On behalf of Vision Expo, we sincerely thank you for being with us this year.

Vision Expo Has Gone Green!

We have eliminated all paper session evaluation forms. Please be sure to complete your electronic session evaluations online when you login to request your CE Letter for each course you attended! Your feedback is important to us as our Education Planning Committee considers content and speakers for future meetings to provide you with the best education possible.

VISION EXPO

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Financial Disclosure – Justin Schweitzer, OD, FAAO

- Aerie – C/L
- Alcon – C/L
- Allergan – C/L
- Bausch + Lomb – C/L
- Ocular Therapeutix - C
- EyePoint – C
- Sight Sciences – C/L
- Dompe – C
- Zeiss – C/L
- Visus - C
- Science Based Health – C
- Kala – C
- RVL - C
- Sun – C/L
- Equinox - I
- Reichert - C
- J&J – C/L
- Glaukos – C/L
- Horizon – C
- Quidel – C
- MediPrint – C
- LKC – C/L
- Avellino – C
- Novartis – C
- Iveric bio – C
- Occuphire - C

2

Case Challenges of the Cornea

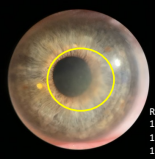
Justin Schweitzer, OD, FAAO
Vance Thompson Vision
Sioux Falls, South Dakota
Optometric Externship Director

3

Case

JS 44-year-old female presents with blurry VA, photophobia, and unspecified corneal edema OS Treated 2 months ago with some "big pills"

Dcc: 20/15 -2 OD; 20/600 OS
IOP: 12 OD; 14 OS
Pachymetry: OD 542; OS 684



Round area of 2+ edema
1+-2+Guttata
1 + injection
1+ cell in AC

KP's present

4

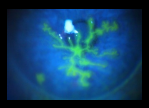
My Treatment

Valacyclovir 500 mg 3 x a day
Topical corticosteroid qid

1 week later, edema was resolved, some mild scarring present, with some guttate and VA improved to 20/40.

7

HSV Keratitis Features



Unilateral presentation → always suspicious for HSV

Iritis with high IOP → always suspicious for HSV

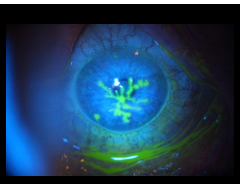
After 2nd episode , 70-80% had another recurrence within 10 years

Bilateral involvement or prolonged HSV suggests comorbid disease (immunodeficiency or immunosuppression)

8

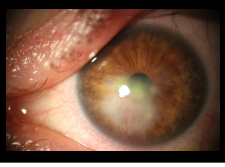
Epithelial

Dendritic epithelial ulcer
Geographic epithelial ulcer
Marginal epithelial ulcer



Stromal

Non-necrotizing keratitis
Interstitial keratitis
Immune stromal keratitis
Necrotizing keratitis



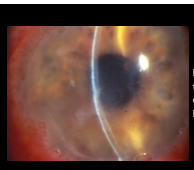
9

Endothelitis

Disciform keratitis

Area of corneal edema

No epi involvment pseudo-guttae and Descemet's folds



http://webeye.ophth.uiowa.edu/eyeforum/cases/160-hsv.htm

Neurotrophic

Ulcerated

Results from altered corneal innervation and decreased tear production

10

HSV Keratitis Treatment

Acyclovir (Zovirax)

400 mg 5 x daily for 7-10 days

Valacyclovir (Valtrex)

500 mg 3 x daily for 7-10 days

Famciclovir (Famvir)

250 mg 3 x daily for 7-10 days

Trifluridine ophthalmic solution 1% (Viroptic)

1 drop 9 x a day for 7 days; can decrease to 5 x a day after 7 days if ulcer not healed.

Ganciclovir ophthalmic gel 0.15% (Zirgan)

1 drop 5 x a day until ulcer heals followed by 1 drop 3 x a day for 7 days.

Acyclovir ophthalmic ointment (Avaclyr)

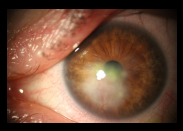
1 cm ribbon in lower cul-de-sac 5 x per day until healed then 3 times per day for 7 days.

11

HSV Keratitis Prophylaxis

Why?

