FOCAL MICROPULSE LASER FOR MANAGING MACULAR EDEMA

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1

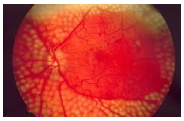
LASERS AND THE EYE

- Laser impact in the eye depends on:
  1. Wavelength
  2. Irradiance (energy/area)
  3. Pulse duration
  4. Tissue being targeted

2

PRINCIPLES OF CONVENTIONAL LASER PHOTOCOAGULATION

- Increases the temperature of the retinal tissues, creating a burn/scar at the level of the RPE
- Consequences:
  - Destruction of overlying photoreceptors
  - Decreases hypoxia and thus vascular endothelial growth factor (VEGF) levels
- Needed in cases of:
  - Retinal tears/holes
  - Increased levels of VEGF
- Risks associated:
  - Visual field defects
  - Secondary choroidal neovascular membrane (CNVM)
  - Epiretinal and subretinal fibrosis



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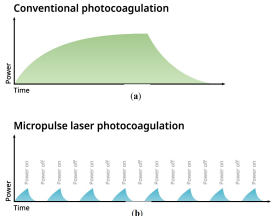
COMPARISON OF CONVENTIONAL VS. SUBTHRESHOLD MICROPULSE PHOTOCOAGULATION



- Conventional laser has a continuous wave pulse of 0.1-0.5 seconds
- In micropulse mode, a train of repetitive short laser pulses is delivered within the same time frame, but the length of each pulse is 100-300 microseconds (0.0001-0.0003 seconds)

4

PRINCIPLES OF FOCAL/MICROPULSE LASER TREATMENT

- The laser impact is divided into many repetitive short "on" and "off" impulses to deliver the minimum laser irradiance to allow the retinal tissue to cool down
- Thus, the temperature to achieve protein denaturation is not exceeded
- Unlike conventional laser treatment, micropulse laser leaves no visible traces on the retina
- In essence, it is tissue-sparing and scarring seems to not be necessary in order to achieve a therapeutic effect
- Types of subthreshold micropulse laser: 810nm diode laser or 577nm
  - Both are negligibly absorbed by xanthophyll pigment which allows for treatment near the fovea

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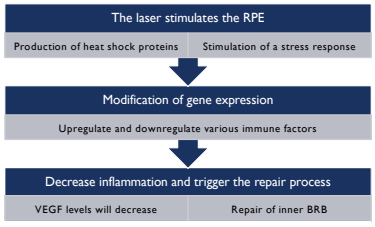
MECHANISM OF FOCAL/MICROPULSE LASER TREATMENT



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PRINCIPLES OF FOCAL/MICROPULSE LASER TREATMENT

- Treatment is applied with a contact lens and laser in office
- Total treatment time is less than 1 minute
- No known risk or adverse effects associated with laser treatment
- The effect of micropulse laser is more significant in patients whose initial macular thickness is less than 400um
- Effects of subthreshold micropulse laser lasts ~3 months
- Cost is less expensive (when compared to anti-VEGF injections)

7

CLINICAL APPLICATIONS IN TREATING MACULAR EDEMA

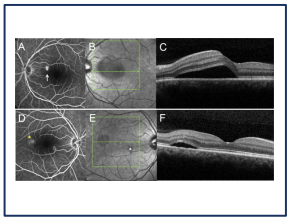
- Macular edema, if persistent, can damage photoreceptors and decrease visual acuity
- Thus, the goal of treatment is to decrease duration and extent of edema present

- Clinical Applications:

1. Central Serous Chorioretinopathy (CSCR)
2. Diabetic Macular Edema (DME)
3. Macular Edema secondary to Retinal Vein Occlusion
4. Others
   1. Proliferative Diabetic Retinopathy
   2. Wet Macular Degeneration
   3. Parafoveal Telangectasia

8

CENTRAL SEROUS CHORIORETINOPATHY



- Serous detachment of the neurosensory retina
- Causes: Mainly idiopathic but associations exist with young males (20-50), type A personality, use of exogenous steroids, or Cushing disease
- Acute cases are often self-limiting and invasive treatment is delayed for 3-6 months
- Possible treatments:
  1. Observation
  2. Medications (i.e. spironolactone)
  3. Photodynamic therapy (PDT)
  4. Laser photocoagulation
  5. Micropulse laser therapy

9

CENTRAL SEROUS CHORIORETINOPATHY

- PDT used in patients with juxtafoveal or subfoveal leakage (as determined by an FA)
  - Procedure involves IV administration of verteporfin in combination with a low power infrared laser over a long duration
  - Not commonly used anymore
  - Complications/Disadvantages:
    - Possible RPE atrophy and/or CNVM development
    - 5% vision loss noted in TAP study (Treatment of AMD using PDT)
    - Labor intensive (IV infusion and post-treatment observation)
    - Higher cost from verteporfrin dye use
    - Dye is phototoxic – Patient to avoid sunlight for 5 days

10

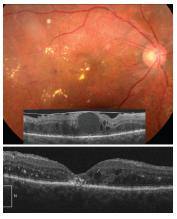
CENTRAL SEROUS CHORIORETINOPATHY

- Laser photocoagulation used in patients with extrafoveal leakage
  - Will accelerate resolution of fluid but will not improve VA and cause further complications
  - Lower success rate than micropulse
- Micropulse Laser:
  - Most studies show treatment to be effective in decreasing central retinal thickness and improving VA
  - Allows for earlier intervention and thus earlier resolution of macular edema that can be repeated several times since it is non-damaging
  - Micropulse laser has higher efficacy in improving both morphology and visual function compared to PDT or no treatment

