

Differentiating Keratitis

Pamela Theriot, OD, FAAO
 Public Awareness Sub-Committee Member
 TFOS Lifestyle Workshop

Pam Theriot - Financial Disclosures

<p>Speaker Bureau: RVL Pharmaceuticals Viartis Pharmaceuticals Johnson & Johnson Vision Sun Pharma Lumenis Be Tarsus Pharmaceuticals Dompe</p> <p>Brand Ambassador: Eyes are the Story UNClug Mask</p>	<p>KOL/Consultant: Novartis Merakris Therapeutics Scope Eyecare NuLids Tear Film and Ocular Surface Society, Public Awareness Committee Member Twenty/Twenty Beauty NovaBay Mallinckrodt Pharmaceuticals Bruder Healthcare Company Alcon</p>
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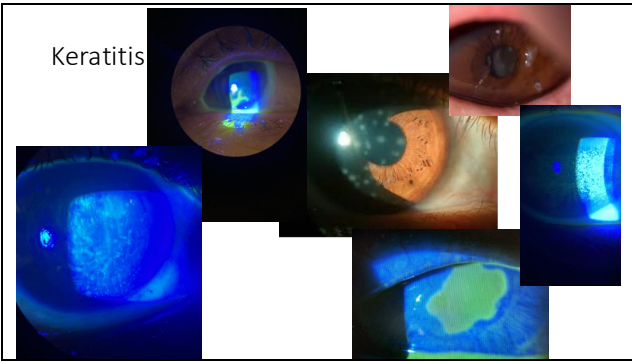
Pam Theriot, OD, FAAO



- Lusk Eye Specialists
 - Clinical Director of Dry Eye Relief Center
- TFOS Lifestyle Workshop:
 - Public Awareness committee Member
- 2025 Dry Eye Columnist
 - Optometric Management
- Author
 - Alleviate Dry Eye
- Website / Blog / Courses
 - www.pamtheriot.com

Learning Objectives

- Keratitis can be hard to differentiate and Diagnose
- Thygesons Keratitis (TSPK), Staph Marginal Keratitis (SMK), Neurotrophic Keratitis (NK), Filamentary Keratitis (FK), Herpes Simplex (HSK), Keratitis Sicca (KCS), Microbial Keratitis
- Learn their causes, signs, and symptoms
- Do a deeper dive into their differential diagnoses
- Explore some newer treatment modalities



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What the heck is TSPK anyway?

- Exact etiology remains unknown
- Auto-immune processes have been suspected
- Genetic association with HLA-DR3 – an antigen associated with several auto-immune disorders (like Sjogren's Syndrome)
- This antigen may alter the immune response in these patients which gives way to the prolonged disease course, and the fact that it waxes and wanes throughout years to decades

Who Gets TSPK?

- Slight female predilection
- Ages 3 - 70, mean age 29
- No racial bias

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Signs

- Usually bilateral, but can be unilateral
- Multiple white-grey intra epithelial deposits,
- Lesions cause an elevation of the epithelium and classic negative staining with FL
- 1 – 50 lesions in the central cornea
- Typically 5 – 10 lesions

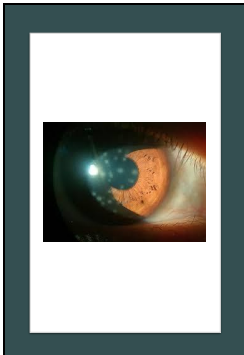
Conjunctiva is Clear

- Corneal sensation remains Normal – unlike in HSK
- Minimal to no conjunctival involvement
- Can be stellate or snowflake in appearance
- Vision is minimally affected
- Does not respond to antibiotic treatment



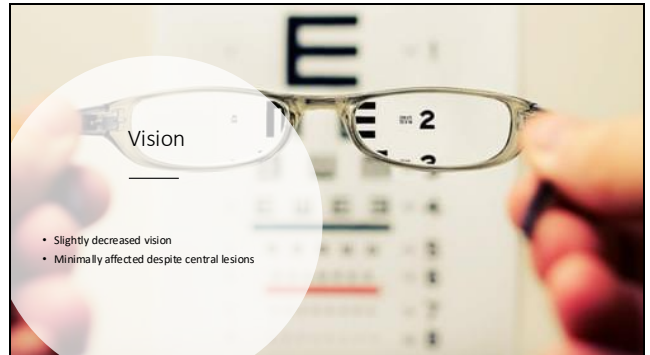
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Symptoms

