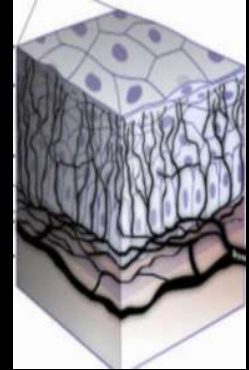
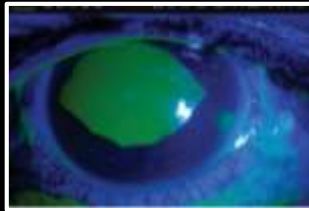
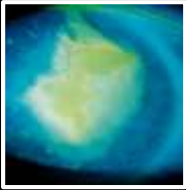


# Recent Management of Neurokeratopathies

## Mohamed Sameh ElShorbagy

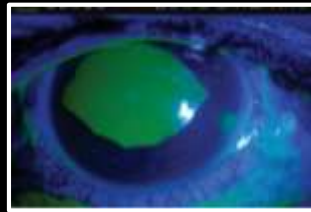
MD

Professor of Ophthalmology  
Fellow LMU Munich Germany

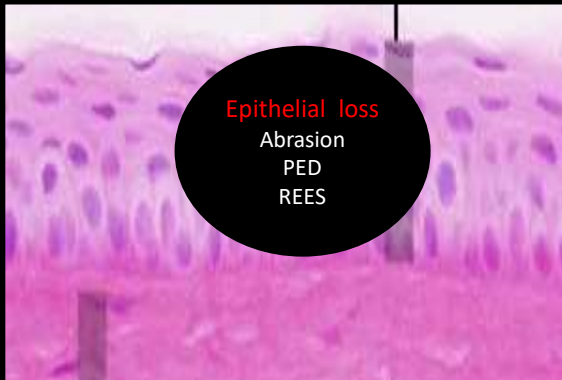


We must answer  
two questions

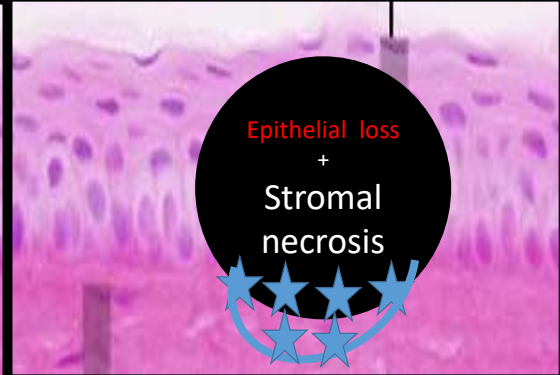
# Positive Fluorescence stains Means Corneal ulceration ??



## Epithelial loss

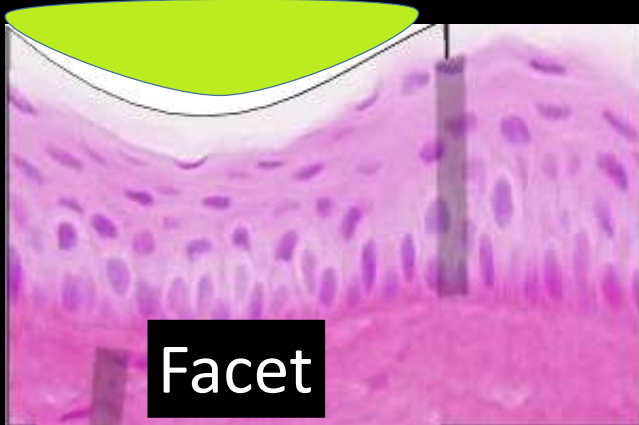


## Ulcer



# Stain and wash

Pooling

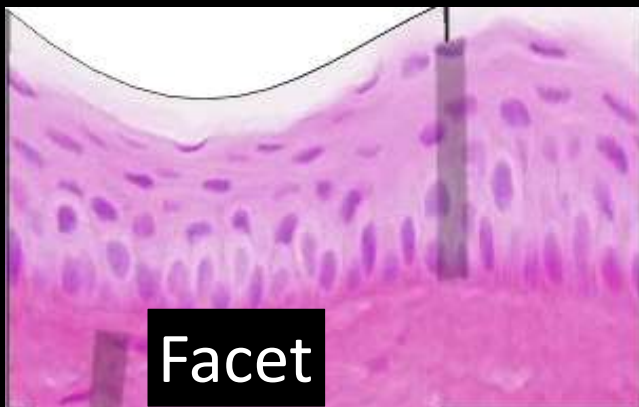


Staining



# After wash

Facet



Staining



If it is a corneal ulcer  
**Needs**  
Antimicrobial drugs??

