

## Pathologic Keratitis: Diagnosis and Management of Infectious Keratitis

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## Financial Disclosure

- I have no financial disclosures.

## Introduction CORNEAL ULCERS

## Corneal Ulcers

- **Definition**
  - Epithelial defect with underlying stromal inflammation, infiltration, or melting

## Corneal Ulcers

- **Incidence**
  - Keratitis
    - CDC estimated 988,000 annual visits to ophthalmology offices or ED for (2010)\*<sup>1</sup>
  - Infectious corneal ulcers
    - Population-based study (1998-1999)<sup>2</sup>
      - 27.6 per 100,000 person-years in non CL wearers
      - 130.4 per 100,000 person-years in CL wearers

\* Results did not include visits to Optometrists

1. Center for Disease Control. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5845a2.html>. 2. Jang BM, Goto GC, Kozar AS, Holbrook DL, Peto TC, Smith SD, Whitcher PS, Margolis TP, Wang SC. Epidemiology of Infectious Keratitis and Corneal Ulcers. *Arch Ophthalmol*. 2010;128(10):1273-1278. doi:10.1001/archophth.128.10.1273

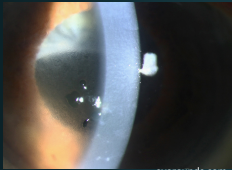
## Corneal Ulcers

- **Risk Factors**
  - Contact lens wear
    - Extended wear soft > daily soft > gas permeable



### Corneal Ulcers

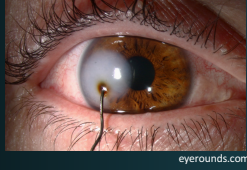
- Risk Factors
  - Contact lens wear
  - Epithelial breakdown
    - Dry eye, bullous keratopathy, hydrops



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### Corneal Ulcers


- Risk Factors
  - Contact lens wear
  - Epithelial breakdown
  - Trauma or corneal surgery



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### Corneal Ulcers

- Risk Factors
  - Contact lens wear
  - Epithelial breakdown
  - Trauma
  - Eyelid disease
    - Trichiasis, blepharitis, malposition, facial nerve palsy



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### Corneal Ulcers

- Risk Factors
  - Contact lens wear
  - Epithelial breakdown
  - Trauma
  - Eyelid disease
  - Systemic disease and immunosuppression
    - HIV/AIDS, DM, iatrogenic

### Clinical Examination

## CORNEAL ULCERS

### Corneal Ulcers


- Clinical findings
  - Documentation is critical
    - Diagnosis
    - Determining response to therapy

Pertinent Findings
Epithelial defect
Presence of infiltrate(s)
Stromal edema
Stromal thinning
Anterior chamber
Keratic precipitates
Intraocular pressure
Perineuritis
Eye Pain
Eye Sensitivity

## Corneal Ulcers

Pertinent Finding

Epithelial defect



Clinical Relevance

reviewofcontactlens.com

## Culturing CORNEAL ULCERS

## Culturing: When to Culture



Figure 4. A small peripheral infiltrate (A) does not require culture, but any corneal ulcer that is large or central (B) or presents with suspicious features should be cultured.

<https://www.aao.org/young-ophthalmologists/yo-info/articles/beginner-s-guide-to-corneal-ulcers>

## Culturing: When to Culture

- **When to culture**
  - High Suspicion
  - Unresponsive to initial treatment
  - 3-2-1 Rule

3-2-1 Rule	
3	mm or larger infiltrate
2	or more infiltrates
1	mm or less from visual axis

## What diagnostic techniques do we have?

- **Corneal Culturing**
  - Scraping
  - Biopsy
- **Imaging**
  - Confocal microscopy
  - UHR-OCT


## Culturing: Options

Single Sample

Multiple Sample

Biopsy

- Also known as “Quick Culture”
- Components:
  - Single swab to obtain sample
  - Transport media
- Sent to pre-specified microbiology lab
  - Lab plates onto multiple media
- No significant difference in growth compared to direct plating<sup>1</sup>



McLeod SD, Kumar A, Cavallio V, Srivastava M, Wittacher JF. Reliability of transport medium in the laboratory evaluation of corneal ulcers. Am J Ophthalmol. 2003;146(5): Pa 1027-1031.

