and growing</td>
</tr>
<tr>
<td>Multiple, arcuate</td>
<td>Individual, satellite</td>
</tr>
<tr>
<td>Peripheral</td>
<td>Central</td>
</tr>
<tr>
<td>No discharge, watery</td>
<td>Mucopurulent discharge</td>
</tr>
<tr>
<td>Epithelium intact-PEE</td>
<td>PEE-full defect</td>
</tr>
<tr>
<td>Flat to elevated</td>
<td>Flat-excavated-thinning</td>
</tr>
<tr>
<td>AC quiet</td>
<td>AC reaction, lid edema</td>
</tr>
</tbody>
</table>

CLPU: CONTACT LENS PERIPHERAL ULCERS

- Small round lesions with epithelial loss, anterior stromal excavation and slight surrounding infiltration
- Usually single or small in number, located near the limbus, ≤1 mm
- Stains NaFl, may have AC reaction, and limbal redness
- Patient may have FBS to moderate pain
- Often upon wakening
- 20% of CL wearers per year

ETIOLOGY OF CLPU

- Toxins from gram + bacteria
  - (staph. aureus/strep pneumonia) adhere to contact lens.
- Under hypoxia or epithelial trauma, chemical messengers are released and if in the peripheral cornea, activate the limbus to initiate an immune response

TREATMENT

- Discontinue lens wear and consider different modality (high dK, DW)
- Use of cool lubricants, topical FQ-AB, steroids*, oral AB*

ETIOLOGY OF INFILTRATIVE KERATITIS

- Etiology - multifactorial
  - FB entrapment
  - Mechanical trauma
  - Bacterial toxins
  - MPS Reaction
- Risk factor - CL wear (DW or EW)
- DDx: Viral KC, Clare, CLPU

INFILTRATIVE KERATITIS TX

- D/C CL wear temporarily
- Steroids if moderate symptoms or VA ↓
  - q.i.d X 5-7 days +/- taper
  - resolution quick vs. Viral KC
- Ocular lubricants
- Rarely scars vs. CLPU (Bull’s eye scar)
- Recurrence possible - esp. if toxic rxn
- Switch to Single Use lenses or Preservative - Free system if in DW
Why is the CL wearer at risk

**DEFENSE**
- Normal lid flora
- Epithelial Structure
- Basal Lamina
- Tears/ Glycocalyx coa
- Regeneration YOU !!!

**CL WEARERS**
- Not hypoxia
- CL divides the normal tear layer and alters the distribution
- BIOFILMS: Bacteria build up under lens & in case
- CL solutions dilute the tear components

Fleiszig SM. *The Pathogenesis of Contact Lens-Related Keratitis*. OVS, 2006; 83-12

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Why are CL wearers prone to Bacterial Keratitis

- Bacteria are attracted to the biofilm
- Proteins can build-up on lenses and cause abrasions: Mucin Balls
- U/R can cause traumatic erosions
- Hypoxia can increase inflammation
- CL solutions that are bacterial-static
- Patients are lazy and cheap
- Alternative sources

---

Microbial Keratitis in CLS

**INCIDENCE**
- 1989 Schein et al
- 4 per 10,000 DW
- 20 per 10,000 EW
- 2005 Holden et al
- 4.6 per 10,000 DW
- 19.3 per 10,000 CW
- 2006 Mathers extrapolates data to 1/100 over 30 years. Can we apply accumulated risk to CLS

**RISK FACTORS**
- Previous CL red eye
- Male, poor hygiene, $
- HSV, OSD
- Smoking (3X)
- Alternative Sources
- Conflicting results with disposable use
- Swimming
  - Daily disposable

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Risk Factors for Microbial Keratitis with Contemporary Contact Lenses

*A Case-Control Study*

J. K. G. Dart, DM, FRCOphth, 1,2 C. F. Radford, PhD, 1 D. Minassian, FRCOphth, MSc(Epidem), 2 S. Verma, MD, FRCOphth, 1 F. Stapleton, PhD 3


**Objective:** To assess the relative risks (RR) of microbial keratitis (MK) for contemporary contact lens (CL) types and wearing schedules.