11

DIABETIC MACULAR EDEMA

- The leading cause of vision loss in diabetic patients is DME, which can occur at any stage of diabetic retinopathy
- Most successful treatments for central DME are anti-VEGF injections (first line) and/or steroid injections
- Micropulse laser therapy can be used as a stand-alone treatment in cases of very mild or noncentral macular edema
  - Morphological improvement is better than a functional one
- More commonly though it is used soon before or after anti-VEGF injections
  - Reduces the amount and burden of additional injections by increasing the duration between injections
  - 'Resensitizes' the retina to anti-VEGF medications
  - Better VA was maintained
- Provides an option in patients who respond suboptimally to or struggle with anti-VEGF injections (high costs, poor compliance, contraindicated for systemic reasons)



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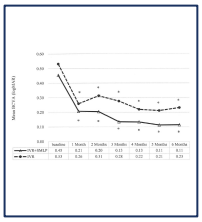
MACULAR EDEMA SECONDARY TO RETINAL VEIN OCCLUSION



- Retinal vein occlusions are the second most common retinal vascular disease after diabetic retinopathy with the main cause of reduced visual acuity being macular edema
- Most successful treatments are anti-VEGF injections and/or steroids
- Similar to DME, micropulse laser provides an option for adjunctive therapy to decrease the overall number of injections needed
- Intravitreal injections and micropulse laser treatment in macular edema due to BRVO has been shown to significantly decrease edema and increase visual potential when compared to injections alone

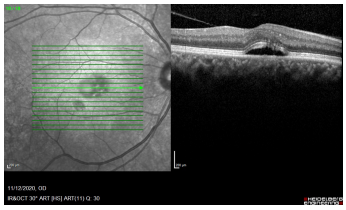
13

CASE EXAMPLES

14

CASE 1: CHRONIC CSCR

- 60-year-old Indian male
- Hx of chronic CSCR in right eye
- Reported 'shadow' in vision
- Focal micropulse laser performed 11/19/20



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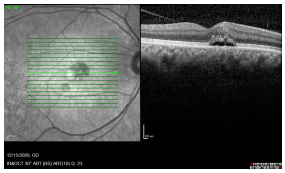
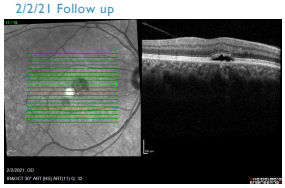
CASE 1: CHRONIC CSCR

12/15/20 Follow up



2/2/21 Follow up

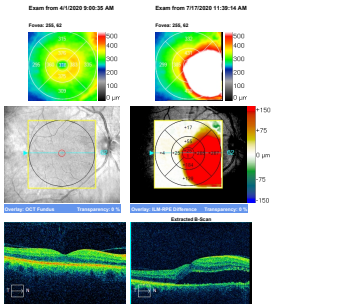


- Vision remained stable at 20/25 but patient reported improvement in symptoms at 2/2/21 follow up.

16

CASE 2: CSCR

- 58-year-old Caucasian male
- Hx of NPDR
- Seen previously in the retina clinic (VA 20/25)
- 7/17/20 visit:
  - VA: 20/80-2 OD
  - Large area of serous detachment between ONH and macula
  - Treated with focal laser
  - Had to rule out peripapillary CNVM with FA



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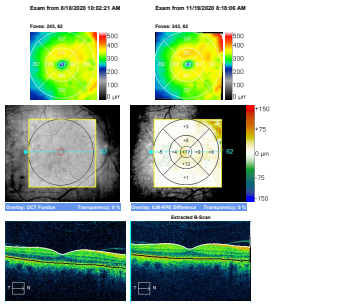
CASE 2: CSCR

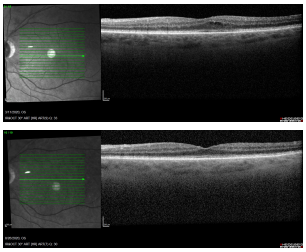
- 8/18/20 Follow-up:
  - VA improved to 20/40+1
- 11/19/20 Follow-up:
  - VA improved to 20/25



18

CASE 3: DIABETIC MACULAR EDEMA

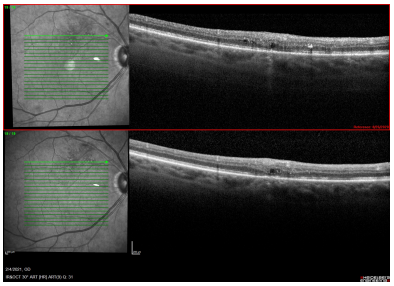
- 85-year-old Caucasian female
- Type 2 Diabetes Mellitus
- DME treated in different times with just focal micropulse laser
- DME present OS on 3/11/20
- SC VA: 20/50
- Focal Laser on 5/5/20
- 8/26/20 and 2/4/21 Follow ups: Mild NPDR with no DME
- Improvement in VA to 20/40



19

CASE 3: DIABETIC MACULAR EDEMA

- 8/26/20 follow up: OD shows noncentral DME
- Focal laser on 9/10/20
- Follow up on 2/4/21 shows slight improvement in DME
- Vision remained stable at 20/25