### Culturing: Options

Single Sample

Multiple Sample

Biopsy

- "Classic" culturing technique with multiple plates
- Growth Media:
  - Plates: blood, chocolate
  - Slant Tubes: potato dextrose, Lowenstein-Jensen
  - Broth: thioglycolate, TSB
- Slides: gram stain, fungal
- PCR Tube: HSV



### Culturing: Options

Single Sample

Multiple Sample

Biopsy

- Pathology specimen gathered with blade or trephine
- Only recommended:
  - Unresponsive to treatment
  - Culture-negative (NGTD)
  - Strong suspicion for infectious cause
- Examination done by **pathology** laboratory

### Culturing: Technique

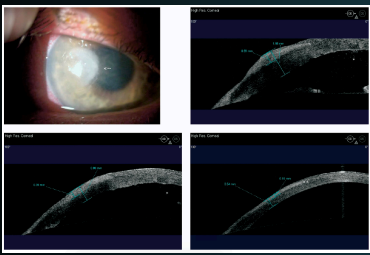
- **How:** anesthetize cornea
- **What:** *sterile* spatula, spud, blade, swab
  - Pre-moistened swabs (saline or broth) to improve sample collection
- **Where:** advancing borders
  - Purulent material may provide inadequate yield
  - AVOID EYELIDS

### Imaging CORNEAL ULCERS

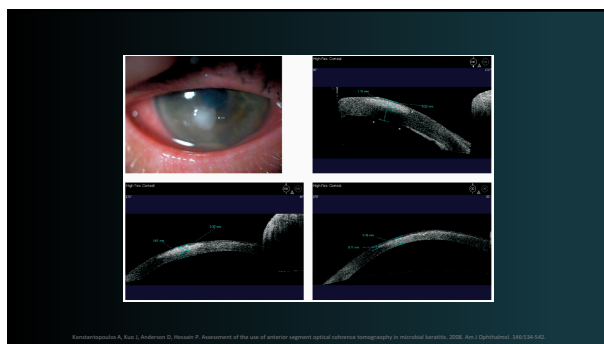
### Imaging

- **Ultra high resolution OCT**
  - Supportive tool in diagnosis and management, including objective treatment response, of microbial keratitis<sup>1,2</sup>

1. Konomatsopoulos A, Kuo J, Anderson D, Hsuan P. Assessment of the use of anterior segment optical coherence tomography in microbial keratitis. 2008. Am J Ophthalmol. 146:538-542. 2. Schimm W, Fathallah A, El-Solhoy O, Al-Rustolji A. Spectral domain anterior segment optical coherence tomography in microbial keratitis. Arch Clin Exp Ophthalmol. 2013; 2(1):249-253.



Konomatsopoulos A, Kuo J, Anderson D, Hsuan P. Assessment of the use of anterior segment optical coherence tomography in microbial keratitis. 2008. Am J Ophthalmol. 146:538-542.



**TABLE. Summary of Corneal Infiltrate Characteristics**

Case No.	Patient Age (yrs)	Risk Factor	Location	Recurrent AS OCT Infiltrate Thickness (µm)	Recurrent AS OCT Corneal Thickness at Infiltrate Area (µm)	Recurrent AS OCT Infiltrate Thickness (µm)	Recurrent AS OCT Corneal Thickness at Infiltrate Area (µm)
1	28	CL wear	ST	190	800	110	860
2	63	CL wear	Inferior	130	670	120	690
3	35	RCS	IT	370	910	250	810
4	57	CL wear	Central	530	1180	170	<50
5	40	CL wear	Temporal	580	1560	160	540
6	72	Trauma, lagophthalmos	Central	580 <sup>a</sup>	NP <sup>b</sup>	0 <sup>c</sup>	160
7	61	CL wear	Central	370	800	800	630

AS OCT = anterior segment optical coherence tomography; CL = contact lens; IT = inferior temporal; RCS = recurrent corneal erosion syndrome; ST = superior temporal; yrs = years.  
<sup>a</sup>In Case 6, measurements refer to AS OCT inflammatory plaque width; infiltrate thickness could not be measured.  
<sup>b</sup>In Case 6, measurement of corneal thickness was not possible at presentation, because the endothelium could not be distinguished clearly from the endothelial inflammatory plaque.

**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

May help differentiate residual scarring from active infection.

- Intact epithelium
- Anterior stromal hyperreflectivity without stromal thickening
- Hyperreflectivity with compact stroma and mild thinning

### Imaging

- **Confocal microscopy**
  - Supportive tool in diagnosis of microbial keratitis
  - Helpful in cases of atypical infections
- **Pros:**
  - Excellent resolution and magnification allows visualization of full thickness corneal planes
- **Cons:**
  - Acquiring and interpreting images is difficult and requires experience

### Confocal Imaging

Fusarium<sup>1</sup>

Branching fungal hyphae through stroma

Acanthamoeba

Double walled cysts, highly reflective round bodies

Nocardia asteroides<sup>2</sup>

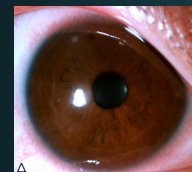
Reflective, thin branching filamentous bacteria

1. Graff JM, Gohs KM, Saphin E. Fungal keratitis - Fusarium: 41-year-old female contact lens wearer with persisting keratitis. EyeFindings.org. date accessed. Available from: http://www.EyeFindings.org/Case/59.