- Burning
- Irritation / foreign body sensation
- Tearing
- Photophobia



- Slightly decreased vision
- Minimally affected despite central lesions

Mon	Tue	Wed	Thu
1	2	3	
8	9	10	
15	16	17	
22	23	24	
29	30		

Recurrence

- Frequent bouts of recurrence
- May reoccur despite medical treatment.
- The classic symptoms - they continue to have recurrent episodes.
- Average recurrence ~11 years

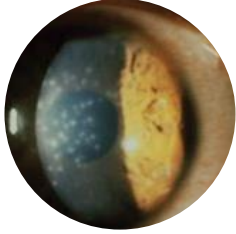
The Differentials

- Viral Conjunctivitis
- Superficial Punctate Keratitis
- Recurrent Corneal Erosion
- Staph marginal Keratitis
- Herpes Simplex Keratitis

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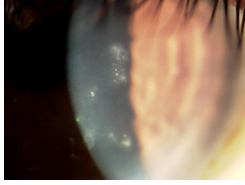
Epidemic Keratoconjunctivitis (EKC)



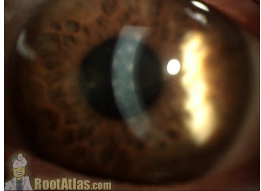
- Infectious keratitis
- Usually caused by Adeno virus
- Often has systemic flu like symptoms
- Spreads quickly from eye to eye (70% bilateral in 1 week)
- Spreads easily from person to person
- redness, eyelid edema, tearing, irritation, foreign body sensation, and photophobia

TSPK vs. EKC

TSPK



EKC



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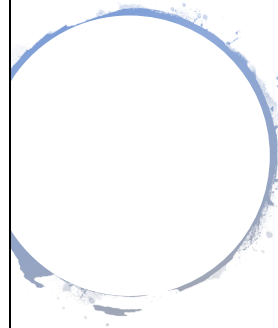
Signs of TSPK vs. EKC

Similar

- Lesion appearance
- Bilateral lesions
- Photophobia
- FB sensation

Different about EKC

- Spreads from one eye to other
- Vision significantly affected
- Can take a long time to respond to steroid treatment
- Conjunctival involvement- SCH
- Systemic flu like symptoms
- Adeno-Plus positive



In Office Testing

- Approximately 1 in 4 patients with acute conjunctivitis have confirmed adenoviral conjunctivitis
- Detects all known serotypes of adenoviral conjunctivitis.
- Early and accurate diagnosis of pink eye may prevent serious consequences including morbidity.
- Overlap exists in the clinical signs and symptoms of acute conjunctivitis
- Can be easily misdiagnosed by eye care professionals
- Help reduce antibiotic resistance

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Superficial Punctate Keratitis

Epi defects, FB sensation, redness

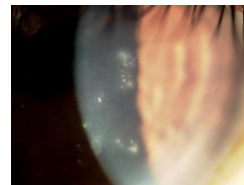
Photophobia, irritation and tearing

Causes:

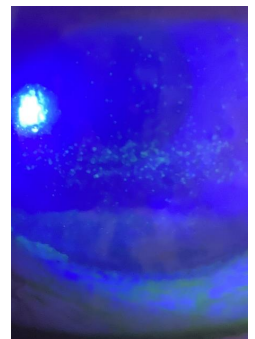
- Exposure
- Chemical
- KCS
- Medicamentosa
- Allergy
- Infection: viral or bacterial

TSPK vs. SPK

TSPK



SPK



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Signs of TSPK vs. SPK

Similar

- Lesion appearance
- Bilateral lesions
- Photophobia
- FB sensation

Different about SPK

- Lesion is superficial TSPK is intra-epithelial
- Lesions can be more confluent
- Appear in bands
- Vision may be more affected
- Usually conj involvement