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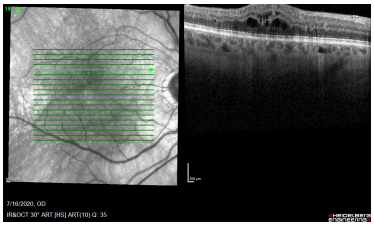
CASE 4: BRVO

- 69-year-old Caucasian male
- BRVO OD onset in 2018
- Long history of Avastin and focal mircopulse laser treatment
- Treatment:
  - 1/2/20: Avastin Injection
  - 3/13/20: Avastin Injection
  - 5/19/20: Avastin Injection
  - 7/16/20: Avastin Injection
  - 7/23/20: Laser treatment
  - 9/10/20: Avastin Injection



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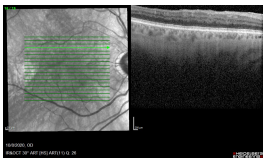
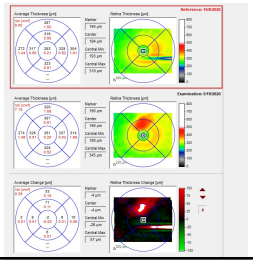
CASE 4: BRVO

10/08/20 Follow up

- Improvement in VA from 20/50 to 20/30





22

CONCLUSIONS

- Subthreshold micropulse laser is a non-invasive and effective treatment in selective cases
- It is less expensive and contrary to conventional laser photocoagulation, it leaves retinal cells intact
- High efficacy in resolving serous fluid in CSCR
- Can be used as adjunctive therapy in DME and retinal vein occlusions
- Micropulse laser can play an important role in treatment of macular edema, even in an era dominated by anti-VEGF therapy

23

ACKNOWLEDGEMENTS AND REFERENCES

- Thank you to Specialty Eye Institute for letting me be their resident and Dr. Gordon for letting me shadow her each week

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24

COMMON OCULAR DISEASES & TREATMENT

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1

FINANCIAL DISCLOSURE:

- None

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PRESENTATION OUTLINE

- Review various common ocular infections and diseases
- Discuss the clinical presentation and management of these ocular diseases
- Review the treatment and management of these conditions, including common pharmacological treatment modalities

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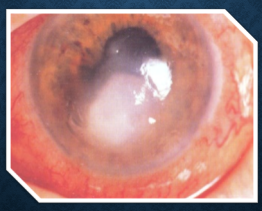
WHAT IS THIS?



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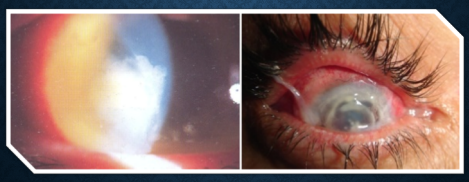
AND THESE?



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BACTERIAL KERATITIS OR CORNEAL ULCER?

- Bacterial Keratitis is also often referred to as a 'corneal ulcer'
- In practice, these terms are not directly interchangeable because a cornea may harbor a bacterial infection (i.e bacterial keratitis) without having a loss of tissue (an ulcer) *and* a cornea may have an ulcer without a bacterial infection

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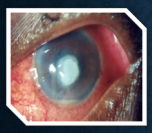
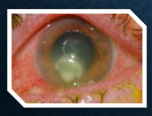
CORNEAL ULCER





- **Etiology**: fungi, viruses, mycobacteria and protozoa bacteria are the most common cause of infectious keratitis
- Risk factors for bacterial keratitis are those that cause disruption of the integrity of the corneal epithelium
- CL wear is most common risk factor 19%-42%
- **Other risk factors**: trauma, contaminated ocular solutions, changes in the corneal surface (from dry eye, eyelid misdirection/exposure, blepharitis and viral keratitis

7

- Bacterial keratitis usually develops only when ocular defenses have been compromised
- Some bacteria are able to penetrate a healthy corneal epithelium, this includes:
  - Neisseria gonorrhoeae
  - Neisseria meningitidis
  - Corynebacterium diphtheriae
  - Haemophilus influenzae

8

RISK FACTORS

- Contact lens wear, particularly if extended, is the most significant risk factor. Corneal epithelial compromise secondary to hypoxia and minor trauma is thought to be important, as is bacterial adherence to the lens surface. Soft lens wearers are at higher risk than those that are rigid lens users
- Trauma, including refractive surgery, has been linked to bacterial infection
- Ocular surface disease such as herpetic keratitis, bullous keratopathy, dry eye, chronic blepharitis, trichiasis, entropion, exposure, severe allergic eye disease and corneal anesthesia

9

COMMON PATHOGENS

- Pseudomonas aeruginosa is a ubiquitous gram-negative bacillus (rod) The infection is typically aggressive and is responsible for over 60% of contact lens-related keratitis
- Staphylococcus aureus is a common gram-positive and coagulase-positive (nasal mucosa, skin and conjunctiva)
- S. pyogenes is a common gram-positive found in the throat
- S. pneumoniae (pneumococcus) is a gram-positive of the upper respiratory tract. Infections with streptococci are often aggressive

10

SIGNS AND SYMPTOMS

SIGNS:

