

المؤتمر السنوي الدولي للجمعية المصرية
INTERNATIONAL CONGRESS OF THE

EGYPTIAN OPHTHALMOLOGICAL SOCIETY

EOS 2023



HSV KERATITIS is NOT that SIMPLEX!!

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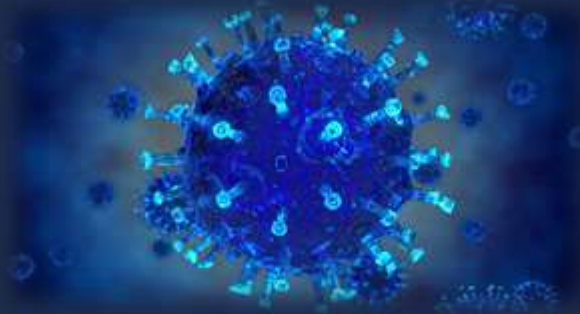
Introduction...

- **Human Herpesviruses:**
 - HSV-1, 2
 - VZV
 - EBV
 - CMV
 - HHV-6
 - HHV-7
 - HHV-8/KSHV

- **Various Human Diseases:**

Mononucleosis, Roseola, Chickenpox and Ocular Involvement

- **Achieve a state of latency (inactivity with occasional reactivation)**

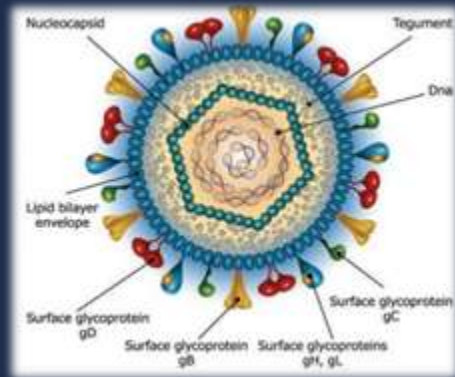
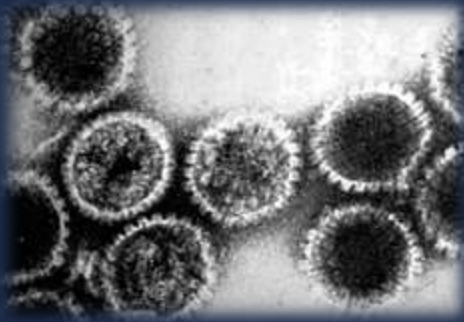


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Herpes Simplex Virus (type I & II) ...

Neurotropic Viruses
(Attack Nervous System Preferentially)



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Epidemiology of HSV keratitis* ...

- Leading infectious cause of blindness in the world
- 2nd cause of blindness after cataract in developing countries
- In **Developed Countries**: Incidence from **10 - 30 / 100,000** population/year
- **Global incidence** 1,5 million (40,000 new cases/year)



Recurrence rate after the first episode:

- 9.6% at 1 year
- 22.9% at 2 years
- 63.2% at 20 years

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*McQuillan G, Kruszon-Moran D, Flagg EW, Paulose-Ram R. Prevalence of Herpes Simplex Virus Type 1 and Type 2 in Persons Aged 14-49: United States, 2015-2016. *NCHS Data Brief*. 2018(304):1-8.

PATHOGENESIS...

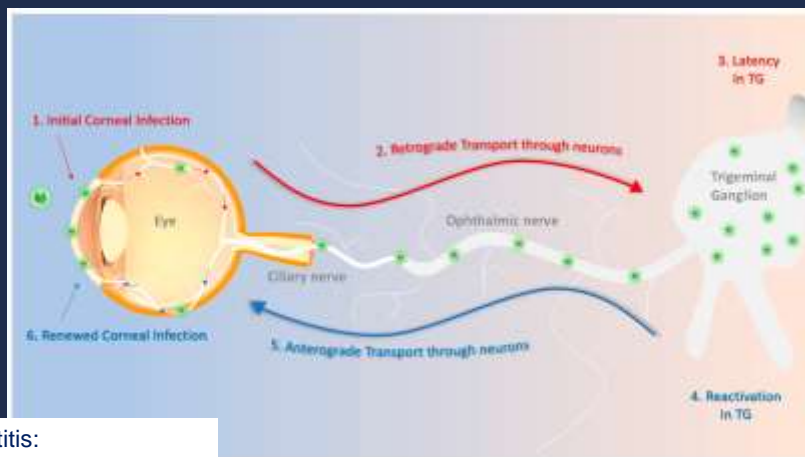
Primary infection (Childhood Usually)