## Treatment CORNEAL ULCERS

## Treatment

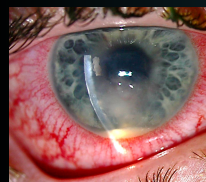
- **Small peripheral ulcers**
  - Broad spectrum antibiotics
  - Fluoroquinolones (3<sup>rd</sup> or 4<sup>th</sup> generation)



## Treatment

- **Culture-worthy ulcers**
  - **Rule of thumb:**
    - Suspicious enough to culture should be treated with fortified antibiotics
  - **Strong gram-positive and gram-negative**
    - Ex:
      - Vancomycin 50mg/mL q1-2h, around the clock
      - Tobramycin 14mg/mL q1-2h, around the clock
  - **Not all pharmacies compound ophthalmics**

## Treatment



- **Fortified example dosage schedule:**
  - Every 1-2 hours around the clock until improvement
  - Then every 2 hours
  - Every 3-4 hours while awake
  - Discontinue

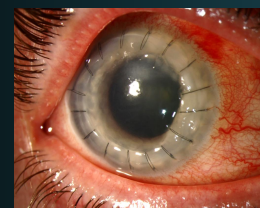
## Treatment

- **Amniotic Membranes**
  - Avascular fetal placental membrane used to decrease inflammation and aid in corneal healing
  - **Two types**
    1. Cryopreserved (*ProKera*<sup>®</sup>, *BioTissue*)
    2. Dehydrated (*AmbioDisk*<sup>®</sup>, *IOP* or *Ophthalmics BioDOptix*<sup>®</sup>, *Derma Sciences*)

Should not be used as a first-line therapy for infectious keratitis

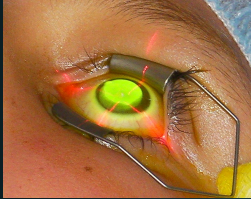
## Treatment

- **The Big Guns**
  - Therapeutic penetrating keratoplasty



## Treatment

- **The Big Guns**
  - Photodynamic therapy with photosensitizing agent



## Cross-Linking Corneal Ulcers

1. Inhibit microbial growth
2. Induce oxidative damage to pathogens
3. Strengthens stroma to reduce susceptibility to enzymatic digestion

## Cross-Linking Corneal Ulcers

**Ultraviolet (UVA) with Riboflavin**

- First non-infectious corneal melt (2000)<sup>1</sup>
- First infectious microbial keratitis (2008)<sup>2</sup>
- Meta-analysis (2016)<sup>3</sup>
  - 96 bacteria, 32 fungi, 11 acanthamoeba, 2 herpes simplex, 13 co-infections, 21 inconclusive etiology
  - Stronger evidence for effectiveness in bacterial cases vs fungal or protozoan

1. Schwabatz C, Sporf E, Seiler T. Irradiation of corneas with ultraviolet light and riboflavin administration as a new treatment for various corneal processes, preliminary results in four patients. *Klin Monatsbl Augenheilkd*. 2002;217:1285-1289. 2. Jankó B, Tóth Gy, Kálmán B, Kemény Z, Székely Z. Ultraviolet A/Riboflavin Corneal Cross-linking for infectious keratitis. *Investigative Ophthalmology and Visual Science*. 2008; 49(12):3260-3263. 3. Papanicolaou A, Papanicolaou G. Corneal Collagen Cross-linking for Infectious Keratitis: A Systematic Review and Meta-Analysis. *Invest Ophthalmol Vis Sci*. 2016; 57(11):4273.

## Cross-Linking Corneal Ulcers











**Green light with Rose Bengal**

- Inhibition of fungal keratitis isolates (2014)<sup>1\*</sup>
- Inhibition of MRSA keratitis isolates (2016)<sup>2\*</sup>
- Successful treatment of resistant fusarium keratitis (2017)<sup>3</sup>

\*Denotes in vitro study

1. Arshady A, Miller D, Cabot T, Tenza M, Kessler M, Almeida K, Amescua G, Yao S, Patel J. Assessment of rose bengal versus riboflavin photodynamic therapy for inhibition of fungal keratitis isolates. 2014. *Am J Ophthalmol*. 158(1):104-107. 2. Jankó B, Arshady A, Duchon A, Duchon M, Miller D, Almeida K, Aguilera M, Amescua G, Patel J, Patel J. Rose bengal and riboflavin mediated photodynamic therapy to inhibit methicillin-resistant staphylococcus aureus keratitis isolates. 2016. *Am J Ophthalmol*. 156:191-202. 3. Arshady A, Kricheldorf H, Nguyen B, Duchon A, Wilson R, Kessler M, Hsu H, Miller D, Patel J. Rose bengal photodynamic antimicrobial therapy (PAMP) treatment for resistant fusarium keratitis. 2017. *Cornea*. 35(14):1514-1518.