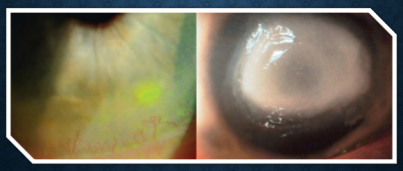
- STROMAL EDEMA
- FOLDS IN DESCEMET MEMBRANE
- ANTERIOR UVEITIS (COMMONLY WITH A HYPOPYON AND POSTERIOR SYNECHIAE IN MODERATE-SEVERE KERATITIS)
- PLAQUE-LIKE KERATIC PRECIPITATES THAT FORM ON THE ENDOTHELIUM CONTIGUOUS WITH THE AFFECTED STROMA
- CHEMOSIS AND EYELID SWELLING IN MODERATE-SEVERE CASES

SYMPTOMS:

- PAIN
- PHOTOPHOBIA
- BLURRED VISION
- MUCOPURULENT OR PURULENT DISCHARGE

11

EPITHELIAL DEFECT WITH INFILTRATE INVOLVING A LARGER AREA AND SIGNIFICANT CIRCUMCORNEAL INJECTION



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LARGE CORNEAL INFILTRATION IN BACTERIAL KERATITIS

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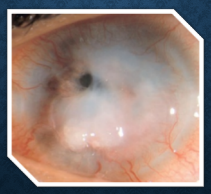
SEVERE ULCERATION MAY LEAD TO DESCEMETOCOELE FORMATION AND PERFORATION, PARTICULARLY IN PSEUDOMONAS INFECTION



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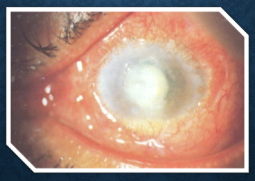
PSEUODOMONAS KERATITIS WITH HYPOPYON



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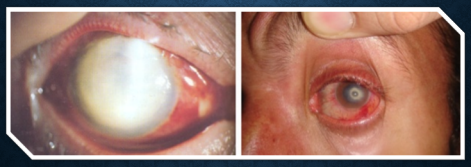
ADVANCED PSEUDOMONAS KERATITIS



16

DIFFERENTIAL DIAGNOSES

- Keratitis due to other microorganisms (fungi, acanthamoeba, stromal herpes simplex keratitis and mycobacteria)
- Marginal keratitis
- Sterile inflammatory corneal infiltrates associated with contact lens wear
- Peripheral ulcerative keratitis
- Toxic keratitis

17

THE WORK-UP MAY INCLUDE:

- Corneal scraping for culture & sensitivity
- Conjunctival swabs
- Contact lens cases, as well as bottles of solution and lenses themselves..(The case *should not* be cleaned by the patient first!)
- Gram staining
- If small infiltrate without epithelial defect & away from visual axis, then no work up required

18

ANTIBIOTICS AND DUOTHERAPY

What is duotherapy?

- Combination of two fortified antibiotics, typically a cephalosporin and an aminoglycoside, in order to cover common Gram-positive and Gram-negative pathogens.

Abx Sensitivity needed ?

- Aggressive disease or if microscopy suggests streptococci or a specific microorganism that may be more effectively treated by a tailored regimen

Disadvantages of fortified antibiotics include high cost, limited availability, contamination risk, short shelf-life and the need for refrigeration

19

MANAGEMENT AND TREATMENT

Single agent vs. double agent Rx

- Gram-positive agent
  - Fortified cefazolin
  - Fortified vancomycin
- Gram-negative agent
  - Fortified gentamycin
  - Fortified tobramycin
  - Fortified amikacin

20

SINGLE AGENT Rx: FLUOROQUINOLONES

- Broad-spectrum (early generations less active against gram-positives)
- Commercially available
- Shown in several studies to be as efficacious as double-agent fortified Abx, with less epithelial toxicity
- Stable at room temperature

COMMON FLUOROQUINOLONES	
CIPROFLOXACIN (CILOXAN)	1ST GENERATION
OFLOXACIN (OCUFLOX)	2ND GENERATION
LEVOFLOXACIN (IQUIX, QUIXIN)	3RD GENERATION
MOXIFLOXACIN (VIGAMOX)*	4TH GENERATION
GATIFLOXACIN (ZYMAR)	4TH GENERATION
BESIFLOXACIN (BESIVANCE)	4TH GENERATION

*1 DS minutes x 5 (loading dose) then Q hour for first day
Reduce Abx as clinical situation allows (to Q2 hour, then Q6hr)
Discontinue from Q6hr, don't taper (promotes resistance)

21

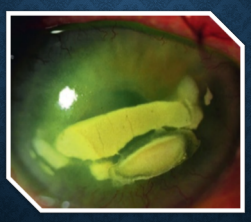
THE BOTTOM LINE

Single agent therapy without cultures probably adequate for most small, mild ulcers- especially those located peripherally

- How soon to evaluate?
  - same day
  - central more urgent than peripheral
- Do you need oral Antibiotics?
- Follow up: Daily
- If no improvement, consider referral→ culture and fortified abx

22

CIPROFLOXACIN CORNEAL PRECIPITATES



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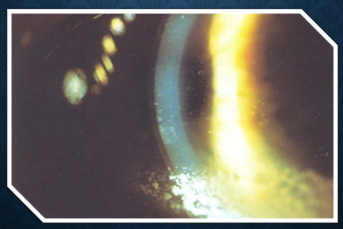
DEPOSITS OF CIPROFLOXACIN