- ❖ Asymptomatic
- ❖ Oral
- ❖ URT
- ❖ Ocular surface
(conjunctivitis or blepharo-conjunctivitis)



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PATHOGENESIS...



- ↓ Type I interferon (IFN-I)
- ↓ Host immune response

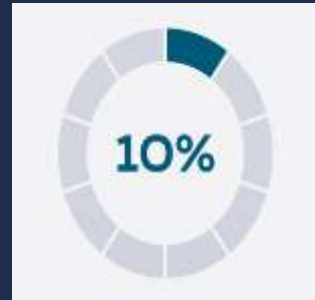
- Stress
- Sun exposure or other UV light exposure
- Fever
- Trauma (injury or surgery)
- Menstruation (hormonal disturbances)
- Certain medications, LVC & Cross Linking

HSV keratitis:

- Epithelial (commonest)
- Stromal
- Endothelial

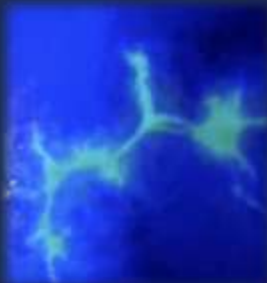
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HSV keratitis may present bilaterally in up to **10%** of individuals and it is more likely to develop in: children, Atopic and immunocompromized individuals.



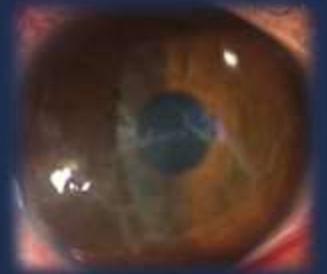
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I. EPITHELIAL KERATITIS (Epitheliitis)...

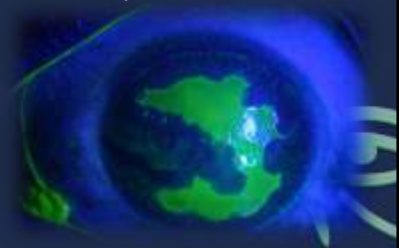


- Active Viral Replication

- Single or multiple **Arborizing Dendritic** Epithelial Ulcers with terminal **bulbs** (raised above corneal surface)



- Coalesce to form **Geographic Ulcer** (Steroids & Immunosuppression)



Differentiate the Dendrite...

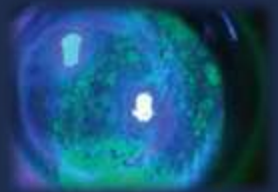
- **Varicella Zoster (Herpes Zoster Ophthalmicus)...**
 - ❖ More epithelial, No central ulcer, No terminal Bulbs.
- **Early Fungal/Acanthamoeba keratitis...**
 - ❖ Not responding to topical antiviral ttt
 - ❖ Scrapping for **staining and culture**



Epithelial Keratitis...Treatment..

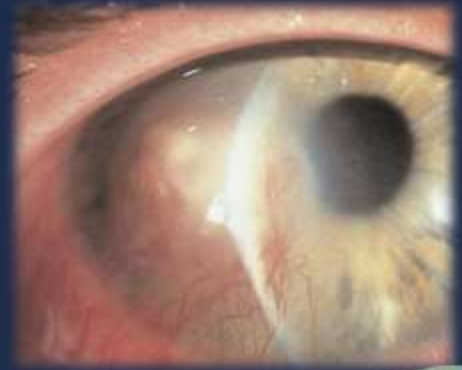
- Topical Antivirals- **Acyclovir 3% E** ... **5% ED** - 5/daily/2 weeks
- Prolonged ttt- cornea
- Oral Acyclovir 400 mg ... children-calculate dose)
- **Debridement** (2mm)... reduce ... long term complications
(Not effective if alone)

OVER 90 % HEALING



II. Stromal Keratitis...

- **Immune Mediated** / Inflammatory response to the HSV/activation
- Infiltration of **myeloid-derived cells, CD4+ T-cell and NK cells**



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Types of Stromal Keratitis...