## Cross-Linking Corneal Ulcers

	Control	RB only	Irradiation only	Riboflavin PDT	RB PDT
Day 0					
Day 7					

10.1186/1475-2875-2014-144 15911144-76-62 doi: 10.1186/1475-2875-2014-144 76-62 Apr 2014

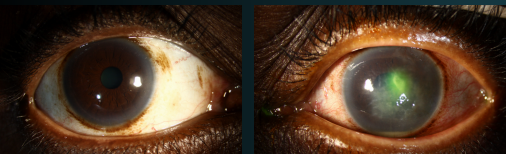
**Assessment of rose bengal versus riboflavin photodynamic therapy for inhibition of fungal keratitis isolates.**

Arshady A<sup>1</sup>, Miller D<sup>2</sup>, Cabot T<sup>2</sup>, Tenza M<sup>2</sup>, Kessler M<sup>2</sup>, Almeida K<sup>2</sup>, Amescua G<sup>2</sup>, Yao S<sup>2</sup>, Patel J<sup>2</sup>

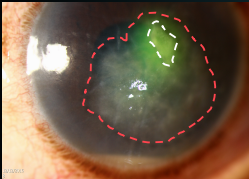
## Case Examples

# CORNEAL ULCERS

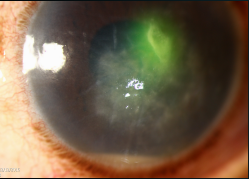
### Case 01



- 52 yo male
- CC: blurred vision OS x 1 week
- Ocular history: Recent stromal keratitis, self-discontinued acyclovir




- Pertinent Findings:
  - Small, anterior infiltrate
  - Small epithelial defect
  - Hypopyon
  - Excessive stromal edema
  - No pain



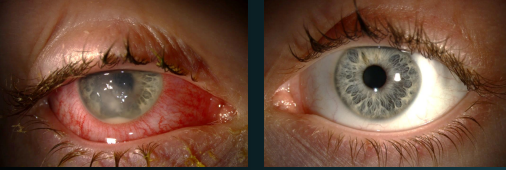
- Management
  - Culture, fortified antibiotics, oral antivirals
- Diagnosis
  - Herpes simplex stromal keratitis
  - Secondary non-sterile infection
    - Streptococcus oralis, sensitive to vancomycin

### Clinical Pearls

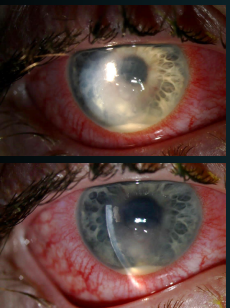
1. Consider herpetic infection if stromal edema is out of proportion to epithelial defect
2. Hypopyon can occur with severe microbial infections, but is also common in herpetic keratouveitis
3. Herpes-associated epithelial defects can provide nidus for secondary bacterial infection



### Case 02

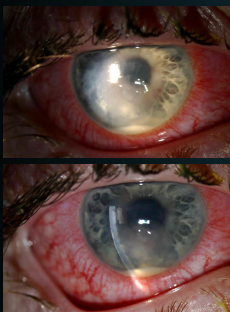


- 19 yo male
- CC: redness, blurred vision, burning OD x 3 days
- Ocular history: slept in CLs last week, rinsed with tap water



- Pertinent Findings:
  - Poorly defined, full-thickness infiltrate
  - 5/10 pain
  - Large epithelial defect
  - Hypopyon
  - Expected stromal edema





- **Management**
  - Culture, fortified antibiotics
- **Diagnosis**
  - No growth
  - Confocal:
    - Suggestive of yeast

### Clinical Course


- Initiated fortified therapy
  - Vancomycin + tobramycin around the clock
- Stalled improvement at 1.5 weeks
  - Added fungal coverage
    - Ketoconazole/fluconazole
- Resumed improvement to resolution

### 2.5 months later




### Clinical Pearls


1. Consider fungal etiology with ill-defined borders
2. If you see initial improvement on antibiotics that stalls, consider fungal co-infection