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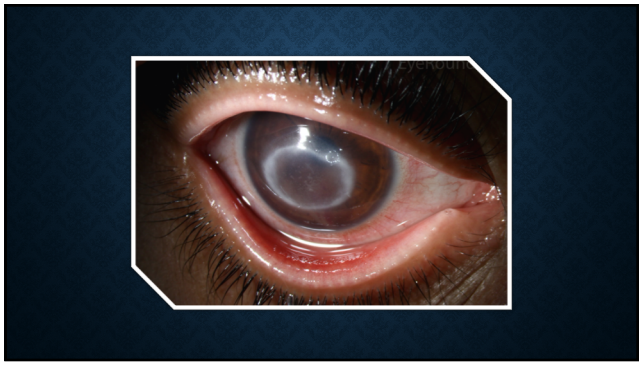

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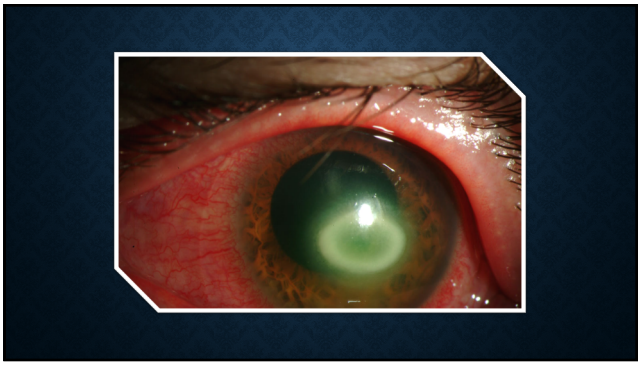


26

ACANTHAMOEBA KERATITIS

Methods of infection:

- Direct corneal contact with organism
- Contact with FB or liquid contaminated with organism
- Contact lens use
- Contaminated contact lens solutions- made from distilled water/tap water

- Relatively uncommon - First case reported in 1974

27

SIGNS AND SYMPTOMS

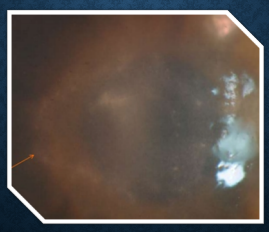
SIGNS	REPORTED IN % OF PATIENTS
PAIN	50-100%
REDUCED CORNEAL SENSATION	29%
EPITHELIAL DEFECTS, EROSIONS	60%
STROMAL RING INFILTRATE	6-29%
RADIAL KERATONEURITIS	2-57%

SYMPTOMS:

- SEVERE EYE PAIN
- REDNESS
- IRRITATION
- FB SENSATION, PHOTOPHOBIA
- REACTIVE PTOSIS
- ENLARGED PRE-AURICULAR LYMPH NODE

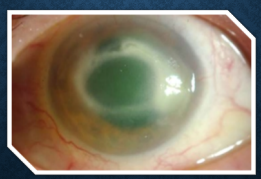
28

STROMAL INFILTRATES APPEAR AS TINY WHITE LESIONS OR GREY WHITE PATCHY LESIONS



29

ENLARGE AND COALESCE TO FORM PARTIAL OR COMPLETE RINGS- PATHOGNOMONIC. EPITHELIUM MAY BE INTACT OR DEVELOP RECURRENT EROSIONS



30

TREATMENT

1. **Biguanide cationic antiseptic agents (PHMB, chlorhexidine)**
   - Disrupt membranes
   - Only agents active against cysts
2. **Aromatic diamidines (Brolene, Pentamidine)**
   - Interfere with DNA synthesis (can cause toxic keratopathy)
3. **Aminoglycosides (Neomycin, Paromycin)**
   - Used in combination with other agents
   - Act by disrupting membranes and inhibiting protein synthesis

Early treatment is more effective, especially when organisms are confined to the epithelium only

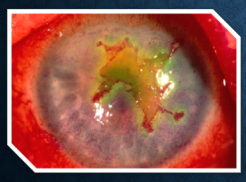
31

ANTI-FUNGAL AGENTS

1. **Polyenes: Amphotericin B, Natamycin, Nystatin**
   - Amphotericin B
     - 0.15 or 0.30% from IV form (in distilled H_2O)
     - Excellent for candida and useful for deep filamentary keratitis
   - Natamycin 5% suspension
     - Only commercially available FDA-approved topical antifungal
     - Broad spectrum of activity
     - Many consider this as first line Rx
2. **Pyrimidines: Flucytosine**
3. **Azoles**
   - Imidazoles:
     - Clotrimazole, miconazole, ketoconazole
   - Triazoles:
     - Fluconazole, itraconazole, voriconazole

32

HERPES SIMPLEX KERATITIS

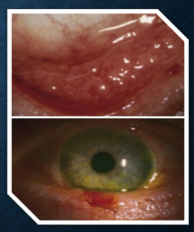


- Herpes simplex is the leading cause of infectious corneal blindness
- While not all humans manifest herpes infection, more than 90% carry the latent virus
- HSV keratitis is the Herpes simplex viral infection of the cornea

33

PRIMARY HSV INFECTION

- Blepharoconjunctivitis
- Follicular conjunctivitis
- Lid vesicles and conjunctival dendrites
- Kaposi's varicelliform eruption
- Severe morbidity- multi-system failure or bacterial superinfection