1. Multiple recurrences of HSV keratitis
2. Recurrent inflammation with scar/vascularization
3. Post-keratoplasty performed for HSV reasons
4. Postoperatively in patients with history of HSV undergoing any type of ocular surgery
5. In patients with a history of ocular HSV during immunosuppressive treatment



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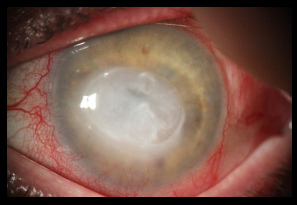
HSV Keratitis Prophylaxis



Acyclovir (Zovirax)

400 mg 2 x daily for 1 year

Valacyclovir (Valtrex)

500 mg 1 x daily for 1 year

Famciclovir (Famvir)

250 mg 2 x daily for 1 year

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Treatment Principles

Treat epithelial disease 1st and stromal 2nd

When using steroids use either therapeutic or prophylactic dose of orals to prevent reoccurrence

In stromal cases that are controlled taper steroid gradually. Patient may never be able to get off in stromal disease and prophylactic orals may be required indefinitely.

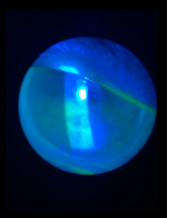
14

82 yr, male, Caucasian OU

CC: Vision has been declined, and I am not sure why? Eye feels fine I just don't see well at all. Seeking another opinion.

VAcc: 20/250 OD; 20/50 OS
IOP: 17 mmHG OU

PMHx: Diabetes (poorly controlled)
PEHx: Cataract Extraction OU, Blepharoplasty OU 2013
Mild POAG OU 2000 – treated with PGA
Current Treatment: Cyclosporine 0.05% bid OU, PF AT's
Fundus Exam: WNL OU
OCT: Normal, with no macular edema present



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Corneal Assessment

- Assessment of corneal sensation is essential to diagnose NK
- Methods of assessing corneal sensation:
  - **Clinical: "Wisp" of cotton, dental floss**
    - **Performed easily in the clinic**
    - **Patient's reaction is noted and compared between each eye**
  - Cochet-Bonnet esthesiometer
    - Different lengths (60 to 5 mm) of nylon filament applied to the cornea
    - Longer the length, the higher (normal) the sensitivity
  - Belmonte noncontact gas esthesiometer
    - Cornea stimulated with calibrated air jet; blink response is observed
    - Not widely available

Dua HS, et al. *Prog Retin Eye Res.* 2018;66:107-131.

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Patient Characteristics to Prompt Corneal Sensitivity Testing

Strongly Recommended	May Be Considered
• Persistent epithelial defect that does not improve within 14 days • Painless, newly observed epithelial defect of unknown etiology • History of herpetic eye disease • History of procedures that might have damaged the trigeminal nerve or conditions that might have involved the trigeminal nerve • Pain in the affected eye and multiple, concurrent risk factors, such as persistent poorly controlled diabetes and either reduced blink or a history of corneal procedures	• Acquired limbal stem cell deficiency • Newly observed epithelial staining and persistent poorly controlled diabetes • Persistent poorly controlled diabetes and vision changes not ascribed to diabetic retinopathy or cataract (even in the absence of corneal findings)

Dana R, et al. *BMC Ophthalmol.* 2021;21(1):327.

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Patient Information	• 82 yr, male, Caucasian, OU
History of Presenting Illness	• Cataract Extraction OU 2013 • Blepharoplasty OU 2013 • Chronic DES • Mild POAG OU 2000 – being treated with a topical prostaglandin analogue
Relevant Medical History	• Diabetes (poorly controlled)
Corneal Sensitivity	• Complete anesthesia • Sensitivity testing performed with cotton swab
Diagnosis	• Stage 1 NK – Central superficial punctate keratitis
Previous Treatments for NK	• Cyclosporine 0.05% bid OU • Preservative free artificial tears
Management Plan	

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Treatment Considerations

Topicals	In-office Procedures	Surgical Intervention
Artificial Tears (PF)	Contact Lenses	Tarsorrhaphy
Corticosteroids	Punctal Occlusion	Conjunctival flap
Autologous serum	Non-surgical eyelid closure	Corneal transplant
Antibiotics	Amniotic Membrane	Direct neurotization
Cenegermin-bkbj	Tissue adhesives	Sutured AMT