NECROTIZING



NON-NECROTIZING

Diminished Corneal Sensation

- | | |
|--|---|
| ✓ Overlying epithelial defect | ✓ No epithelial defect |
| ✓ Stromal melting and thinning | ✓ No Stromal melting |
| ✓ Immune mediated destruction / viral ?? | ✓ Immune/interstitial disease |
| | ✓ Vascularization +/- lipid keratopathy |

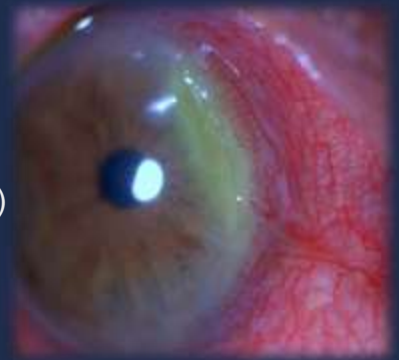
✓ Role of **ANTIVIRAL ttt SYSTEMIC**

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HSV marginal keratitis...

- Special, rare form of stromal and epithelial keratitis
- Difficult to differentiate from other forms of MK (PUK)
- Laboratory testing (PCR)
- Diminished corneal sensation is a clue (DD)



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Endotheliitis... Disciform Keratitis...

- Host Immune response-endothelial dysfunction +/- Wessley immune ring

Diminished Corneal Sensation

- AC reaction (KPs), IOP rise - Trabeculitis
- Topical steroids + systemic antivirals



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DD.. Endotheliitis...

Endothelial specific inflammation:

- I. KPs
- II. Localized edema
- III. Ac inflammation
- IV. Endothelial damage

- I. Herpes simplex virus (HSV)
- II. Varicella zoster virus (VZV)
- III. Cytomegalovirus (CMV)

DIFFICULT



- Shiraishi A, et al. Am J Ophthalmol, 2007
- Kobayashi, et al. Am J Ophthalmology, 2012



Diagnostic Dilemma...

Active Disease

- **PCR (S. 100%)** of HSV should be attempted if:
 - Ulcer may have dendritic appearance (without a prior confirmed diagnosis)
 - Corneas with a history of HSV developed a new ED without characteristic features
- **Scraping:** for obtaining a corneal sample for laboratory investigation
 - **Viral culture (Gold standard)**
 - **Immunohistochemistry (S. 80%)**
 - **Serology for Ab (For exclusion)**
- **(Co-infection or Different infection)**



Challenges in diagnosis...



Inactive disease: to determine if corneal scars are herpetic in origin ???

Keratoplasty
Explaining the prognosis

CXL
Reactivation

Refractive procedure
Reactivation

PTK
Reactivation

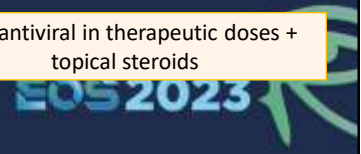
Cataract surgery
steroids

- **History of Recurrent Keratitis**
- **Diminished Corneal Sensation**



HSV Keratitis ttt.. Be Wise Layer Wise...

HSV CATEGORY	COMMON NOMENCLATURE	BASIC TREATMENT APPROACH
Epithelial Keratitis	<ul style="list-style-type: none"> •Dendritic keratitis •Geographic Keratitis 	Antiviral (topical+/- systemic)-debridement
Stromal Keratitis without Ulceration	<ul style="list-style-type: none"> •Interstitial keratitis •Immune stromal keratitis •Non necrotizing stromal keratitis 	Oral antiviral prophylaxis+Topical steroids
Stromal Keratitis with Ulceration	<ul style="list-style-type: none"> •Necrotizing stromal keratitis 	Oral antiviral in therapeutic doses + topical steroids
Endothelial Keratitis	<ul style="list-style-type: none"> •Disciform keratitis •Endotheliitis 	Oral antiviral in therapeutic doses + topical steroids



Antiviral Agents for HSV keratitis...