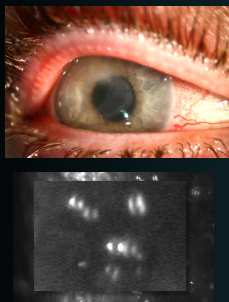
### Case 03



- 49 yo female
- CC: severe eye pain, photophobia, blurred vision OD
- Ocular history: airbag injury to eye 1 month ago while wearing CLs, persistent irritation, worse with increased steroids



- **Pertinent Findings:**
  - Epithelial defect overlying poorly defined infiltrate
  - Minimal stromal edema
  - CL wear
  - 9/10 pain
  - Worse with steroids



**Diagnosis**

- No growth on culture
- Confocal:
  - Double-walled cysts consistent with acanthamoeba keratitis

**Management**

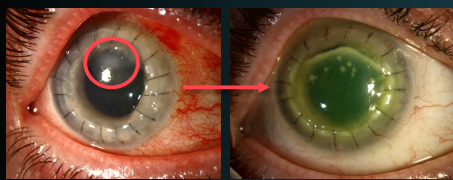
- Fortified antibiotics
- Chlorhexidine + PHMB

Confocal microscopy

### Clinical Course

- Despite heroic efforts, she required therapeutic PKP
- Recurrence was seen in graft at 2 weeks

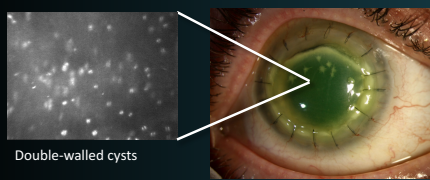
### Clinical Course



Therapeutic PKP  
Question of recurrence in graft

Infectious crystalline keratopathy

### Clinical Course




Double-walled cysts

Infectious crystalline keratopathy

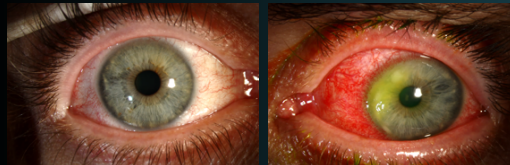
### Clinical Pearls

1. Consider acanthamoeba when:
  - Pain out of proportion to findings
  - Steroids make it worse
2. May require confocal or biopsy for definitive diagnosis
3. Difficult to manage

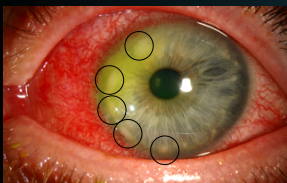


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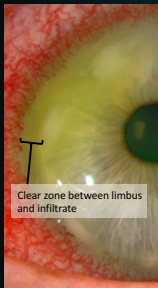
### Case 04



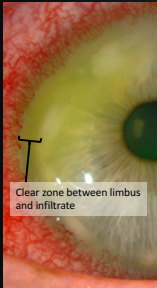
- 45 yo male
- CC: redness, photophobia OS x 4 days
- Ocular history: Polymixin B-trimethoprim use for 3 days without resolution, no contact lens wear



- **Pertinent Findings:**
  - Curvilinear infiltrates with small (<1:1) overlying epithelial defects
  - Minimal stromal edema
  - No stromal thinning
  - Mild pain
  - **Lucid interval between limbus and infiltrates**
  - **Blepharitis**



- **Pertinent Findings:**
  - Curvilinear infiltrates with small (<1:1) overlying epithelial defects
  - Minimal stromal edema
  - No stromal thinning
  - Mild pain
  - **Lucid interval between limbus and infiltrates**
  - **Blepharitis**




- **Diagnosis**
  - Staphylococcal marginal keratitis
- **Management**
  - Broad spectrum topical antibiotic
  - Steroid (i.e. prednisolone acetate 1%)
  - Eyelid hygiene
  - (+/-) doxycycline

5 days later



### Clinical Pearls

1. Consider staph hypersensitivity when you see a lucid interval and lack of corneal thinning
2. Should be managed with antibiotics and steroids
3. Treatment doesn't stop when patient feels better
  - Lid scrubs
  - Warm compresses
  - Artificial tears (lipid-based, emollient)
  - Omega-3 fish oil supplements (EPA+DHA)



3

### Diagnosis & Management

## VIRAL KERATITIS

## Viral Anterior Segment Disease

- Common viral infections
  - Adenovirus
  - Varicella Zoster Virus (VZV)
  - Herpes Simplex Virus (HSV)

## ADENOVIRUS

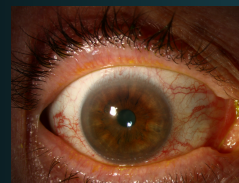
## The Adenovirus Family

- Causes variety of respiratory conditions, rashes, gastroenteritis, etc
- Over 50 serotypes identified, A thru G
  - A: gastrointestinal
  - B/C: respiratory
  - B/D: conjunctivitis
  - E: respiratory and conjunctivitis
  - F and G: gastroenteritis