20

Patient Information	• 82 yr, male, Caucasian, OU
History of Presenting Illness	• Cataract Extraction OU 2013 • Blepharoplasty OU 2013 • Chronic DES • Mild POAG OU 2000 – being treated with a topical prostaglandin analogue
Relevant Medical History	• Diabetes (poorly controlled)
Corneal Sensitivity	• Complete anesthesia • Sensitivity testing performed with cotton swab
Diagnosis	• Stage 1 NK – Central superficial punctate keratitis
Previous Treatments for NK	• Cyclosporine 0.05% bid OU • Preservative free artificial tears
Management Plan	• Oxervate 20mcg/ml, 1 drop 6 times daily, for 8 weeks • Concomitant Medications: • Preservative free artificial tears

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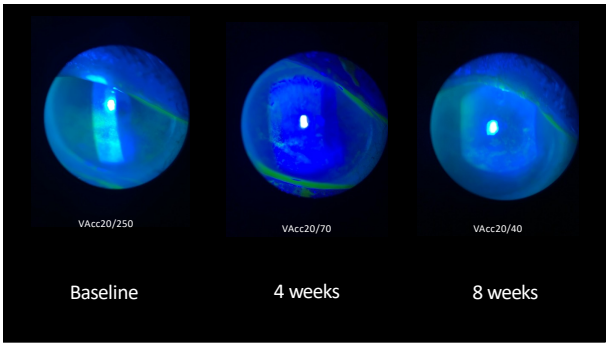

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Neurotrophic Keratitis: Etiology

1. Infectious: HSV, VZV, leprosy
2. CN V palsy
   - Surgery for trigeminal neuralgia, neoplasia (acoustic neuroma), aneurysm, facial trauma, congenital, familial dysautonomia (Riley-Day syndrome), Goldenhar-Gorlin syndrome, Möbius syndrome, familial corneal hypesthesia
- Topical medications: anesthetic abuse
- Iatrogenic: LASIK/PRK, corneal incisions (RK, AK), contact lens wear, scleral bands, vitrectomy and photocoagulation to treat diabetic retinopathy[1,2]
- Chemical and physical burns
- Systemic: DM, multiple sclerosis, Vit A deficiency
- Increasing age, chronic DED[3]

1. Banerjee P.J. JAMA ophthalmology 2014;132:750-2.
2.Tinley CG. Eye 2009;23:1819-23
3. Ocul Surf. 2007 Apr;5(2):75-92.

23

Neurotrophic Keratitis: Classification

Mackie classification

- Stage I is characterized by hyperplasia and/or irregularity of the epithelium, evolving to punctate keratopathy, corneal edema, neovascularization, stromal scarring.
- Stage II is defined by a recurrent or persistent epithelial defects or a PED without stromal thinning.
- Stage III: stromal involvement leads to corneal ulcer, melting and perforation

Mackie IA. Neuroparalytic keratitis. Current Ocular Therapy. Philadelphia, PA: WB Saunders; 1995:452-4.

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Amniotic Membranes
Amniotic Membrane Extract Eye Drop (AMEED)

Cryopreserved Membranes

Dry Membranes

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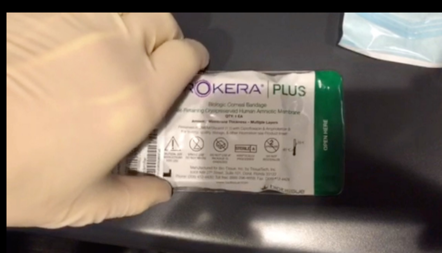

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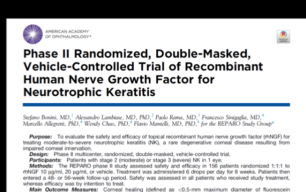
cenegermin-bkbj 20 mcg/ml was approved by FDA in August 2018



AMERICAN ACADEMY OF OPHTHALMOLOGY®

Phase II Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis

*Stefano Bonini, MD,[1] Alessandro Lambiase, MD, PhD,[2] Paolo Rama, MD,[3] Francesco Sinigaglia, MD,[4] Marcello Allegretti, PhD,[4] Wendy Chao, PhD,[4] Flavio Mantelli, MD, PhD,[4] for the REPARO Study Group**

Purpose: To evaluate the safety and efficacy of topical recombinant human nerve growth factor (rhNGF) for treating moderate-to-severe neurotrophic keratitis (NK), a rare degenerative corneal disease resulting from impaired corneal innervation.

Design: Phase II multicenter, randomized, double-masked, vehicle-controlled trial.