**No**

Even it can worsen the condition

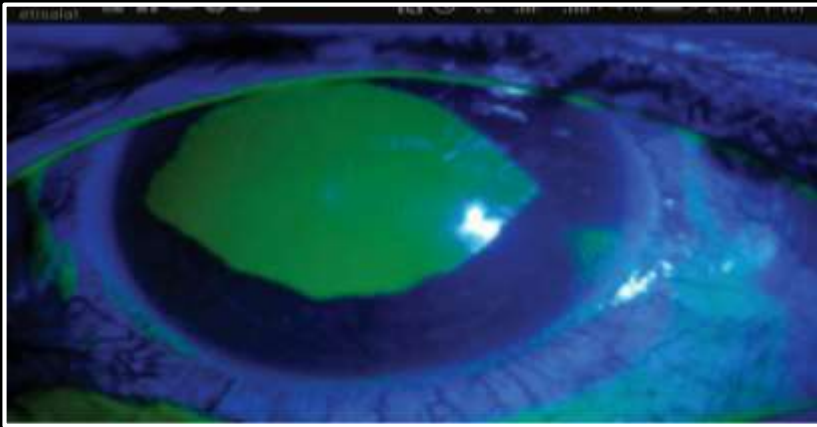
- Epithelial Toxicity
- Predispose to other infections

# Nomenclatures

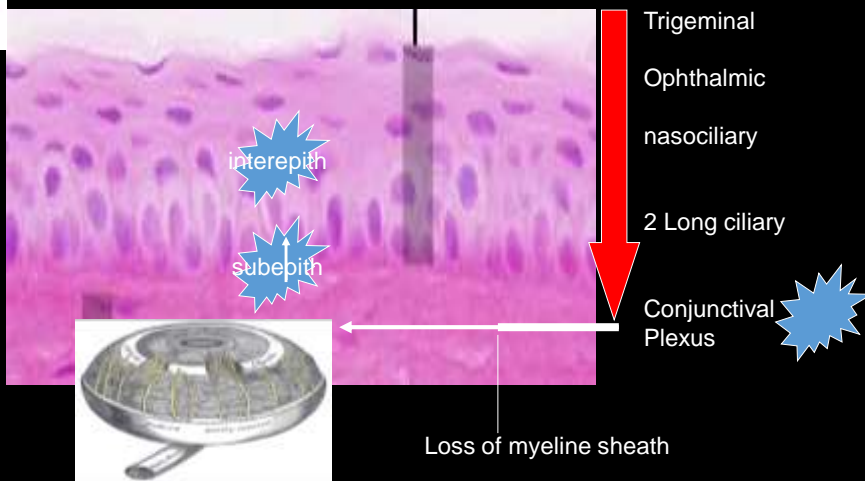
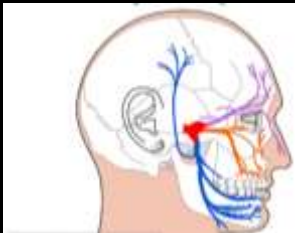
Neuro-keratopathies (nomenclatures)

- \* Neuroparalytic
- \* **Neurotrophic**
- \* Factitious keratitis
- \* Neurogenic keratitis

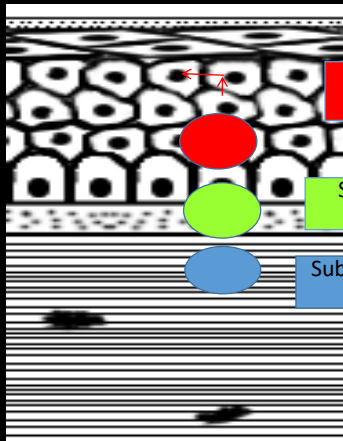
# Neurotrophic Keratitis



## Corneal innervation



Cornea is the richest part of the body  
Contains  
16000 nerve Endings /mm<sup>3</sup>