+ A: 10, 16, 31  
 + B: 3, 7, 11, 14, 16, 21, 34, 35, 50, 55  
 + C: 1, 2, 5, 6, 59<sup>(H)</sup>  
 + D: 8, 9, 10, 13, 15, 17, 18, 20, 22, 23, 24, 25, 26, 27, 28, 29, 30, 32, 33, 36, 37, 38, 39, 42, 43, 44, 45, 46, 47, 48, 49, 51, 53, 54, 56<sup>(H)</sup>  
 + E: 4  
 + F: 40, 41  
 + G: 36<sup>(H)</sup>

## Adenoviral Conjunctivitis

- **Definition**
  - Highly contagious virus-induced red eye with an incubation period of 4-10 days
  - Makes up 65-90% of all viral conjunctivitis infections



## Adenoviral Conjunctivitis

- **Risk Factors**
  - Recent contact with infected individual
    - Via hand-eye contact, respiratory droplets
- **Diagnosis**
  - Clinical examination
  - Point-of-care testing
    - Adenovirus Detector (Adenoplus<sup>®</sup>, Rapid Pathogen Screening)

## Adenoviral Conjunctivitis

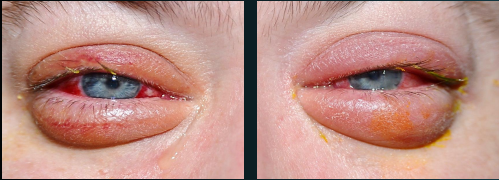
1. **Acute nonspecific follicular conjunctivitis**
  - Conjunctival injection and follicles
  - Tearing, irritation, (+) PAN
2. **Pharyngoconjunctival Fever**
  - Fever, sore throat, headache
  - Most common in children
3. **Epidemic Keratoconjunctivitis**
  - Additional corneal findings (i.e. SEIs, erosions)
  - +/- conjunctival exudates (pseudomembranes)
  - +/- subconjunctival hemorrhages

### Treatment

- **Steroids:**
  - Reduce symptoms, but promotes viral shedding
  - Use in case-by-case situation
- **Topical anti-virals:**
  - Ganciclovir 0.15% gel has been shown to hasten reduction in signs and symptoms of EKC\*
- **Antiseptic povidone-iodine:**
  - Hastens clinical resolution, may reduce long-term sequelae
  - Off-label (*Betadine*®, *Purdue Pharma*)
- **Povidone-iodine/dexamethasone:**
  - Currently in Phase III clinical trials
    - Hastened clinical resolution and adenovirus eradication

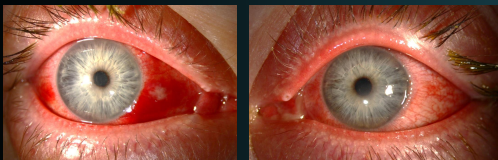
\*Not statistically significant

### Case 01



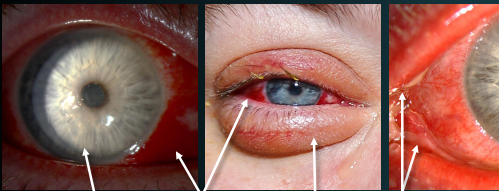
- 37 yo female
- CC: pain, redness, photophobia, eyelid edema OU
- Other history: OS first, then OD. Concurrent URTI.

### Case 01




- 37 yo female
- CC: pain, redness, photophobia, eyelid edema OU
- Other history: OS first, then OD. Concurrent URTI.

### Case 01



Corneal haze, epithelial erosion      Subconjunctival hemorrhage      Severe lid edema      Pseudomembranes

### Case 02



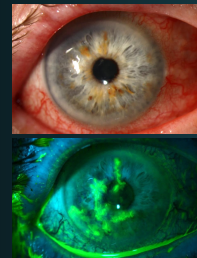
### Epidemic Keratoconjunctivitis

- **Management**
  - (+/-) Betadine rinse (if caught early)
  - Treat SEIs and epithelial defects
    - Steroids
    - Prophylactic antibiotics
  - Peel pseudomembranes
    - Numb, peel, repeat
      - Sheets of inflammation will lead to increased risk of conjunctival scarring and corneal haze after resolution of acute phase

## HERPES SIMPLEX KERATITIS

## Herpes Simplex Keratitis

- SS DNA virus in the herpes simplex group that lies dormant in the sensory ganglia (i.e. trigeminal nerve)
- Painful, acute red eye with photophobia and blurred vision
- Herpes simplex infections are often called “masqueraders”