Recurrent Corneal Erosion

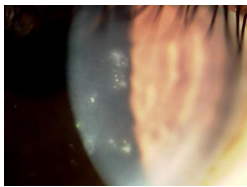
- Symptoms occur most often in the morning or middle of the night
- Usually only one lesion
- Significant sudden onset pain
- Sometimes resolve on their own
- May occur months after an initial abrasion

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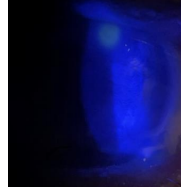
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TSPK vs. RCE

TSPK



RCE



Signs of TSPK vs. RCE

Similar

- Lesion appearance
- Photophobia
- FB sensation

Different about RCE

- Usually only one lesion at a time
- Vision may be more affected
- Initial onset is sudden

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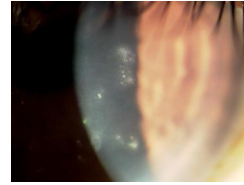
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Staph Marginal Keratitis (SMK)

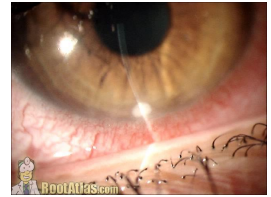
- Small round infiltrates at limbus
- Can be one or multiple
- Redness
- If untreated, lesions will coalesce into larger areas and stain
- Injection of bulbar conjunctiva adjacent to infiltrate
- Zone of clear cornea between limbus and lesion
- Red, watery, photophobia, FB sensation

TSPK vs. SMK

TSPK



SMK



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Signs of TSPK vs. SMK

Similar

- Lesion appearance
- Photophobia
- FB sensation
- Vision not significantly affected

Different about SMK

- Lesions are peripheral
- Presents with blepharitis as well

Herpes Simplex Keratitis

- Check corneal sensitivity
- HSK will have decreased sensitivity
- Severe infection that can lead to scarring and blindness
- Worsens with steroid

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What triggers HSK

- Fever
- hormonal changes
- ultraviolet exposure
- psychological stress
- ocular surgery
- ocular trauma
- Immunosuppression
- Pregnancy

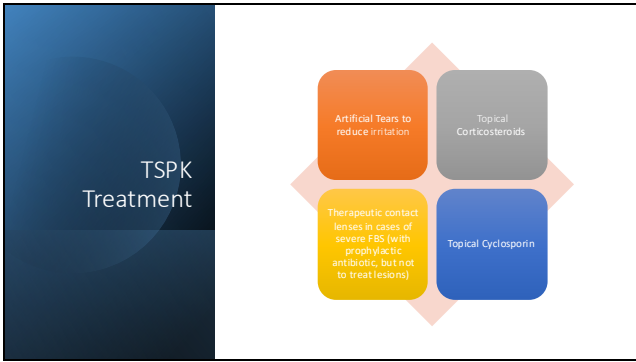
TSPK vs. HSK

TSPK vs. HSK

<p>TSPK</p> <ul style="list-style-type: none"> • Stellate or snowflake lesion • Little conjunctival injection • Normal corneal sensation • Does not respond to antibiotic or antiviral treatment • High rate of recurrence • Culture negative • Usually no scarring 	<p>HSK</p> <ul style="list-style-type: none"> • Dendritic lesion • Conjunctival redness • Decreased corneal sensation • Responds to antivirals • 50% recur in five years and 63% at 20 years • Can culture active lesion • High probability of scarring
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TSPK Management

- Not necessary to culture
- Can take slit lamp photos
- Follow up Q1week until lesions begin to resolve
- Q2-3 weeks to monitor IOP, depending on IOP elevation risk



Topical Treatment

- Topical Steroids mainstay: QID until the deposits resolve, slow taper.
- Can use topical Cyclosporine when steroids are contraindicated
- Steroid responder
- Cataract formation
- Long term treatment safe with Cyclosporine

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TSPK Surgical Intervention?