ORAL ANTIVIRALS

Agent	Treatment dose	Prophylaxis Dose
Acyclovir	Adults: 400 mg 3-5/day Children: 12-15 mg/kg/day in 3-5 divided doses	400 mg twice daily
Valacyclovir	500 mg 3/day	500 mg once daily

TOPICAL ANTIVIRALS

Agent	Treatment dose (short term use only)
Acyclovir 3%	5/ day/ 2 weeks
Ganciclovir 0.15%	5/day/ 2 weeks (less surface toxicity)



Ophthalmology

Volume 101, Issue 12, December 1994, Pages 1871-1882



Herpetic Eye Disease Study: A Controlled Trial of Oral Acyclovir for Herpes Simplex Stromal Keratitis

- Potency of steroid ... according to **level of corneal inflammation**
- Epithelial defect.... **Delay the onset of steroid use**
- Systemic antiviral coverage (**Roughly Single Drop=200mg**) (**maximum 4 drops**)
- Instead of sudden discontinuation of stronger steroid, consider replace with a weaker one (**avoid a rebound increase in inflammation**)
- Gradual tapering is mandatory over at **least 10 weeks**

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For How Long Prophylactic oral Acyclovir Can Be Used in Preventing Recurrence of HSV Keratitis?



CLINICAL SCIENCES

Oral Acyclovir for Herpes Simplex Virus Eye Disease

Effect on Prevention of Epithelial Keratitis and Stromal Keratitis

Conclusions: Long-term suppressive oral acyclovir therapy reduces the rate of recurrent HSV epithelial keratitis and stromal keratitis. Acyclovir's benefit is greatest for patients who have experienced prior HSV stromal keratitis.

tients to receive oral acyclovir, 800 mg/d, and 346 to receive placebo; and followed up patients during a 12-month treatment period for the development of HSV eye disease.

Results: The cumulative probability of a recurrence of any type of ocular HSV disease during the 1-year treatment period was 19% in the acyclovir group compared with 32% in the placebo group. Sixteen patients in the acyclovir group and 30 in the placebo group had more

The benefit in preventing stromal keratitis was seen solely among patients with a history of stromal keratitis.

Conclusions: Long-term suppressive oral acyclovir therapy reduces the rate of recurrent HSV epithelial keratitis and stromal keratitis. Acyclovir's benefit is greatest for patients who have experienced prior HSV stromal keratitis.

Arch Ophthalmol. 2000;118:1030-1036



Neurotrophic Ulcer / Metaherpetic Ulcer...

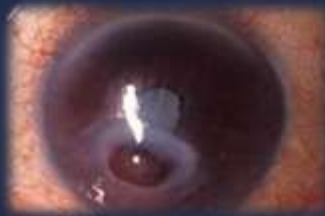
Different entity (No virus activation, Lower inflammatory level)

Dua et al.* have proposed a 3-stage classification system:

❖ Mild NK (epithelial / absence of epithelial defect)

- Chronic viral trigeminal ganglionitis
- Toxicity from antiviral medications
- Lack of NGF
- Nerve damage (Recurrent Keratitis)

Corneal Hypo-aesthesia or Anesthesia

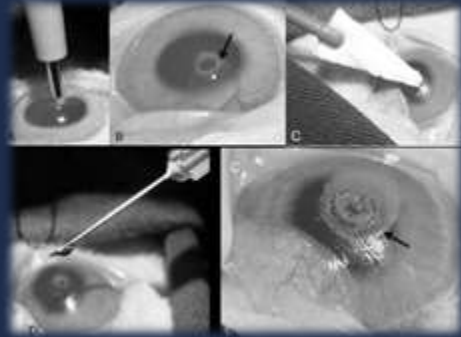


*Dua HS, Said DG, Messmer EM, et al. Neurotrophic keratopathy. Prog Retin Eye Res 2018;66:107–31.

MANAGEMENT of ADVANCED PERFORATED CASES...