Inter epith  
Plexus

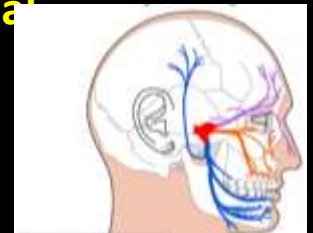
Sub basal  
Plexus

Sub bowmen  
Plexus



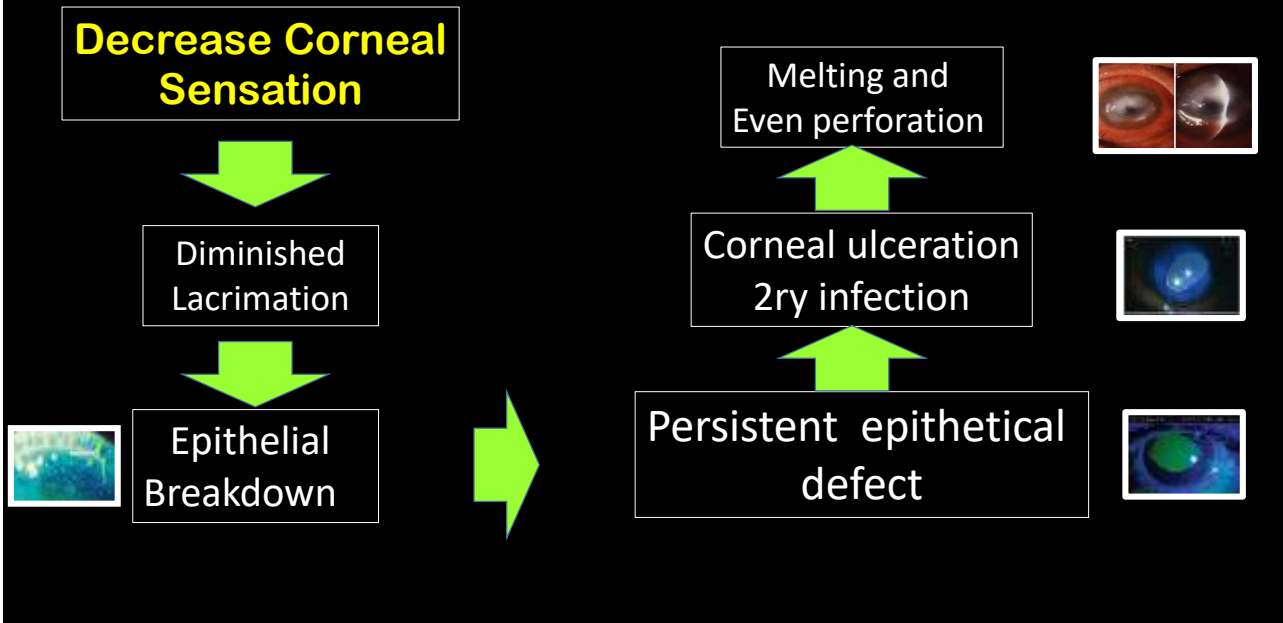
= Sub bowman  
= Sub basal plexus  
= Interepithelial

**Lesion of 5<sup>th</sup> n lead to interruption of normal corneal sensation lead to:**



- Edema, exfoliation of epithelial cells
- Decrease cell division
- Disruption of metabolic activity of epithelium

*NT keratitis is a Degenerative corneal disorder*



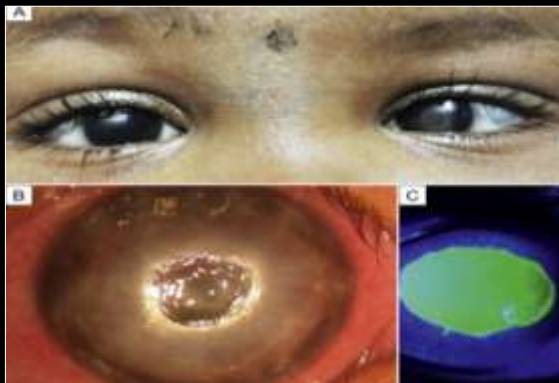
Etiology



- Congenital Corneal anesthesia
- Lesion in trigeminal ganglia or nerve
- Infection
- DM
- CL
- Topical drugs
- Post LASIK , PRK and PKP and vitrectomy
- Post irradiation