Participants: Patients with stage 2 (moderate) or stage 3 (severe) NK in 1 eye.

Methods: The REPARO phase II study assessed safety and efficacy in 156 patients randomized 1:1:1 to rhNGF 10 µg/ml, 20 µg/ml, or vehicle. Treatment was administered 6 drops per day for 8 weeks. Patients then entered a 48- or 56-week follow-up period. Safety was assessed in all patients who received study treatment, whereas efficacy was by intention to treat.

Main Outcome Measures: Corneal healing (defined as <0.5-mm maximum diameter of fluorescein staining in the lesion area) was assessed by masked central readers at week 4 (primary efficacy end point) and

- Approved for the treatment of neurotrophic keratitis in adults and children age 2 and older
- Available for ordering since January 2019
- Developed by Dompé pharmaceuticals, available through specialty pharmacy

Bonini S, Lambiase A, Rama P *et al.* Phase II Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis. *Ophthalmology* 2018;125:1332-1343.

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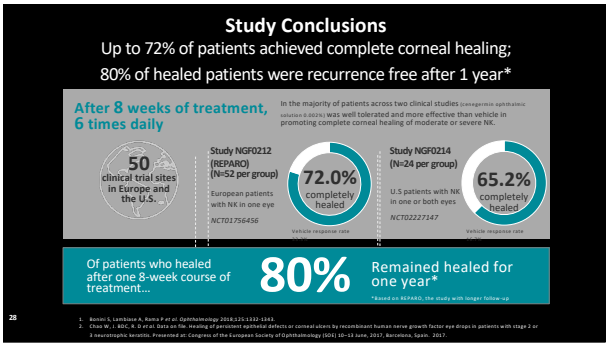

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29-year-old WF with complaints of fluctuating vision, irritated eyes, and some redness. She owns a flower business, but states this has never been a problem in the past. I am tired of wearing my contact lenses and is interested in refractive surgery.

PMHx: Unremarkable
POHx: Contact Lenses x 14 years
Systemic Meds: None
Topical Meds: AT's off and on
Allergies: NKDA
FMHx: None
Social Hx: Nothing to report

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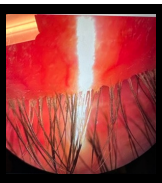
SPEED: 6/28
BCVA: 20/15 OD 20/15 OS
MRX: -3.50 OU
IOP: 12 OD 12 OS
MMP-9 Testing: Positive OU
Osmolarity: 300 OD. 322 OS

SLEx:
Lids/Lashes: See photo's; Minimal meibum secretions noted
Conjunctiva/Sclera: Trace injection noted OU, no staining
Cornea: Clear; TBUT: 7 seconds OU
A/C: Deep and Quiet OU
Iris: Flat OU
Lens: Normal



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Case Considerations

- OK To Proceed Refractive Surgery?
- How do you educate this patient?
- Treatment Considerations?

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What I Did

1. Heat and gland clearing treatment in clinic OU
2. Start loteprednol bid x 1 month OU
3. Start lotilaner bid OU x 6 weeks OU
4. At home maintenance
5. RTC in 6 weeks for a recheck

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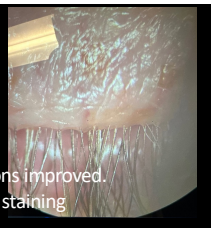
Patient states VA seems better.
BCVA: 20/15 OD 20/15 OS
IOP: 14 OD 14 OS
Osmolarity: 300 OD 300 OS

SLEx:
- Lids/Lashes: See photo; Meibum secretions improved.
- Conjunctiva/Sclera: Clear, no injection or staining
- Cornea: Clear; TBUT: >10 seconds OU
- A/C: Deep and Quiet OU
- Iris: Flat OU
- Lens: Normal



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Case

19-year-old female with a painful, red, cloudy left eye. Does wear CL's but states that she does not sleep in them and cares for them well.
Has had a FB sensation for a few weeks.

Primary MD put in a BCL for comfort and started Neo-Poly-Dex

20/40 BCVA OS

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Slit Lamp Examination

Branching ulcer with satellite lesion
1+ cell
2+ injection of the conjunctiva

35

Culturing is Essential!

Bacterial
Gram stain
KOH prep
Fungal
Viral

1.Positive result for Nocardia farcinica

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Aggressive Treatment is Essential!