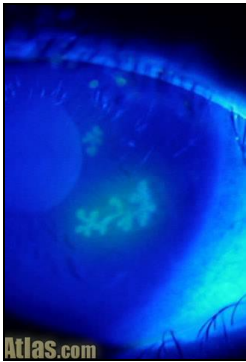
- PRK, and epi debridement have shown to be insufficient in alleviating the inflammation in these patients

Case Report JG

- 45 yo Caucasian Male
- Referred in from local optometrist
- Pain, light sensitivity OD X 3 weeks
- VA = 20/30
- Current Medications: Moxifloxacin TID

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Most Important Differential

- Rule Out Herpes Simplex Keratitis
- History of fever blister
- Previous HSK infection
- Lesions on lids

Atlas.com

Treatment Plan 1

- Oral Anti-viral
- Review of Dosages:
 - Acyclovir – Zovirax – 400mg 5x/day
 - Valacyclovir – Valtrex – 500mg TID
 - Famciclovir – Famvir - 250mg TID
- 7 - 10 days

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Treatment Plan 2

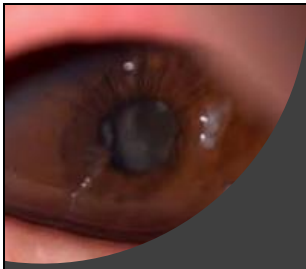
- Pt did not respond to oral Acyclovir
- HSK Ruled Out!
- Now okay to add steroid
- Pred Forte QID until the deposits resolve
- Slow taper
- Can Rx QD or QOD steroid long term to reduce recurrences

Filamentary Keratitis

New Treatments

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Filamentary Keratitis


Key Findings

- Strands or filaments attached to the cornea
- Increased mucus to aqueous ratio in the tear film
- Schirmer's test shows low aqueous production
- Patient notes foreign body sensation

Tests for Filamentary Keratitis

- Slit lamp exam
- Vital dyes (lissamine, fluorescein, rose bengal)

<ul style="list-style-type: none"> • Topical lubricants (tears/ung) • Acetylcysteine Drops • Bandage Contact lenses • Biologic Membranes <ul style="list-style-type: none"> • Dehydrated AMT • Cryopreserved AMT • Biologic Drops <ul style="list-style-type: none"> • Serum Tears • PRP • AM Drops 	<ul style="list-style-type: none"> • Steroids <ul style="list-style-type: none"> • Loteprednol • Fluoromethalone • Immunomodulators <ul style="list-style-type: none"> • Cyclosporine • Lifitegrast • Scleral Contact Lenses
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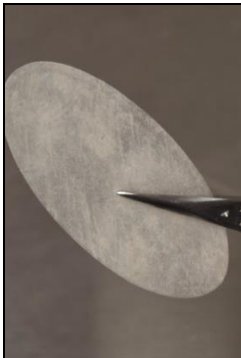
Cryopreserved Amniotic Membrane

- Approved by the FDA for:
 - Protective
 - wound healing
 - anti-inflammatory effects.
- Why is it so powerful:
 - extracellular matrix components
 - heavy-chain hyaluronic acids
 - growth factors
 - Fibronectin
 - Collagen
- promote anti-inflammatory effects and healing



Dehydrated Amniotic Membrane

- Room temperature stable allograft derived from human placental tissue collected from consenting donors
- Extra cellular matrix acts as a reservoir of bioactive peptides:
 - Growth factors
 - Cytokines
 - Glycosaminoglycans
- Basement membrane interface acts as a substrate that supports:
 - cellular adhesion
 - transplanar migration
 - proliferation.




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Neurotrophic Keratitis

It's not rare when it's in your chair.