## Herpes Simplex Keratitis

- **Incidence**
  - 90% of adults are infected with HSV-1 by age 60
- **Risk factors**
  - Stressed immune system
  - CL wear, eye surgery
  - Diabetes
  - Immunocompromised
    - Cancer, organ transplant, medication-induced, HIV/AIDS

## Herpes Simplex Keratitis

- **Recurrence rates of HSK<sup>1</sup>**
  - 32% by 1 year
- **Ocular findings that increase risk of recurrence<sup>1,2</sup>**
  - Stromal keratitis
  - History of prior flare-ups



## HERPES ZOSTER OPHTHALMICUS

## Herpes Zoster Ophthalmicus

- DS DNA virus in the herpes simplex group that lies dormant in sensory ganglia (i.e. trigeminal nerve)
- Painful, acute, vesicular rash in limited dermatome (usually V<sub>1</sub>) with ophthalmic findings

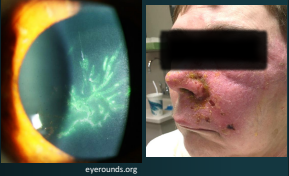


## Herpes Zoster Ophthalmicus

- **Incidence**
  - 98% of adults in United States are infected
  - 1 in 3 will experience zoster during their lifetime
    - 10-20% of Zoster cases are HZO
- **Risk factors**
  - Age > 60
  - Woman
  - Caucasian
  - Immunocompromised
    - Cancer, organ transplant, medication-induced, HIV/AIDS

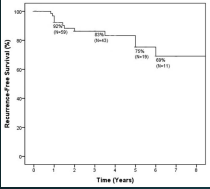
## Herpes Zoster Ophthalmicus

- **Common:**
  - Dermotome blistering and pain
  - Corneal pseudodendrites
  - Conjunctivitis
  - Anterior uveitis
  - Subepithelial infiltrates
    - Usually 1-2 weeks after presentation



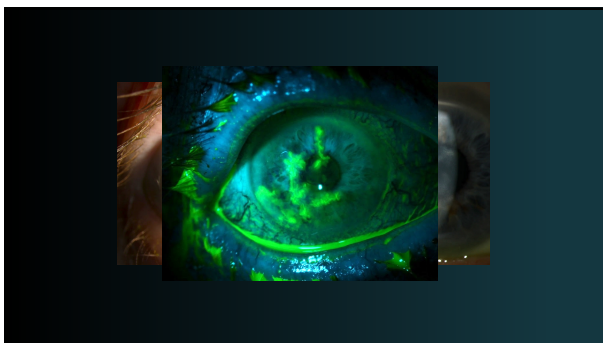
## Herpes Zoster Ophthalmicus

- **Recurrence rates of HZO<sup>1</sup>**
  - 8% by 1 year
  - 31% by 6 years
- **Ocular findings on presentation that increase risk of recurrence<sup>1</sup>**
  - Ocular hypertension
  - Uveitis
- **Zoster Eye Disease Study (2017-2020)**
  - Does suppressive acyclovir reduce recurrence rates
  - Does suppressive acyclovir reduce post herpetic neuralgia



1. Tan ET, Fakhry MM, Chou DS, Sridharan P, Pang CS, Dunn B, Sedor A. Ophthalmology. 2018 Jul;127(7):1492-75. doi: 10.1016/j.ophtha.2018.03.001. Epub 2018 Apr 8. Epidemiology of Herpes Zoster Ophthalmicus: Recurrence and Ocularity.

## MANAGEMENT OF VIRUS-RELATED EYE DISEASE



## Management of Epithelial Keratitis

Antivirals with proven efficacy against HSV	FDA approval HSK	Minimum concentration met (Aqueous)	Typical dosage
Ganciclovir 0.15% gel	Yes	Not clear	5x/day, then 3x/day for 1 week
Trifluridine drops	Yes	Yes*	Q2h
Acyclovir ointment	No	Yes	5x/day for 1-2 weeks
Oral Acyclovir	No	Yes	HSV: 400mg 5x/day HZO: 800mg 5x/day
Oral Valacyclovir	No	Yes	HSV: 500mg 3x/day HZO: 1000mg 3x/day
Oral Famciclovir	No	Yes	HSV: 250mg 3x/day HZO: 500mg 3x/day

\*if there is an epithelial defect

## Management of Stromal Keratitis

Antivirals with proven efficacy against HSV	FDA approval HSK	Typical dosage
Oral Acyclovir	No	HSV: 400mg 5x/day HZO: 800mg 5x/day
Oral Valacyclovir	No	HSV: 500mg 3x/day HZO: 1000mg 3x/day
Oral Famciclovir	No	HSV: 250mg 3x/day HZO: 500mg 3x/day