1.Treatment w/ Amikacin q1h OS

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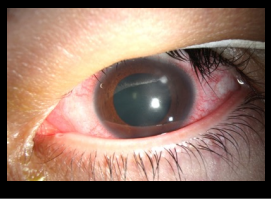
Clinical Findings: Location, location, location!

- Central –likely more virulent pathogen
- Peripheral – more likely staph marginal



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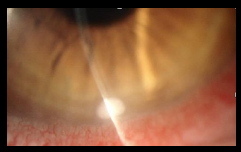
Clinical Findings: Epithelial defect

- Measure in mm
- Relative size
  - Compared to underlying infiltrate



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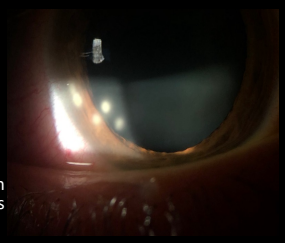
Clinical Findings: Infiltrate

- Presence **or** absence!
- What do the borders look like?
  - Hazy/feathered → think fungal
- Single lesion or multiple?
  - Multiple infiltrates may be seen in satellite, atypical, or staph species



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Sterile vs Infectious

Sterile	Infectious
Mild Pain	Moderate to Severe Pain
Peripheral	Central
Small	Large
Multiple and arcuate	Individual
Epithelium intact	Full defect
AC quiet	AC reaction
No discharge and watery	Muco-purulent discharge
Mild injection	Red, injected eye

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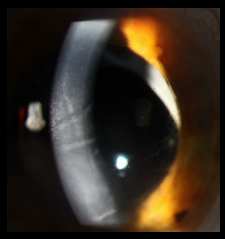
Clinical Findings: Stromal thickness

- Corneal edema
  - Often present!
  - Excessive edema
- Is there any thinning?
  - Monitor closely for melt



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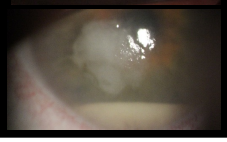
Clinical Findings: Anterior chamber reaction

- May be present in *any* ulcer, uveitis, or epithelial defect
  - AC reaction ≠ (always) infectious
- Hypopyon may be present in severe cases
- Granulomatous KPs could suggest herpetic



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Clinical Findings: Pain

- Critical question!!
- Less than expected?
  - Check sensitivity in clinic!
  - Consider neurotrophic or herpetic
- More than expected?
  - Consider acanthamoeba

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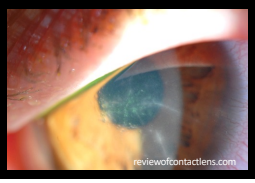
Clinical Findings: Perineuritis

- Uncommon finding
- Hallmark of acanthamoeba



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Evaluation: Imaging

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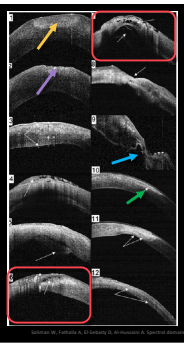

Example OCT findings:

1. Stromal infiltrate
2. Epithelial defect
6. Small stromal cystic spaces*
7. Full thickness cystic spaces* (necrosis)
9. Desmetocele
10. Stromal scar

*Cystic spaces were found to be present for fungal etiologies

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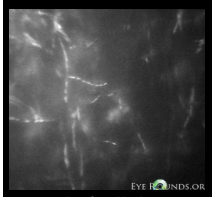
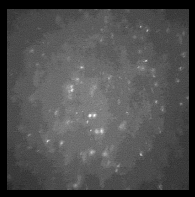
Confocal Imaging

Fusarium[1]	Acanthamoeba	Nocardia asteroides[2]
		
Branching fungal hyphae through stroma	Double walled cysts , highly reflective round bodies	Reflective, thin branching filamentous bacteria

1. Graff JM, Goins KM, Sutphin JE. Fungal Keratitis - Fusarium. 41-year-old female contact lens wearer with persisting keratitis. EyeRounds.org. date accessed ; Available from: http://www.EyeRounds.org/cases/59-fusarium-fungal-keratitis-ReNu-Moisture-Loc.htm. 2. Vaddavalli PK, Garg P, Sharma S, Thomas R, Rao G. confocal microscopy for Nocardia keratitis. Ophthalmology. 2006; 113(8): 1645-1650.

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When to Culture?