Neurotrophic Keratitis Definition



Degenerative corneal disease
 Damage to the trigeminal nerve (cranial nerve V)
 Loss of corneal sensation
 Breakdown of the corneal epithellum
 Impaired corneal healing
 Persistent epithelial defect → corneal ulceration → stromal melting and perforation

Hallmark: decreased sensation, decreased or no pain

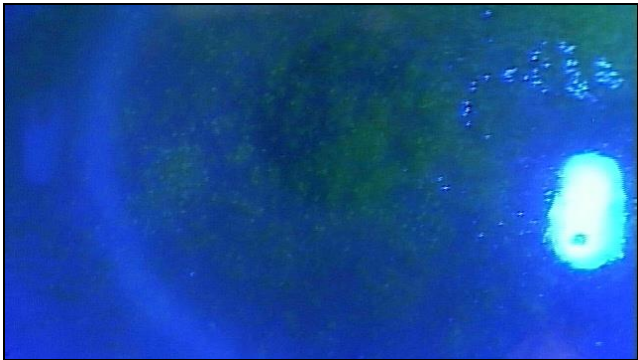
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Severity-Based Therapy

Stage	Therapy
1	<ul style="list-style-type: none"> • Preservative-free artificial tears formulations • Punctal occlusion • Hydrogel contact lens (consider large diameter) • Recombinant human NGF (rhNGF, cenegelein) • Serum/plasma/platelet rich plasma
2	Supportive therapies plus: <ul style="list-style-type: none"> • rhNGF • Scleral lens (± serum/plasma) • Amniotic membrane • Botulinum induced ptosis, Tarsorrhaphy
3	<ul style="list-style-type: none"> • rhNGF • Keratoplasty + scleral lens, tarsorrhaphy, neurotization

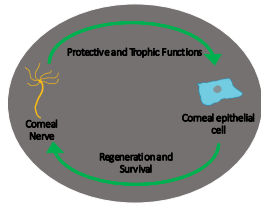
Saricubiric M, Lambiasi A. Diagnosis and management of neurotrophic keratitis. *Clin Ophthalmol*. 2014;8:571-579. Sheth H, Tigh S, Hashem O, Hayashida Y. Update on cenegelein eye drops in the treatment of neurotrophic keratitis. *Clin Ophthalmol*. 2015;10:187-191. Pub Med Oct 17, 2015.



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Corneal Innervation



The cornea is the most sensitive and densely innervated tissue in the human body^{1,2}

Corneal innervation is essential. Corneal epithelial cells act in a mutually supportive relationship with corneal nerves^{3,4}

- Corneal nerves: maintain corneal integrity
- Protective functions: blinking and tearing
- Trophic support: neuropeptides (eg, substance P) promote epithelial cell proliferation, migration, adhesion
- Epithelial cells: neurotrophic factors (neuronal extension and survival)

Corneal nerve damage = loss of corneal sensation, epithelial breakdown, poor healing^{1,2}

1. Shehata H. Clinical Ophthalmology. 2019; 13: 1973-1983
 2. Verwee P, et al. Eye and Brain. 2018; 10: 37-45.
 3. Dua HS, et al. Prog Retinal Eye Res. 2018;64:107-131.
 4. Saad S, et al. Ocular Surf. doi:10.1016/j.jaos.2019.11.008.

Etiology



- INFECTIOUS^{1,2}**
 - Herpes (simplex, zoster)
 - Leprosy
- ATROGENIC^{1,2}**
 - Trauma to ciliary nerves by laser treatment and surgery
 - Corneal incisions
 - LASIK
- SYSTEMIC DISEASE^{1,2}**
 - Diabetes
 - Multiple sclerosis
 - Vitamin A deficiency
- CORNEAL DYSTROPHIES^{1,2}**
 - Lattice
 - Granular
- TOXIC^{1,2}**
 - Chemical burns
 - Carbon disulfide exposure
 - Hydrogen sulfide exposure
- FIFTH-NERVE PALSY^{1,2}**
 - Trigeminal neuralgia surgery
 - Neurosistia (acoustic neuroma)
 - Aneurysms
 - Facial trauma
 - Congenital
 - Riley-Day syndrome
 - Goldenhar-Gorlin syndrome
 - Möbius syndrome
 - Familial corneal hypesthesia
- TOPICAL MEDICATIONS^{1,2}**
 - Anesthetics (abuse)
 - Timolol
 - Betaxolol
 - Sulfacetamide
 - Diclofenac sodium
 - Ketorolac
- MISC^{1,2}**
 - CTL
 - Increasing age
 - Dark eye color
 - Adie syndrome
 - Limbal stem cell failure (chronic)