I. Small Off-Axis Perforation:

Tissue adhesive & BCL or AA grafting

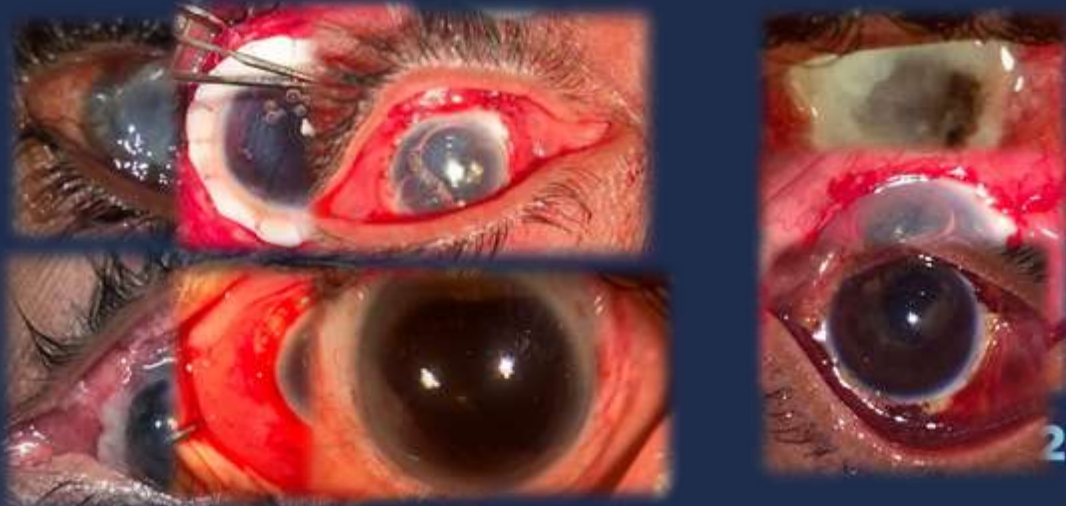


II. Larger Peripheral Perforation

Patch Grafts ... Eccentric Grafts



Hot therapeutic KP & Croneoscleral grafts...



HSV & HZV Differentiation...

- Important & Relevant- **Obvious skin lesions**- Immunocompromised
- Whenever in doubt **over treat as VZV- 800mg Acyclovir 5/day for 1 month**
- Stromal & endothelial involvement/ **Difficult**
- **Serological** tests - PCR



IN COVID-19 pandemic...

Increased Incidence of HSV Reactivation....!!!

DOI: 10.14744/ijq.2022.81994
 Sryoglu Eye J. 2022; 7(2): 140-142

Cureus Open Access Case Report DOI: 10.7755/cureus.20907

Received: 2 April 2022 | Revised: 31 August 2022 | Accepted: 21 September 2022
 DOI: 10.18001/ijq.81994

Herpetic Keratitis and Corneal Endothelitis Following COVID-19 Vaccination: A Case Series

medicina Original Article

Spectrum of herpetic eye pandemic

Her vaccines

MDPI

Hindawi

Case Report
Recurrence of Herpetic Keratitis after COVID-19 Vaccination: A Report of Two Cases

Ali Mahdavi Fard,¹ Jeffrey Desilets,¹ and Sangita Patel^{1,2}

ABSTRACT
Purpose: To analyze clinical presentation, outcome and upsurge in the ac Herpes Zoster Ophthalmicus) cases during coronavirus disease 2019 (COVID-19) pandemic. **Methods:** We reviewed the medical records of all cases of acute Herpes Zoster Ophthalmicus (HZO) from April 2020 to August 2022. **Results:** We had 71 patients being HZO. The majority (84.78%) of the patients were <50 years of age.

Take Home Messages....

- HSK is a major cause of blindness in developing countries.
- **Multiform occurrence / challenging in diagnosis in clinical practice.**
- In any patient with stromal scar, examine corneal sensation 1st before prescribing topical steroids.
- **While managing HSK be wise layer wise.**
- Ocular surface homeostasis should be always considered.



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**Thank You For
Your Attention**