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The Incidence of Contact Lens-Related Microbial Keratitis in Australia


DW-SCL 3x risk of MK or EW-SCL 5X risk of MK vs. DW-GP

CONCLUSIONS: Prospective 12 month study via surveillance. N= >35K.

New types have not reduced risk for VA loss due to MK in EW or DW lens wearers.

**RISK FACTORS:** overnight use, poor storage case hygiene, smoking, internet purchase of CLS, < 6 months wear experience, higher socioeconomic class
MATERIALS AND METHODS

- **Participants:** Cases were 367 CL wearers attending Moorfields Eye Hospital with proven or presumed MK. Controls were 1069 hospital controls, who were CL wearers with a disorder unrelated to CL wear, and 639 population-based controls who were CL wearers randomly selected from the Moorfields catchment area.
- **Hospital patients completed a self-administered questionnaire; population-based controls were interviewed by telephone.**
- **Definitions:** MK (Severe vs. Moderate), Wear
- **Testing:** Multivariate analysis was done both for all cases of MK, and for the moderate and severe MK subgroups alone.
- **Main Outcome Measures:** The RR for developing MK, and vision loss, for all lens types compared with planned replacement soft lenses (the referent).

CL COMPLIANCE

- 12 MC Q’s with a weighted scoring system
- Disinfection or lens disposal 0-20
- Storage replacement 0-4
- Storage case hygiene 0-8
- Hand-washing before handling 0-8
- **Maximum score 40**
  - O = reuse cls w/o disinfection, never emptied or air dry their case, replaced cl<annual, who washed hands only sometimes
  - DD lost 32 points if they re-used contact lenses.

RESULTS

- Compared with planned replacement soft lenses (the referent), the RR of MK was significantly increased with daily disposable (DD) CLs (RR, 1.56 [95% confidence interval (CI), 1.1–2.1]; P = 0.009) and differed between different brands of DD lens, was reduced for rigid lenses (RR, 0.16 [95% CI, 0.06–0.4]; P = 0.001), and no different for silicone hydrogel or other types of soft lens.
- Although the risk of MK was higher overall among DD lens users, the risk of vision loss was less than for planned replacement soft CL users (P = 0.05); no DD lens users lost vision to the level of 20/40.
- The RR for overnight wear, for any lens type, was 5.4 times higher (95% CI, 3.3–10.8; P = 0.001).
- Comparison of the DD soft CL types with planned replacement soft lenses (the referent), showed significant differences between brands for the risk of MK.

CONCLUSION

- **Largest MK case series to date since DD and SiHi**
- **Conclusions:** The risk of MK has not been reduced in users of DD and silicone hydrogel CLs. However, vision loss is less likely to occur in DD than in reusable soft CL users.
- Different brands of CL may be associated with significantly different risks of keratitis; understanding these differences should lead to the development of safer soft lenses. These findings suggest that lens/ocular surface interactions may be more important in the development of corneal infection than oxygen levels and CL case contamination.
- **Financial Disclosures:** The authors have no proprietary or commercial interest in any materials discussed in this article.

OTHER CONSIDERATIONS

**CONFLICTING REPORTS of SiHy**
- 30 days vs. 7 days from previous
  - Leaves us to believe that other factors are in play-tear stagnation, tear compartmentalization, reduced epithelial turnover

**DAILY DISPOSABLES!**

- Consider patient population
  - At Risk patients-
    - OSD, allergy
  - For sports, water activities, occasional use
- Handling Concerns
  - Infrequent user, poor handling, stuck lenses or unavoidable overnight
- **The Bugs**
  - Worse pathogens in the PRP cases

**Most Likely Organisms Overall**

- 51% Bacterial
  - 25% Coagulase (-) Staphylococcus (epi)
  - 23% Staphylococcus aureus
  - 14% Pseudomonas aeruginosa
  - 13% Streptococcus
- 26% Fungal
  - 40% Acremonium 15% Fusarium
Most Likely Organisms in the Contact Lens Population

- **Pseudomonas aeruginosa**: gram -
  - 50% of CL related ulcers, also post sx or trauma
  - Can penetrate an intact cornea & perforate in 24 h
- **Staphylococcus aureus** (gram + non mobile)
  - Colonizes eyes, nose axillae
- **Serratia marcesens** (gram - bacteria)
  - Develops over time and requires a break in epithelium
- **Acanthamoeba** (protozoa)
  - A minor corneal break allows it to enter from contaminated CL solutions, cases, or tap water. Ring