1. Dua, HS, et al. Prog Retinal Eye Res. 2018;64:107-131.
 2. Mardipati R. Neurological aspects. https://doi.org/10.1016/j.jaos.2019.11.008

Endogenous nerve growth factor (NGF) and its role in NK:

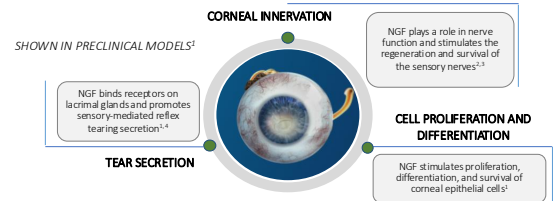
Neurotrophic keratitis (NK) is a result from impaired trigeminal corneal innervation

- ↓ Lacrimation and blink reflex
- ↓ Epithelial cell vitality, metabolism, mitosis
- ↓ Epithelial trophism and repair
- ↑ Stromal and intracellular edema
- ↓ Microvilli
- ↓ Development of the basal lamina

Martini-paqueo et al. (2021) | Cell Physiol 232:717-24

Endogenous NGF Maintains Corneal Integrity By Three Mechanisms

Endogenous nerve growth factor acts through specific high-affinity (ie, TrkA) and low-affinity (ie, p75NTR) nerve growth factor receptors in the anterior segment of the eye to support corneal innervation and integrity.¹



1. Mochly-Rosen D, et al. Understanding the pathogenesis of neurotrophic keratitis: the role of corneal nerves. J Cell Physiol. 2017; Apr; 232(4):717-724. J. Müller U, Marfurt CF, Krause J, Tamm ER. Corneal nerve structure, contents and function. Exp Eye Res. 2003; May; 76(5):521-42. S. Sachdev RN, Lambert A. Diagnosis and management of neurotrophic keratitis. Clin Ophthalmol. 2014; 8:575-84. Mui G, Callanan C, Srinivasan S, et al. Nerve growth factor in the development and adult lacrimal gland of rat (RBN) and its role in neurotrophic keratitis in humans. Cornea. 2010; 29:1010-1018.

Treatment

- Continue:
 - Cyclosporine 0.05% BID OU
 - Heat Mask
- Stop
 - Oral ceterizine
- Order
 - Cenegermin 20 mcg/mL – Patient to call once meds come in to review meds / demo proper usage
 - Ceterizine ophth sol BID OU
- Follow Up
 - 3-4 months glaucoma / Dilate OCT - G

Staph Marginal Keratitis

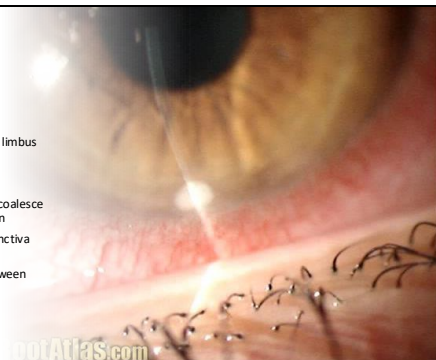
Is it an ulcer or not... That is the question.

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Signs of SMK

- Small round infiltrates at limbus
- Can be one or multiple
- Redness
- If untreated, lesions will coalesce into larger areas and stain
- Injection of bulbar conjunctiva adjacent to infiltrate
- Zone of clear cornea between limbus and lesion



Symptoms of SMK



- Pain, Irritation
- Photophobia
- Watering
- Foreign Body Sensation
- Blurred vision

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Causes and Co-Conspirators

- Overgrowth of Staph aureus bacteria
- Co-Conspirators:
- Contact Lenses
- Poor makeup hygiene
- Ocular rosacea
- Blepharitis – almost 100%
- Meibomitis



Differentials

- Vernal keratoconjunctivitis
- HSV keratitis
- Bacterial keratitis and ulceration
- Old corneal scars
- Exposure keratopathy
- Contact lens induced peripheral ulcer



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SMK vs. VKC

SMK

- Peripheral lesions
- Little conjunctival injection
- Does not respond to antibiotic or antiviral treatment
- High rate of recurrence
- No itching
- Little watery discharge