# • Congenital

Congenital corneal anesthesia

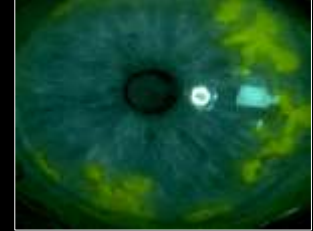
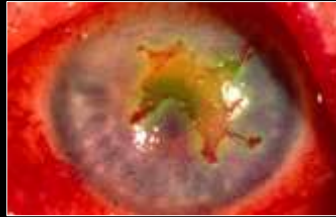


# • Infections

HS

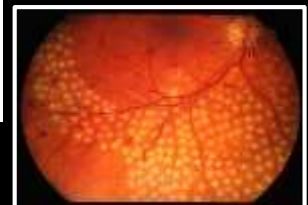
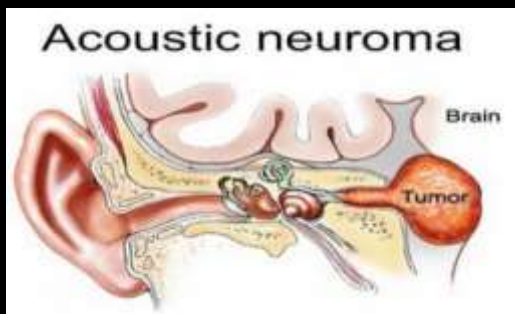
HZ

Leprosy



# • Postsurgical after :

- Treatment of trigeminal neuralgia and acoustic neuroma
- Post lasik and PRK
- After PKP
- After vitrectomy
- Heavy endolaser
- After PRP in DR



## •Corneal dystrophy

- Advanced lattice and granular dystrophy

## •Topical drugs

- Anesthetics
- Timolol / Betaxolol
- NSAI ( diclofenac sodium )
- Sulphonamides



## •Systemic disorders

- DM
- Vitamin A deficiency
- MS

## •Toxic

- Chemical burns
- Hydrogen and carbon disulphide exposure



## Special Consideration

- DM
- Refractive surgery

### Diabetes M

Decrease density  
of  
sub-basal nerve plexus

Diabetic  
neuropathy

Complications  
of  
Treatment

## Refractive surgery

Lasik

PRK

Femto SMILE



Cause corneal nerves affection  
Regeneration of n differ [smile/PRK/Lasik]

# Stages

# Mackie

# Stages



## Stage 1

### SPK



## Stage 2

### PED



## Stage 3

### ulcer

## Mackie classification of NK

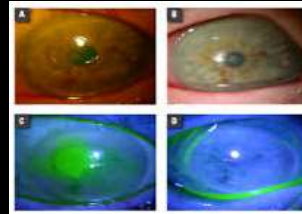
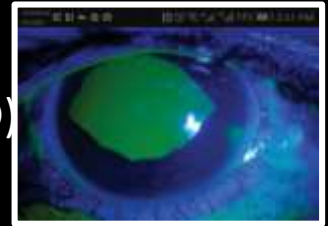
### Stage 1

- Rose Bengal staining of inferior palpebral conjunctiva
- **SPK** with dried epithelial facets
- Decreased tear film break up time
- Increased tears Mucus content



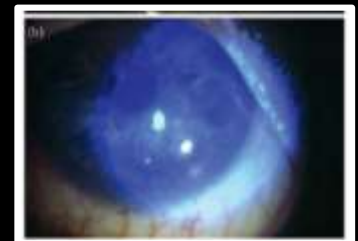
## • Stage 2 (PED)

- Oval epithelial defect in superior cornea (PED)
- Surrounded with loose epithelium
- Stromal swelling
- Folds in DM
- AC reaction