Indications for Culturing

- Central corneal ulcer
- Immuno-compromised patients
- Risk for perforation or non-responsive to tx
- Tertiary settings with atypical and resistant pathogens: hospital or nursing home based
- Suspicion for Fungus or Acanthamoeba
- Yield can be as low as 30% so don’t delay treatment. Study showed that it altered treatment in 6-15% of non-responsive pt

CULTURE MEDIA USED

- **BLOOD AGAR**
- **CHOCOLATE AGAR**
- **THIOGLYCOLATE BROTH**
- **SABOURADE**
- **NON-NUTRIENT AGAR** with E.COLI over-lay
- **GRAM-STAIN SLIDES**
- **GIEMSA-STAIN SLIDES**
- **VIRAL MEDIA**
- Most Bacteria
- Haemophilus, N.gonorhe
- Aerobic,anaerobic bacteria
- Fungus
- Acanthamoeba
- Bacteria or fungus
- Bacteria,Fungus, Acanth.
- HSV

Culture Technique

- Use lid retractor to avoid contamination
- Proparacaine is least bactericidal
- Kimura spatula, blade or Ca+ alginate swabs
- Culture deep and various areas of the lesion
  - Strep.pneumonia found at leading edge
  - Moraxella found at base
- Culture medicine bottles, CL case, makeup
- De-bulking effect is beneficial

Mini-tip Culturette vs. Kimura spatula


Sensitivity = 83.3% - Specificity = 100%

PCR IDs PA

- Polymerase Chain Reaction used to identify PA
- Analysis of short DNA sequence
- Smaller sample needed but can lead to false + (commensals)
- Faster results (hours vs. days)
- Less available $$$
- High concordance rate vs. cultures 66% and would be higher however previous treatment will eradicate bugs in cultures, but not PCR bugs
- Accurate
  - 76% yield for PA, 96% FK
Staph Marginal Disease Signs
- Small (<2mm) solitary gray-white lesions anterior stroma
- Often bilateral
- Clear interval between the limbus and infiltrate
- Minimal (if epithelial defect present) or no staining
- Stromal edema surrounding the infiltrate
- Sectoral conjunctival injection
- Minimal to no AC reaction
- Blepharitis, but not as bad as you think
- Usually between 4-8 o’clock

Staph Marginal DX Etiology
- Delayed hypersensitivity
- Sterile marginal infiltrates develop as a result of a hypersensitivity reaction of the host to the components of the Staphylococcus aureus cell wall.
- It is a noninfectious reaction of the host’s antibodies to staph antigens and exotoxins

Staph Marginal DX Treatment
- Lid Hygiene
- Warm compress
- Erythromycin ung
- Blephamide ung
- AzaSite rub
- Topical Steroid
  - PF, Lotemax qid
- Steroid/AB combo
  - Tobradex, Zylet qid
- Oral AB
  - Doxycycline
  - 100 mg po bid x 2wk-1m
  - 100 mg po qd x 1 month
  - 50 mg po maintenance
  - ALODOX 20mg KIT

AzaSite
- 1% Azithromycin Ophthalmic solution
- Macrolide, Cat B
- Cidal/static
- Gram +/Some gram-
- Indication: bacterial conjunctivitis >age 1
- 1 drop BID x 2 days
- 1 drop QD x 5 days

Peripheral Marginal Ulcer
- **Microbial?** –
  - CTX’s, GM stain, Geimsa stain to evaluate bacterial, GC, fungal, acanthamoeba
- **Herpetic?** –
  - Herpetic Disciform Keratitis – HSV and VZV are clinically indistinguishable
  - Herpetic Necrotizing Keratitis
- **Systemic Immune-Mediated Diseases** –
  - Mooren Ulcer
  - Terrien Marginal Degeneration
  - RA
  - SLE
  - Wegener Granulomatosis
  - Polyarteritis Nodosa
  - Bechet Syndrome
  - Etc………………
  - RF, ANA, P-anca, C-anca, CBC, ESR