VKC

- Shield Ulcer
- Conjunctival redness
- Responds to antihistamine & steroid
- High rate of recurrence
- Itching is hallmark
- Thickened discharge

SMK vs. Exposure Keratopathy

SMK

- Lesions scattered on cornea
- Lesions do not stain
- Mild conjunctival injection
- High rate of recurrence
- Symptoms same all day

Exposure

- Lesions grouped in band
- Band of staining
- May have sig conj Injection
- Recurs until exposure eliminated
- Usually worse in am

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Differentiating an Infiltrate from an Ulcer

SMK - Sterile Infiltrate

- Small lesion <1mm
- Peripheral location – at limbus
- No mucus discharge
- No A/C reaction
- Foreign body sensation
- Mild photophobia
- Mild to no epi defect

Infectious Ulcer

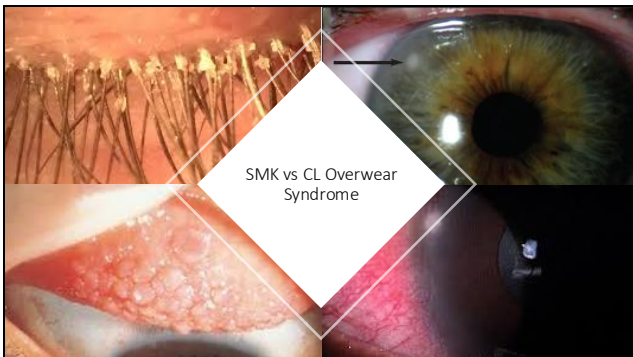
- Large Lesion >1mm
- Central >2mm of limbus
- Mucus discharge
- + A/C reaction
- Significant pain
- Significant photophobia
- Large epi defect

Differentiating SMK vs CL related Ulcer

- Sterile
 - Localized Conjunctival injection
 - Always at limbus
 - Not necessarily a CL wearer
 - Blepharitis
- Infectious
 - Overall conjunctival injection
 - Can be further into cornea
 - Always related to CL wear
 - Giant Papillary Conjunctivitis

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Two Treatment Arms for SMK

Resolve Corneal Infiltrate



Decrease Bacterial Overgrowth

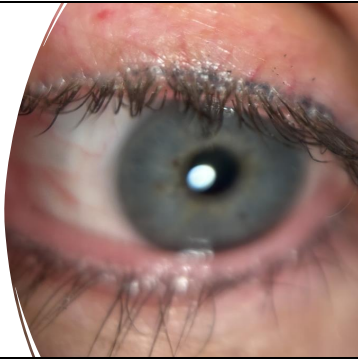


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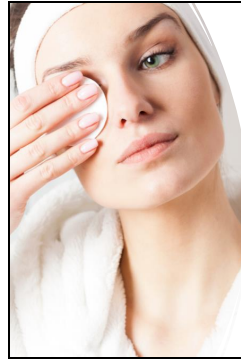
Resolve Corneal Infiltrate

- Antibiotic followed by a steroid if there is significant epi defect
- Antibiotic / Steroid Combo
- Steroid Alone



Treat Bacterial Overgrowth

- D/C Contact lens wear
- In office Treatment- Microblepharoexfoliation
- Topical Antibiotic drops or ointment – azithromycin, bacitracin, erythromycin
- Topical Antiparasitic - lotilaner
- Oral Doxycycline 20mg BID
- Lid Cleansers – Daily maintenance
- Makeup Removal
- Makeup Hygiene



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Treatment Options

Prescription medications

At-home treatments

In-office treatments

Prescription Treatments for Blepharitis

- Antibiotic Drops:
 - Azithromycin 1% ophthalmic solution
- Antibiotic /Steroid Combination Drops:
 - Tobramycin/Dexamethasone suspension
 - Tobramycin/Loteprednol Suspension
 - Neomycin-polymyxin-dexamethasone
- Ointments: antibiotic or antibiotic steroid combination
 - Erythromycin, Neomycin-polymyxin-dexamethasone, tobramycin-dexamethasone
- Topical Anti-parasitic
 - Lotilaner 0.25% solution