Additional topical steroid therapy with long taper indicated for stromal, endothelial, or keratouveitis

## Prevention of Herpes Zoster

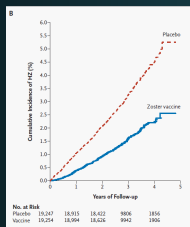
### Vaccination

1. Zostavax® (Merck & Co)
  - Live, attenuated virus
2. Shingrix® (GlaxoSmithKine)
  - Recombinant viral subunit

## Prevention of Herpes Zoster

### Zostavax®

- Shingles Prevention Study (2005)<sup>1</sup>
  - CDC recommended vaccination for those 60 years and older
  - 51% reduction in incidence of Zoster across age groups
  - 66% reduction in incidence of post-herpetic neuralgia (PHN)
  - Works better in younger patients



## Prevention of Herpes Zoster

### Shingrix®

- CDC recommends vaccination those 50 years and older
  - Also recommended for those who have received Zostavax previously
- >90% reduction in incidence of Zoster across age groups
- Similar effectiveness in all age categories
- Requires injection + booster

## Prevention of Herpes Zoster

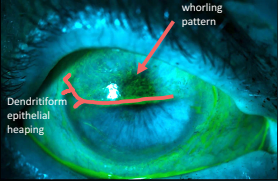
Age Group (Years)	Zostavax		% Efficacy (95% CI)	Shingrix		% Efficacy (95% CI)
	Incidence Rate of HZ per 1,000 Person-Years	Incidence Rate of HZ per 1,000 Person-Years		Incidence Rate of HZ per 1,000 Person-Years	Incidence Rate of HZ per 1,000 Person-Years	
Overall	11.1	5.4	51%	9.1	0.3	97.2%
50-59	-	-	-	7.8	0.3	96.6%
60-69	10.8	3.9	64%	10.8	0.3	97.4%
70-79	11.4	6.7	41%	9.4	0.2	91.3%
>80	12.2	9.9	18%	-	-	-

\*Data adapted from drug inserts

Herpetic Impersonators  
**PSEUDO-PSEUDO-DENDRITES**



### Case 01



Epithelial whorling pattern

Dendritiform epithelial heaping

70yof

**Ophthalmic history:**

- Bilateral panuveitis, uveitic glaucoma

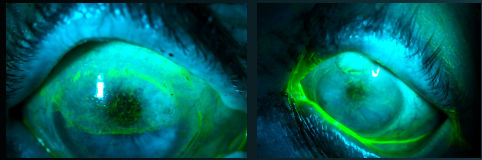
**Ophthalmic surgery:**

- Pars plana vitrectomy OU
- Cataract surgery OU
- Trabeculectomy OS

**Topical medications:**

- Brimonidine, Travatan Z, Timolol-dorzolamide, Lotemax

### Case 01

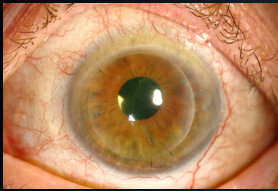


History of bilateral uveitis  
History of 3 daily glaucoma drops  
History of ophthalmic surgery (x2 OD, x3 OS)

Bilateral corneal epithelial whorling  
Quiet anterior chamber

Limbal stem cell deficiency

### Case 02

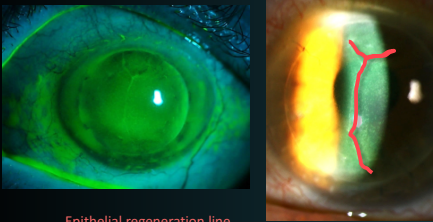


66yof

**Ophthalmic history**

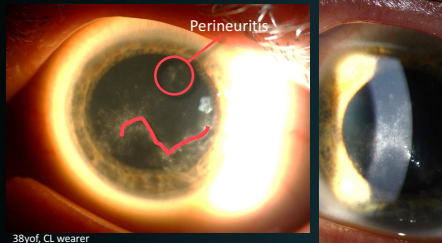
- Primary open angle glaucoma OU
- s/p penetrating keratoplasty for PBK OS
- Recent corneal abrasion

### Case 02



Epithelial regeneration line


### Case 03



Perineuritis

38yof, CL wearer

### Case 03



Confocal revealed acanthamoeba cysts

## Herpetic Impersonators

- Beware of “pseudo-pseudo dendrites”
  - Limbal stem cell deficiency
    - Look for whorled epithelium with a history
  - Epithelial regeneration lines
    - After corneal epithelial insult
  - Acanthamoeba keratitis
    - Signs of perineuritis and pain will clue you in

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## Questions/Comments?

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Thank you for your time and attention.