OFF LABEL USE
- Lid Margin Disease
- Sterile Infiltrate
- Trachoma
- Post-Injury
- In vitro studies show that MMPS suppressed 33.48% corneal epi/endothelium
- Oral form long thought to have anti-inflammatory effects in RTIs
- Can alter MG secretions*
**Pseudomonas Keratitis**

- Consistently Associated with CLS
- Huge Genome dedicated to survival and communicating to enhance virulence
- Invasive (present with better VA but worse by 3 months) vs. Cytotoxic (less response to steroids, kill w/o invading)
- Rapidly progressive. Ground glass edema
- Thick adherent yellow-greenish mucous
- Destructive enzymes: Proteases, Lipases, Exotoxins
- Secretes protective glycocalyx but also sets up its own immune response that it can evade.
- PA found on 1.3-25% of health workers hands but can be reduced 2-3 logs via 30 sec. hand wash: non-med. soap. via mechanical rub

**Antibiotic Therapy for Infectious Bacterial Keratitis**

4<sup>th</sup> Generation Fluoroquinolones

- Commonly used for mild to moderate peripheral ulcers or as adjunct therapy for more severe
- Loading dose while waiting for meds: q5 for 15 minutes, Q1H, QID
- If using 4<sup>th</sup> FQ only, there is limited gram + coverage against MRSA
  - Add Polymyxin or Bacitracin

**Fortified Antibiotics**

- Fortified Tobramycin (15 mg/ml) or Gentamicin (15 mg/ml) AND
- +Fortified Cefazolin 50 mg/ml or Vancomycin 25 mg/ml

Alternate every 30 minutes for first 24 hours

**BACTERIAL KERATITIS TX**

- Loading Dose q 30 minutes -2 h to achieve maximal concentration for first 24-72 hours
- Follow-up in 24 hour
- Taper at 72 h-5 days depending on severity, location, and compliance
- Maintain a lethal dose of QID for 5-7 days after apparent resolution to avoid rebound super-infection or resistance

**CULTURE CONFIRMATION:**

IF PA: Continue Fortified Tobrex + Add Ciloxan. d/c Vancomycin
IF Staph. Ep: FQ + Bacitracin ung
IF MRSA: Continue Vancomycin, add Polymyxin

**ANTIBIOTIC THERAPY**

- ALL FLUOROQUINOLONES* (gati, moxi, levo)
  - Only 20% effective against MRSA
  - 80% effective against MSSA
  - 100% effective against Strep. Pneum., H. influenza
- TRIMETHOPRIM
  - 95% effective against MRSA, 100% MSSA
  - POLYTRIM = Trimethoprim plus Polymyxin B (gram -)
  - Broad static, H. Flu, Strep., Peds*
  - Systemically = Bactrim
- AMINOGlicosides
  - Effective against Gram -, strep
  - Tobramycin, Gentamicin, Neomycin (NOT FOR PA)
- **USE FREQUENTLY!!!** Q2 x 4 then QOD, switch

**IQUIX®**

Levofoxacin 1.5%, Vistakon

3x concentration of Quixin

Penetrates human corneal tissue and aqueous humor to concentrations that exceed MIC90 values of common ocular pathogens

FDA ulcer indications Q 30 min-2h x 4 days, q 1-4 hour

Broad coverage of gram-negative and gram-positive pathogens, including *P. aeruginosa*, *S. marcescens*, *S. aureus*, *S. epidermidis*, and *S. pneumoniae*

**BESIVANCE™**

Besifloxacin .6% Supension, Bausch & Lomb

Chloro-fluoroquinolone

Broad, Cidal, potant, long dwell-time, easy TID dosing

FDA approved for bacterial conjunctivitis

**ZYMAXID™**
(gatifloxacin ophthalmic solution) 0.5%
ophthalmic solution is a topical fluoroquinolone
anti-infective indicated for treating bacterial
conjunctivitis
Allergan (Zymar is .3%)
Haemophilus influenzae, Staphylococcus aureus,
Staphylococcus epidermidis, Streptococcus mitis
Streptococcus oralis*, Streptococcus pneumoniae