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Kill the Bacteria / Mites

- Prescription Medications:
 - Oral Doxycycline 20mg BID
- Topically:
 - Apply (azithromycin, erythromycin, or steroid/antibiotic combo drops) directly to lid margins with clean fingertip
 - QHS OU x 30 nights
 - Lotilaner 0.25% ophthalmic solution

At Home OTC Tx: Lid Cleansers

- Hypochlorous Acid Spray
- Foaming Lid Cleanser
- Lid Scrubs Pads
- **NEVER USE BABY SHAMPOO!!!**



Blepharitis: At-Home Cleansing

- Remove Contact lenses
- Makeup Removal
- Lid Cleansers – Daily maintenance
 - Wipes
 - Foams
 - Spray

Lid and Lash Hypochlorous Acid Cleansing Sprays

- Hypochlorous Acid sprays: naturally produced in the cells of our body
- Natural defense against micro-organisms
- Great for killing staph bacteria around eyes

- Start with clean face
- Remove makeup or moisturizers
- Spray directly to closed lids
- Allow to air dry

PROS:

- Great for all skin types
- Found to kill COVID-19 virus
- Can also be applied to face
- Non-drying, Non-irritating
- Can also help to remove dust, dirt and pollens from lashes

CONS:

- Will not effectively eliminate Demodex when used alone
- Some concentrations can be irritating to very sensitive skin



Foaming Cleanser PROS and CONS

PROS:

- Great to use in the shower
- Can be used after makeup removal to cleanse lids
- Better for oily skin types

CONS:

- Can be drying to the skin as many contain soap
- May Contain Tea Tree Oil

Eyelid Wipes PROS and CONS



- PROS:**
 - Convenient
 - Easy to carry with you
- CONS:**
 - Extra waste products due to individual packaging
 - Most still need to be rinsed away
 - May Contain Tea Tree Oil

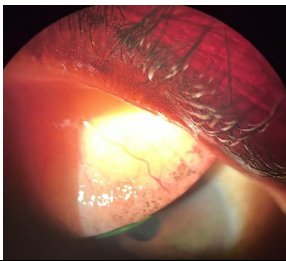


5 Categories of Makeup Removers

- Micellar
- Oil-Free
- Oil-Based
- Wipes
- Cloths


Must Remove Eye Makeup Every Night

Makeup Rules for Best Ocular Health



- Always remove makeup nightly
- No water-proof makeup
- No glitter in your eye shadow
- Avoid powdered eye shadow
- Apply primer to lids before shadow and liner
- Pencil eye liners are best
- No water-lining or tight-lining
- Avoid toxic and irritating ingredients
- Toss out your makeup on time
- Never share your eye makeup
- Never Mix ten cosmetics with saliva
- Never alter your makeup with heat
- Never apply makeup on the go
- Never put a product not intended for the eye on the eye

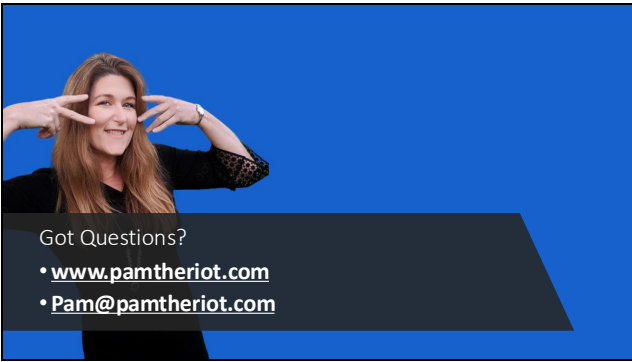
If not you, then who...




the never list™
NEVER compromise on your ingredients. We thought the line up over 1000 harmful or questionable ingredients.


Never compromise on your ingredients. We thought the line up over 1000 harmful or questionable ingredients.

FLAWLESS MAKEUP IN 10 MINS!



Got Questions?

- www.pamtheriot.com
- Pam@pamtheriot.com



Thank You

- Vision Expo West
- All of the Meeting Sponsors
- Attendees

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.