34

RECURRENT HSV INFECTIONS

- Multiple factors are thought to cause recurrence including fever, sunlight, irradiation, and emotional stress
- Recurrent disease most commonly causes keratitis
- HSV Keratitis is broadly classified into epithelial and stromal/endothelial keratitis

35

EPITHELIAL KERATITIS: SIGNS AND SYMPTOMS

Signs:

- Punctate epithelial keratitis
- Classic arborizing dendritic epithelial ulcers with terminal bulbs
- Geographic epithelial ulcer
- Ciliary flush & conjunctival injection
- Dendritic ulcer
- Geographic ulcer
- Marginal keratitis
- Metaherpetic (trophic) ulcer

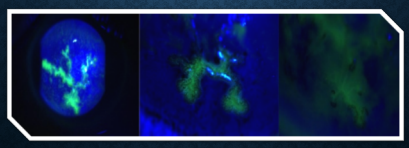
Symptoms:

- FB Sensation
- Photophobia
- Redness
- Blurred vision

36

DENDRITIC ULCER

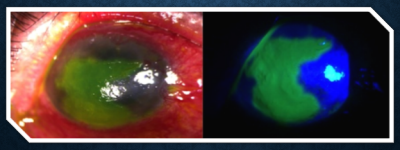
- Classic herpetic lesion
- The boarders are slightly raised, grayish and stain with rose Bengal as they consist of infected cells that have undergone acantholysis
- On resolution, a dendrite-shaped scar, called a ghost dendrite, may remain in the superficial cornea



37

GEOGRAPHIC ULCER

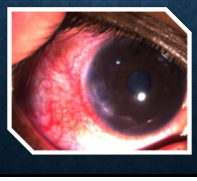
- Occurs when: Immunocompromised, on topical steroids, or have longstanding, untreated ulcers
- Dichotomous branching and terminal bulbs are seen at the periphery



38

MARGINAL KERATITIS

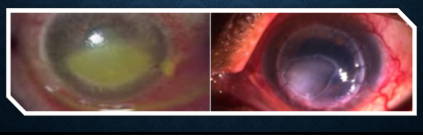
- Located near the limbus
- The presence of an epithelial defect and lack of corneal sensation can aid in diagnosis
- Significant stromal inflammation
- They are more resistant to treatment and frequently become trophic ulcers



39

METAHERPETIC (TROPHIC) ULCER

- Trophic ulcer, if it arises *de novo*, or a metaherpetic ulcer if it follows a dendrite or geographic ulcer
  - Causes:
    - Toxicity from antiviral medications
    - Lack of neural-derived growth factors
    - Poor tear surfacing
    - Low-grade stromal inflammation
- Neurotrophic ulcers start as roughened epithelium, which then breaks down to produce an epithelial defect with smooth margins



40

STROMAL/ENDOTHELIAL KERATITIS

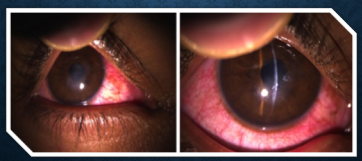
- An immune-mediated response to nonreplicating viral particles
- All layers of the cornea are affected and may involve the trabecular meshwork and iris
- It is classified based on the predominant site and type of involvement

Classifications
1. Endotheliitis
2. Necrotizing keratitis
3. Immune stromal keratitis
4. Keratouveitis

41

1. ENDOTHELIITIS

- Manifests as overlying stromal edema from endothelial dysfunction
- Longstanding stromal edema leads to permanent scarring & is the major cause of decreased vision associated with HSVK



42

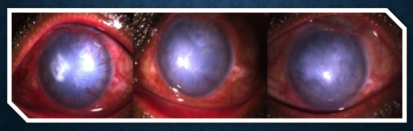
ENDOTHELIITIS CONT.

LOCALIZED ENDOTHELIITIS	DIFFUSE AND LINEAR ENDOTHELIITIS
DISC-SHAPED AREA OF CORNEAL EDEMA (ALSO KNOWN AS DISCIFORM KERATITIS)	ACCOMPANIED BY TRABECULITIS WITH A RESULTING ELEVATED IOP
MINIMAL STROMAL INFLAMMATION	PSEUDO-GUTTAE AND DESCEMET'S FOLDS
NO EPITHELIAL INVOLVEMENT	

43

2. NECROTIZING KERATITIS

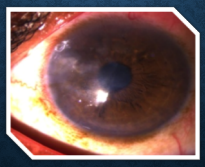
- INFLAMMATION IN THE CORNEA IS DUE TO A REACTION TO LIVE VIRAL PARTICLES IN THE CORNEAL STROMA
- CORNEAL MELTING AND PERFORATION
- ASSOCIATED WITH UVEITIS AND TRABECULITIS THAT MAY LEAD TO RECALCITRANT GLAUCOMA



44

3. IMMUNE STROMAL KERATITIS

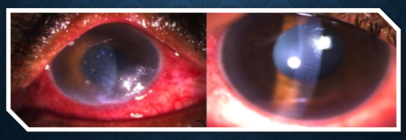
- MANIFESTS AS FOCAL, MULTIFOCAL, OR DIFFUSE STROMAL OPACITIES OR AN IMMUNE RING
- STROMAL EDEMA AND A MILD ANTERIOR CHAMBER REACTION
- IT IS CALLED INTERSTITIAL KERATITIS (IK) IF ACCOMPANIED BY VASCULARIZATION