**MOXEZA™**
moxifloxacin HCL ophthalmic solution) 0.5%
ophthalmic solution is a topical fluoroquinolone
with 8-methoxy FQ and a diazabicyclononyl ring at C7
xanthan gum vehicle which prolongs contact time on the
ocular surface and enhances tissue penetration
anti-infective indicated for treating bacterial
conjunctivitis
BID dosing as young as 4 months
Alcon
Haemophilus influenzae, Staphylococcus aureus,
Staphylococcus epidermidis, Streptococcus mitis
Streptococcus oralis*, Streptococcus pneumoniae,
E.coli* chlamyda*

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**Community Opinions in the Management of Corneal Ulcers and Ophthalmic Antibiotics: A Survey of 4 States**

| 629 questionnaires (10%) returned from ophthalmologists in IL, FL, CA, and MA |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| Gram Stains:                | 42% Eye-MD                 | 75% K-pro                   |
| Cultures:                   | 73% Eye-MD                 | 94% K-pro                   |
| Initiate FQ:                | 89% Eye-MD                 | 76% K-pro                   |
| Fortified AB:               | 12% Eye-MD                 | 41% K-pro                   |
| ↑ Superior?:               | 18% Eye-MD                 | 33% K-pro                   |
| New FQ                      | 65% Eye-MD                 | 58% K-pro                   |

**THE QUESTION OF STEROIDS**

- Inhibits phagocytosis
- Decreases leukocytes
- Interferes with collagen dynamics
- Perforation
- Endophthalmitis
- Promotes HSV, AK or fungal growth
- Wilhelmsen, Ophth.2002 meta-analysis of 4 studies
  - Inconclusive
- Srinivasan Pilot study
  - Aravind Hospital, India
  - N= 40 pts. Vigamox/PF
  - 3 weeks, 2 lines better
  - 3 months, 1 line better

---

**Steroids for Corneal Ulcers Trial: SCUT**
Srinivasan M, et al

**OBJECTIVE**
To determine whether there is a benefit in clinical outcomes with the use of topical corticosteroids as adjunctive therapy in the treatment of bacterial corneal ulcers.

**METHOD**
Randomized, placebo-controlled, double-masked, multicenter.
All culture positive MK
All received moxifloxacin
Additional drop was placebo or prednisolone sodium phosphate 1%

**RESULTS:**
Screen 1769 N= 500
No significant difference was observed in the 3-month BSCVA,
infiltrate/scar size, time to re-epithelialization or corneal perforation

**CONCLUSION**
We found no overall difference in 3-month BSCVA and no safety concerns with adjunctive corticosteroid therapy for bacterial corneal ulcers.
Treatment for Corneal Melting

- **Doxycycline**
  - 100 mg BID po or 50 mg QID po
  - Anticollagenolytic activity by inhibiting MMP and may suppress connective tissue breakdown.

- **Vitamin C** 1-2 g QD po
  - High dose Ascorbic acid
  - A co-factor in collagen formation and tissue repair involved in oxidative reduction & other metabolic rxn
  - Overdose causes DVT
  - Caution for gout, renal calculi, anti-coagulant tx
  - Sodium Citrate 10% gtt

Fungal Keratitis

- Most commonly associated with trauma
- Approx. 1500 cases a year in the US
- **Organisms**
  - Fusarium & Aspergillus (filamentous - hyphae)
  - Candida (yeast - unicellular)
- Can start 48hrs post-trauma
- Feathery stromal infiltrates with dry, gray epithelial surfaces - satellite lesions, ring infiltrates (filamentous fungi)
- Round focal infiltrates with epithelial defects (yeasts)

TREATMENT for Fungal MK

**Natamycin 5%**
- 50 mg/ml q 1-2 H
- Fusarium, Aspergillus

**Voriconazole**
- IV can be made topically
- Fusarium indications

**Concomitant AB TX**

**Amphotericin B**
- Not commercial, IV, Candida

**Fluconazole**
- po, good ocular penetration, may not be effective for filamentous

**Miconazole**
- Subconj injections

Epidemiological Characteristics of a Chicago-area Acanthamoeba Keratitis Outbreak

- Review of AK from June, 2003- November 2005 and compared it to the historical reference period of June 2000-November 2003
- Cases were confirmed via confocal microscopy, histology, cultures, definitive clinical presentation with response to standard AK treatment.
- Referral source due to confocal microscopy
- Results showed 40 confirmed cases vs. 7
- Represents an increased relative risk of 7X
- 38 CLW/ 35 SCL, average age = 30, M=F
- Disproportionate geographic distribution

Why was there a disproportionate increase in cases further from the purification source?