1. Central lesions that threaten vision
2. Risk of perforation
3. Scleral tissue involvement
4. Injury with vegetative matter
5. Institutionalized patients where MRSA is possible
6. Lesion is not responding to treatment
7. Atypical features suggestive of fungal, amoebic or mycobacterial

50

"Quick Culture"

No significant difference in growth compared to direct plating[1]

McLeod SD, Kumar A, Cevallos V, Srinivasan M, Whitcher JP. Reliability of transport medium in the laboratory evaluation of corneal ulcers. Am J Ophthalmol. 2005 Dec; 140(6). Pp 1027-1031.

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Chocolate

Haemophilus and Neisseria
Gram-negative

Blood

Streptococcus
Gram-positive
Fungi

52

Sabouraud's Medium

Fungal growth

Thioglycollate

Anaerobic bacteria

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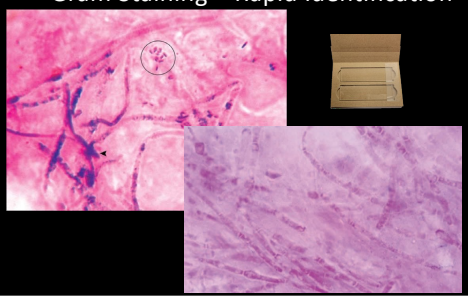
Gram Staining – Rapid Identification



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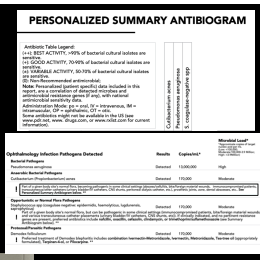
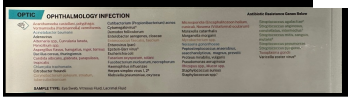
PCR Testing

24-hour turnaround





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Infectious Keratitis Management and Treatment

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Fluoroquinolones

2nd Generation
ofloxacin 0.3%
ciprofloxacin 0.3%

4th Generation
gatifloxacin 0.3% and 0.5%
moxifloxacin 0.5%

besifloxacin – 4th + added benefits




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Fortified Antibiotics

tobramycin - cefazolin
(gram -) (gram +)
(pseudomonas)

vancomycin - tobramycin
(gram +) (gram -)

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ARMOR (2015)

Antibiotic Resistance Monitoring in Ocular Microorganisms

1. *S. aureus* and Coagulase-negative staphylococci (CoNS) have high (42-49%) rates of methicillin resistance
2. Methicillin resistant organisms also showed higher resistance to fluoroquinolones, aminoglycosides, and macrolides
3. Besivance > other 4th generation fluoroquinolones > older 2nd or 3rd
4. S. pneumoniae, P. aeruginosa, H. influenza appeared pan-sensitive
5. Staphylococcal Isolates susceptible to vancomycin

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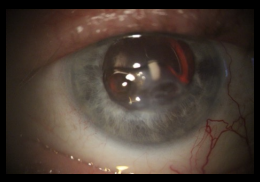
The Role of Doxycycline and Vitamin C



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Steroids for Corneal Ulcers Trial (SCUT) Study

500 eyes received 0.5% moxifloxacin every hour while awake for 48 hours

Randomized to either topical steroids or placebo

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Steroids for Corneal Ulcers Trial (SCUT) Study (3 months)

Steroid group required more time to re-epithelialize

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Steroids for Corneal Ulcers Trial (SCUT) Study (3 months)

Steroid group required more time to re-epithelialize

4 adverse events in the placebo group and none in the steroid group

65

Steroids for Corneal Ulcers Trial (SCUT) Study (3 months)

Steroid group required more time to re-epithelialize

4 adverse events in the placebo group and none in the steroid group

No statistically significant difference in VA between the steroid and placebo group at 3 weeks or 3 months

66

Steroids for Corneal Ulcers Trial (SCUT) Study (3 months)

Steroid group required more time to re-epithelialize

4 adverse events in the placebo group and none in the steroid group

No statistically significant difference in VA between the steroid and placebo group at 3 weeks or 3 months

No statistically significant difference in scar size at 3 weeks or 3 months

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Steroids for Corneal Ulcers Trial (SCUT) Study (12 months)

Trend was…

Better long-term VA outcomes

In the steroid group

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In Conclusion…

Follow 24-72 hours until signs of improvement

Treatment can last months

Q1h treatment day/night

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