45

4. KERATOUVEITIS

- UVEITIS IS USUALLY GRANULOMATOUS WITH LARGE "MUTTON-FAT" KERATIC PRECIPITATES ON THE ENDOTHELIUM
- IT CAN LEAD TO SIGNIFICANT MORBIDITY FROM SYNECHIAE, CATARACTS, AND GLAUCOMA
- UNILATERAL UVEITIS ASSOCIATED WITH HIGH INTRAOCULAR PRESSURE IS ALMOST ALWAYS CAUSED BY HSV



46

HERPETIC EYE DISEASE STUDY (HEDS)

- WHY IT WAS DONE: TO ASSESS THE EFFECT OF ADDING STEROIDS AND ACYCLOVIR TO CONVENTIONAL THERAPY WITH TRIFLURIDINE (TFT)
  - It was a prospective
  - Randomized
  - Double-masked
  - Placebo-controlled
  - Multi-center study
  - Divided into six trials: three therapeutic, two preventive, and one cohort

47

HERPES STROMAL KERATITIS TRIAL - NOT ON STEROIDS	HERPES STROMAL KERATITIS TRIAL – ON STEROIDS
COMPARED WITH THE PLACEBO GROUP, PATIENTS WHO RECEIVED PREDNISOLONE PHOSPHATE DROPS HAD FASTER RESOLUTION AND FEWER TREATMENT FAILURES.	THERE WAS NO APPARENT BENEFIT TO ADDING ORAL ACYCLOVIR TO TOPICAL CORTICOSTEROIDS AND TFT, HOWEVER, VISUAL ACUITY IMPROVED OVER 6 MONTHS IN MORE PATIENTS IN THE ACYCLOVIR GROUP THAN IN THE PLACEBO GROUP.

48

HERPES SIMPLEX VIRUS IRIDOCYCLITIS RECEIVING TOPICAL STEROIDS

THE TRIAL WAS STOPPED BECAUSE OF SLOW RECRUITMENT, BUT TREATMENT FAILURES OCCURRED AT A HIGHER RATE IN THE PLACEBO GROUP THAN IN THE ACYCLOVIR GROUP, INDICATING A POTENTIAL BENEFIT TO ADDING ORAL ACYCLOVIR TO THE REGIMEN OF A TOPICAL STEROID AND AN ANTIVIRAL.

49

HERPES SIMPLEX VIRUS EPITHELIAL KERATITIS TRIAL

IN THE TREATMENT OF ACUTE HSV EPITHELIAL KERATITIS WITH TFT, THE ADDITION OF ORAL ACYCLOVIR OFFERED NO ADDITIONAL BENEFIT IN PREVENTING SUBSEQUENT STROMAL KERATITIS OR IRITIS.

50

ACYCLOVIR PREVENTION TRIAL

- ORAL ACYCLOVIR REDUCED THE RISK OF ANY FORM OF RECURRENT OCULAR HERPES BY 41% AND STROMAL KERATITIS BY 50%. THE RISK OF MULTIPLE RECURRENCES DECREASED FROM 9% TO 4%.
- ALTHOUGH THERE WAS NO REBOUND INCREASE IN KERATITIS AFTER DISCONTINUATION OF THE ACYCLOVIR, THE PROTECTION DID NOT PERSIST ONCE THE ACYCLOVIR WAS DISCONTINUED.

51

OCULAR HSV RECURRENCE FACTOR STUDY

- NO ASSOCIATION WAS FOUND BETWEEN PSYCHOLOGICAL OR OTHER FORMS OF STRESS AND HSV RECURRENCES.
- PREVIOUS EPISODES OF EPITHELIAL KERATITIS WERE NOT A PREDICTOR FOR FUTURE OCCURRENCES WHILE PREVIOUS, ESPECIALLY MULTIPLE, EPISODES OF STROMAL KERATITIS MARKEDLY INCREASED THE PROBABILITY OF SUBSEQUENT STROMAL KERATITIS.

52

TREATMENT

- The mainstay of treatment is topical steroids as they decrease inflammation and therefore scarring
- Oral antivirals
- Topical antivirals
- Aggressive topical and systemic antivirals along with steroids are necessary in necrotizing keratitis and focal iritis

53

CURRENT ANTIVIRALS

DRUG (TRADE NAME)	ROUTE	DOSE	FREQUENCY	ADVERSE EFFECTS
TRIFLURIDINE (VIROPTIC)	TOPICAL DROPS	1.00%	Q2H	FOLLICULAR CONJUNCTIVITIS, EPITHELIOPATHY
VIDARABINE (ARA-A)	TOPICAL OINTMENT	3.00%	5X/DAY	AS ABOVE
ACYCLOVIR (ZOVIRAX)	TOPICAL OINTMENT	3.00%	5X/DAY	HEADACHE, NAUSEA, NEPHROTOXICITY, NEUROTOXICITY
	ORAL- TREATMENT	400MG	5X/DAY	
	ORAL- PROPHYLAXIS	400MG	2X/DAY	
VALACYCLOVIR (VALTREX)	ORAL- TREATMENT	500MG	3X/DAY	AS ABOVE, TTP, HEMOLYTIC UREMIC SYNDROME IN IMMUNOSUPPRESSED
	ORAL- PROPHYLAXIS	500MG	2X/DAY	
FAMCICLOVIR (FAMVIR)	ORAL- TREATMENT	250MG	3X/DAY	AS ACYCLOVIR
	ORAL- PROPHYLAXIS	250MG	2X/DAY	