- EPA Stage I Disinfectants/D-By-Products Rule of 1998 that was implemented in 2002-04
- Required water treatment systems to reduce the residual amounts of the disinfectants in the trihalomethane and chlorine family.
- Linked to reproductive problems and several forms of cancer
- Rules should reduce exposure of chemicals to 140 million people
- Lower levels of residual disinfectants allow bacterial/algae biofilms to build-up, especially further from the source
- EPA does not monitor or regulate the amount of Ac in the water

Acanthamoeba Keratitis

- Extreme pain> signs to FBS
- Initially epithelial stippling, microcystic edema, "dendritic"
- More edematous or necrotic along the nerves (keratoneuritis)
- Decreased corneal sensitivity
- Ring infiltrate typical 4-8 weeks
- Difficult to treat & worsens w/ delay
- Contact lens related (92% in recent study) although changing.
- Joslin, et all study
Acanthamoeba TX

Chlorhexidine (.02-.04%)
Cationic antiseptic agents
that disrupt cell
membrane function
Polyhexamethylene
biguanide = PHMB
Propamidine isethionate
.1% Brolene
Aromatic diamidines that
directly affect the
amoeba’s nucleic acids
and synergistic to above

- Neomycin
- Clotrimazole, Miconazole
- Steroids can convert
trophozites to cysts and
interfere with macrophage activity
- Super-infection
- Debridement

Does Acanthamoeba like the cornea?

- Holden, 1999: The ability of AK to bind to
  normal epithelial cells is the same for non-CLW
  and non-symptomatic CLW.
- AK bind to mannose-glycoproteins which are
  present in all epithelial cells however this
  increases when there is an abrasion.
  *It probably likes the sick ones*

Sharma, S. Holden, B et al. Adherence of Acanthamoeba to human corneal epithelial cells
recovered from normal non-contact lens wearers and asymptomatic contact lens wearers.
BCLA, 1999; 22-4

Achromobacter xylosoxidans

- Motile, aerobic, gram-negative, non-fermentative straight rod with a peritrichous flagella*
- DDX: PA
- Urine, blood, ears, respiratory tract, and spinal fluid
- Opportunistic pathogen to compromised tissue
- Water pathogen found in pools, chlorhexidine
- Reports: post-PKP, EKC, steroid use, NVG
- Therapeutic BCL
- Resistant to many AB
- Sensitive to Polytrim

SIGNIFICANCE OF CASE

- There are only 15 reports of ocular infection from Achromobacter xylosoxidans and this is
  the first to be confirmed with PCR technique
- VITEK 2 rapid panel assays which can ddx from PA and determine specificities
- Recent study showed (excluding PA) a high concordance rate of gram negative rods
  between +CL cultures and – corneal scrapings

Cases are a Source of Contamination

- Clean your case daily with solution and digital rub
- Air dry the case
- Replace the case every 1-3 months
- Micro-waving or boiling the case will kill the cysts.

Why has there been solution Failure?

- American Type Culture Collections (ATCC test for PA, SA, Serratia, Candida, Fusarium) isoaltes are limited and
  needs to be updated since the strains have become overused. Solutions not tested with:
- Lens: Biocidal activity reduced with uptake
- Stiffer materials may block normal response
- Biofilms: contamination, increased virulence, reduced bioavailability of biocide
- Poor Compliance: topping off, 4x risk when hands not washed, test under no rub conditions
- Formulation components contain cellulose derivatives that are nutrition source for pathogens
Less common causes of “MK”
- Crack Cocaine
- Proparacaine
- Vitamin Deficiency
- Foreign body
- Exposure
- Viral

Medical Management Has Improved
Significant improvement in percentage of eyes achieving microbiological cure with medical therapy alone (bacterial keratitis)
- 76.0% in 1995 vs. 92.2% in 2005

Or in combination with surgical intervention
- 92.4% in 1995 vs. 100.0% in 2005

Medical Management Has Improved
Significant improvement in percentage of eyes achieving microbiological cure with medical therapy alone (bacterial keratitis)
- 76.0% in 1995 vs. 92.2% in 2005

Outcomes of Therapeutic PKP
Anatomical cure rate refers to complete eradication of the microbial load.
70.8% to 100% for bacterial. 86-100% for fungal

One study compared outcomes of patients who underwent keratoplasty in the acute stage with patients who were first managed medically followed by a secondary k-plasty at later date.
- Comparable graft clarity rate of 70% with the acute keratoplasty & 72% with secondary keratoplasty group.