## • Stage 3 (ulcer)

- Corneal ulceration
- Corneal thinning
- Corneal melting
- Corneal perforation



## Evaluation

### Corneal Sensation

Corneal Staining  
F/RB

Confocal Microscope  
IVCM

Lacrimal Secretion tests

## Measurement of Corneal Sensation

### Quantitative

- Cotton tip

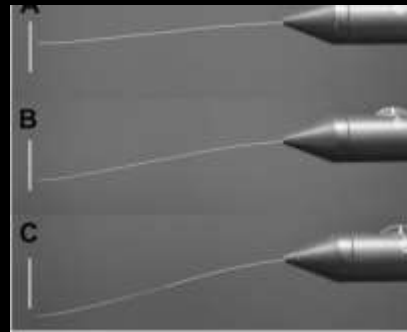
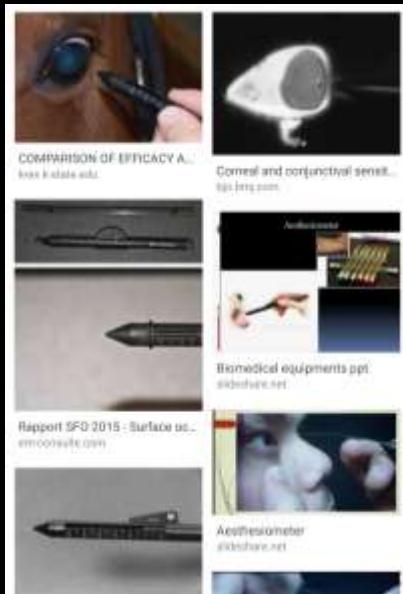


### Qualitative

- Aesithiometer Cochet bonnet
- Air puff
- Thermal stimulation by carbon dioxide laser