54

TROPHIC ULCER TREATMENT

- Stop toxic medications
- Tear film supplementation
- Bandage contact lenses
- Amniotic membrane
- Use topical steroids *carefully* if there is significant underlying inflammation

55

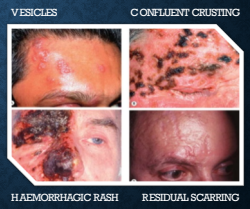
HERPES ZOSTER OPHTHALMICUS

- Known as shingles/Zoster. It is a viral disease characterized by a painful skin rash in one or more dermatome distributions of the fifth cranial nerve, shared by the eye and orbit.
- Risk of Ocular Involvement:
  - Hutchinson Sign
  - Age
  - AIDS

56

EXTRAOCULAR MANIFESTATION

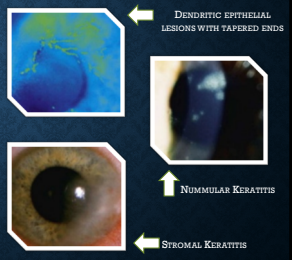
- Acute Shingle
- A Prodromal Phase
- Skin Lesions
- Disseminated Zoster



57

CORNEAL MANIFESTATION

- Conjunctivitis (follicular and/or papillary)
- Episcleritis, Scleritis
- Keratitis (Acute Epithelial, Nummular, Stromal, Disciform)
- Anterior Uveitis with Sectoral iris ischemia and atrophy
- Elevated IOP
- Retinitis, choroiditis
- Neurological Complication



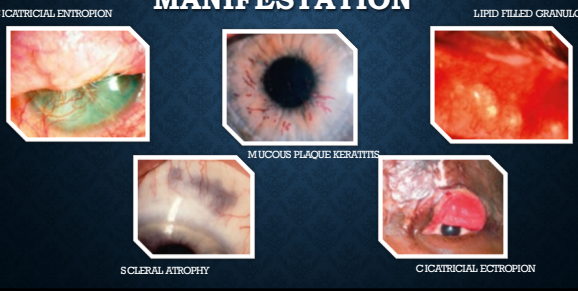
58

POST INFECTIOUS SEQUELA MANIFESTATION

- Neurotrophic keratitis 50% cases
- Scleritis patchy scleral atrophy
- Mucous plaque keratitis 5%, between 3rd and 6th month
- Lipid degeneration in eye with persistent severe nummular or disciform keratitis
- Lipid-filled granulomata under tarsal conjunctiva together with subconjunctival scarring
- Eyelid scarring result in ptosis, cicatricial entropion and occasionally ectropion

59

POST INFECTIOUS SEQUELA MANIFESTATION



60

CLINICAL MANIFESTATION CONT.

- Pain persist >1 month after rash healed
- 75% of patient over 70 Yrs
- Pain (Constant or intermittent), worse at night and aggravated by minor stimuli, touch and heat

61

MANAGEMENT

- Acute Shingles:
  - Oral Acyclovir 800mg 5x/day for 7-10 days, start within 72 hours of onset
  - Intravenous acyclovir 5-10mg/kg Tid is indicated for encephalitis (Retinitis/chroiditis)
  - Other Oral antiviral agents Valaciclovir 1g tid, famiciclovir 500mg tid
  - Systemic steroids (prednisone 40-60mg daily)
  - Oral Gabapentin 100mg TID (titrate to 300mg TID) or Lyrica for pain

62

MANAGEMENT

- Conjunctival involvement
  - Cool compresses and erythromycin ointment bid
- SPK
  - lubrication with preservative-free artificial tears q1-2h and ointment qhs
- Corneal or conjunctival pseudodentrites
  - lubrication with preservative-free artificial tears q1-2h, topical antivirals (e.g ganciclovir 0.15% or vidarabine 3% ointment) tid
- Immune stromal keratitis
  - topical steroid (prednisonolone acetate 1%) tapering over months to years using weaker steroids and less than daily dosing
- Uveitis (with or without immune stromal keratitis)
  - Topical Steroid (prednisolone acetate 1%) and cycloplegic

  Treat increased IOP with aggressive aqueous suppression; avoid prostaglandin analogues

63

MANAGEMENT

- Neurotrophic Keratitis
  - Treat mild epithelial defects with erythromycin ointment 4-8 times/days. if corneal ulceration occurs, smears and cultures to rule out infection. If sterile, no response to ointment, consider a bandage contact lens, tarsorrhaphy, amniotic membrane graft or conjunctival flap.

Increased IOP may be steroid response or secondary to inflammation

- If uveitis, increase frequency of steroid for a few days and use topical aqueous suppressants eg. timolol 0.5% bid, brimonidine 0.2% tid or dorzolamide 2% tie. Oral carbonic anhydrase inhibitors if IOP > 30mmhg.
- If IOP still increased but inflammation controlled, substitute fluorometholone 0.25% or loteprednol 0.5% drops for prednisolone acetate and taper dose

64

SUMMARY

- Early recognition and diagnosis is important
- Recognize patterns
- Early intervention prevents vision loss and decrease morbidity
- Refer Early if needed

65

THANK YOU!

66