Tectonic graft: When medical management fails us
- Use of a corneal graft for terminating or improving active infectious keratitis.
- Primary aim is to re-establish the integrity of the globe and to eliminate the infectious process
- Visual rehabilitation is a secondary outcome

Therapeutic PKP
- For fungal indication, the size of graft also correlates with postoperative outcome
- Smaller sized grafts have higher success rates
- 9mm or less are more likely to have successful anatomical and functional outcomes.
- Overall recurrence rate of 6 to 7%
- Higher rate of recurrence in cases with preoperative hypopyon (10.9%), corneal perforation (12.0%), corneal infection expanding to limbus (20.6%)
## CORNEAL CROSS LINKING TO TREAT RECALCITRANT MK

- Direct Kill of micro-organism
- Enhanced collagen resistance to digestive enzymes
- UV-A can inhibit growth of bacteria and fungi
- Free-radicals interfere with cell wall synthesis and repair of bugs
- On-going studies

**Yaron S. Rabinowitz, Suy Anne Martins, MD, PhD**

## Corneal Ulcers Associated with Crack Cocaine Abuse

- First described in literature by McHenry et al in 1989
- In 1993, Sachs et al proposed mechanisms of injury
  - Direct toxic effect of smoke to cornea
  - Repeat exposure → decreased sensation and decreased blink reflex
  - Corneal nerve damage
  - Alkali burn
  - Mechanical trauma from eye rubbing

## Atypical pathogens

- Corneal cultures
  - Capnocytophaga species
  - Brevibacterium casei
  - Streptococcus sanguis
  - Beta-hemolytic streptococci
  - Streptococcus mitis

## Treatment Recommendations

- Aggressive treatment for patients with drug-related corneal ulcers
- Low threshold for hospital admission
- Routine cultures and fortified antibiotics; use 4th generation FQs when sensitivity available
- Assess corneal sensitivity (Neurotrophic component)
- For patients have persistent epi defect
  - Doxycycline to aid in stromal healing
  - Consider lateral tarsorrhaphy
- Substance abuse counseling

## HERPES: A bad virus with many forms

- DNA virus, Latent in sensory ganglia, multiple
- Herpes Simplex HSV and healthy cornea have similar protein coat UL6.
- HSV also has CD8….SCARRING… NEED STEROIDS
- HZ= Zoster = Varicella= Chicken pox=Shingles
  - Can spread by inhalation, ventilation system!
  - Caution with children, immunocompromised,pg
  - Activation: hypoesthesia, tingling, malaise, pain and then lesions 2-3 days later
  - Follows single nerve Branch CN V-1 (50-70%= HZO)
  - Zostavax- reduces episodes 50%, neuralgia by 67%

## DIFFERENTIAL DIAGNOSIS

**HSV**

- Clear vesicles progress to red that later crust
- SPK-Geographic-or
- Dendrites that stain on edges with RB and collect NAFL in center. They have true bulbs and stain.
- Recurrence/younger

**HZO**

- Rash follows dermatome/midline
- Immuno-compromised
- Dendrites look stuck and bulbs don’t stain
- Recurrence/older
**EVOLUTION OF HSV DENDRITE**

- Discreet Punctate epithelial lesions coalesce within days to form a branching lesion with swollen opaque edges (RB). The epithelial cells in the center eventually get infected with virus and get desquamated (FL). Propensity for center.
  - Border stains with Rose Bengal Center stains with Fluorescein
  - HZO: no bulbs, all heap-up, +RB

**TREATMENT: SKIN INVOLVEMENT**

- **HSV**
  - Clear vesicles progress to red that later crust
  - Warm Compress
  - Keep it clean
  - Erythromycin or Bacitracin ung BID
  - Topical Acyclovir ung not shown to be effective
  - Antiviral drops added if at eyelid margin

- **HZO**
  - Rash follows dermatome/midline
  - Warm Compress
  - Keep it clean
  - Erythromycin or Bacitracin ung BID
  - Acyclovir 800 mg po 5x
  - Valacyclovir 1000 mg TID
  - Within 72 hours
  - Consider Steroid if >60 to reduce post-pain

**TREATMENT for OCULAR DISEASE**

- **HSV**
  - Artificial tears
  - Trifluridine (Viroptic 1%) 9 x/day epithelial
  - Toxic (kills unaffected)
  - Vira-A (Vidarabine 1% ung) 5x for conjunctiva NA
  - Zirgan (.15% ganciclovir) 5 times per day
  - Decrease after therapeutic level is achieved or toxicity
  - Add cycloplegic for AC
  - Steroid for stroma or uveitic involvement: Pred Forte QID

- **HZO**
  - Cool artificial tears
  - No topical anti-virals **
  - Treat po to get to root of disease
  - Steroid and cycloplegic if stromal disease or uveitis
  - ORALS??? For ocular involvement ….

**ZIRGAN™**

Ganciclovir .15% ophthalmic gel
Sirion Therapeutics

Systemic antiviral approved in 1989 (CMV)
An inert compound that is activated via phosphorylation by viral enzymes and only attacks virally-infected cells, so less toxic.
5 g tube with indications for acute Herpetic keratitis
Use 5x/daily for 4-5 days then TID for 3-4 more days
In Europe x 10 years

**ORAL ANTI-VIRALS for EYE**

- Relies on achieving supra-therapeutic levels in tear film
- Can only attack LIVE virus
- SE: NVD, dizziness, asthenia, headache rare, $$
- HSV primary episode
- Improved outcome for HSV-Iritis
  - HEDS 1 if oral added, when added to topical anti-viral & steroid
  - Prophylactic dosage reduced recurrence
  - HEDS 2 41% reduction of all forms after 1 year
  - HEDS 2 50% reduction of severe form
  - HEDS 2 shows no Δ in resolution* or conversion to stromal or iritis for any corneal involvement between topical or po

**VALACYCLOVIR**

- A virustatic antiviral that is converted to acyclovir triphosphate in the pt intestine/liver.
- Pro-drug- achieves higher therapeutic level w/ less drug
- Then becomes part of the viral DNA chain and interferes with the DNA synthesis and replication of HSV/HZO without interfering with human DNA

**INDICATIONS**

- Herpes Zoster HZO
- Shingles/ Skin/ Ophthalmic
- Herpes Simplex HSV
- Oral/Genital/Ocular
- Prophylaxis
- Bell’s Palsy
VALACYCLOVIR

- CONTRAINDICATIONS
  - Category B
  - Adjust dosage for renal impairment
    - Max 1000 mg/day
  - DRUG INTERACTIONS
    - Cimetidine and probenecid may increase drug conc.
    - Cimetidine is an antacid anti-ulcer H2 blocker and has been shown to decrease pain of skin lesion in HZO (400 mg po bid)

DOSAGE
- Cat B-C
- HZO 1000mg TID
  - Within 72 hrs
  - 7(67yo) -10 days (> 67)
  - HSV 500-1000*mg B-TID*
  - Prevent 500mg QD-BID
  - Renal DX: Max 1000 mg/day

ALTERNATIVES
- Zovirax (Acyclovir)
  - HSV 400 mg 5x/day
  - HZO 800 mg 5x/day
  - 7-10 days
  - Prophylaxis 400 mg bid
- Peds IV acyclovir
- Famvir 250 mg TID

HEDS/Archives/ NEJM

- 26% have recurrences, 94% don’t recall primary infection, triggers are questionable
- Some RX orals for primary infection
- Topical steroids aid in stromal only/never epithelial
- Topical antivirals always used for epithelial HSV/HZ?
- Orals don’t improve/speed resolution of corneal dx
- Orals probably aid in HSV iridocyclitis acute
- Orals reduce recurrence of ALL forms HSV by 50%
- Orals aid in skin lesions for HZO

Thank you

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