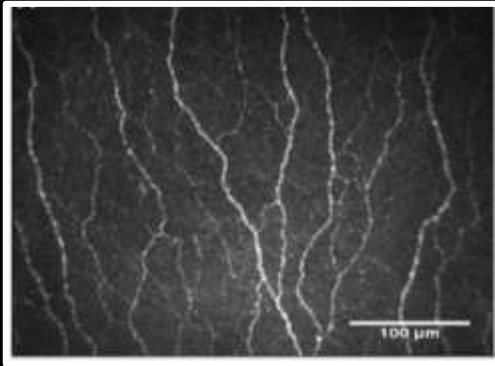
## Cochet –Bonnet Aesthiometer



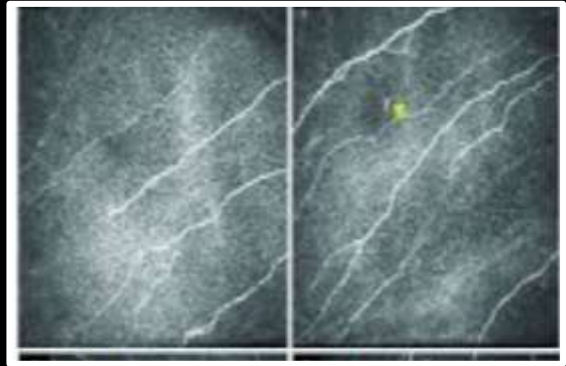
## Corneal nerve imaging

- Confocal microscope
- Wide field fluorescence
- Nerve fiber densities

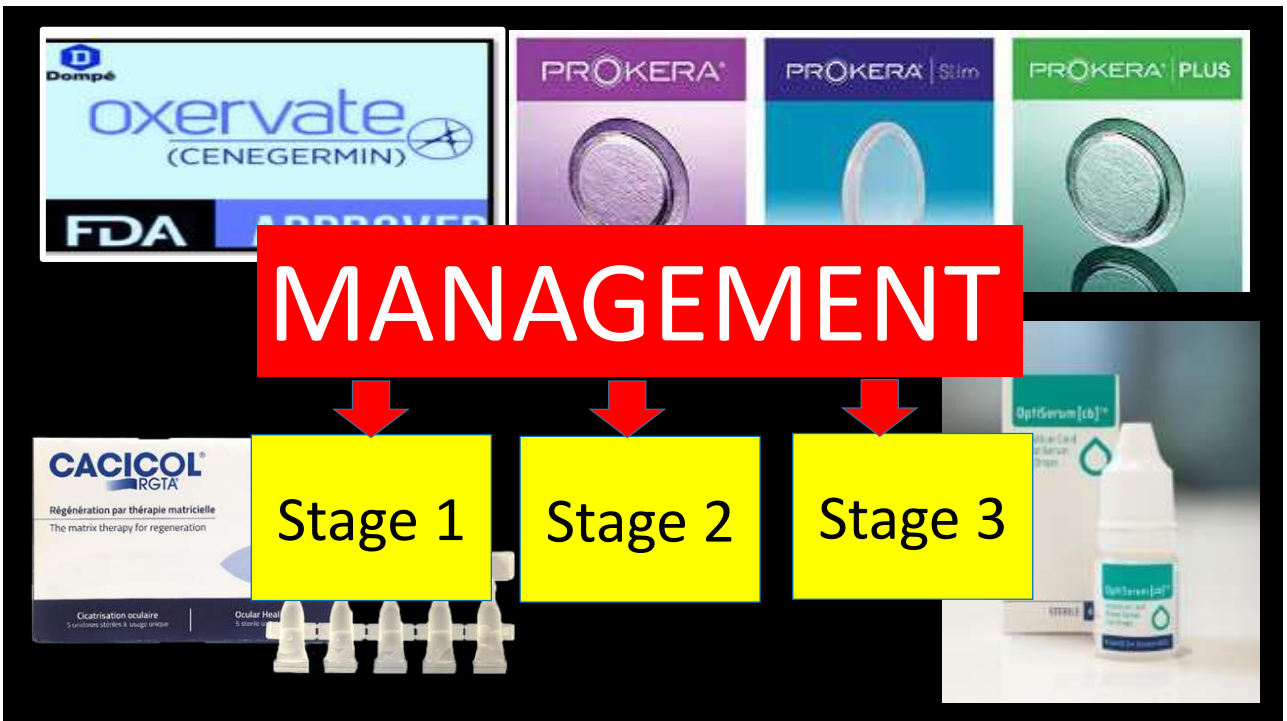
# Confocal Microscopy IVCM



Normal



NK



# Treatment of NTK

## Stage 1

- Stop all topical drugs that can cause epithelial toxicity
- **Preservative free topical lubricant**
- Contact lenses
- Systemic tetracyclin
- **Autologous serum 20%**
- Umbilical cord serum

### Stage 1

- Rose Bengal staining of inferior palpebral conjunctiva
- SPK with dried epithelial facets
- Decreased tear film break up time
- Increased tears Mucus content



## Stage 2

- As stage 1

**Add**

- Topical Tetracycline that help healing of epithelial defect
- Mydriatic cycloplegic for AC reaction

### Stage 2

- Oval epithelial defect in superior cornea (PED)
- Surrounded with loose epithelium
- Stromal swelling
- Folds in DM
- AC reaction



## Stage 3

- All the previous treatment

**Add**

- Surgery
- Drugs prevent corneal melting
- Drugs promote healing

### • Stage 3

- Corneal thinning
- Corneal melting
- Corneal perforation



## Surgery

- Punctal occlusion
- Glue
- Limbal stem cell replacement
- Conjunctival flap
- Amniotic membrane flap
- Tarsorrhaphy
- PKP

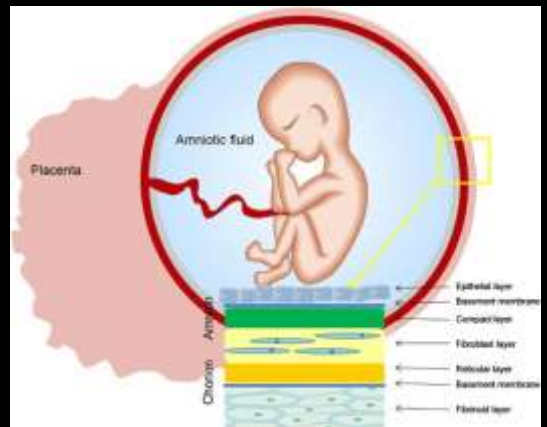


# Recent Management

- Nerve Growth factor eye drops
- Amniotic membrane modalities
- Cyclosporin eye drops
- Autologous serum + Umbilical cord eye drops
- REGTA Ora eye drops
- Omega 3 Fatty acids
- Nicergoline tablets
- Corneal neurotization

## Amniotic membrane contains :

- Pluripotent cells
- Growth factors
- Antiproteolytic activity
- Highly organized collagen
- Immune modulators
- Matrix protein



# Amniotic Membrane Modalities

AMT  
As a whole

Amniotic fluid  
Eye drops

Amniotic membrane  
Eye drops

AMT  
As a contact lens  
Prokera

Amniotic Extracts  
Eye drops

With or  
without  
Umbilical  
blood

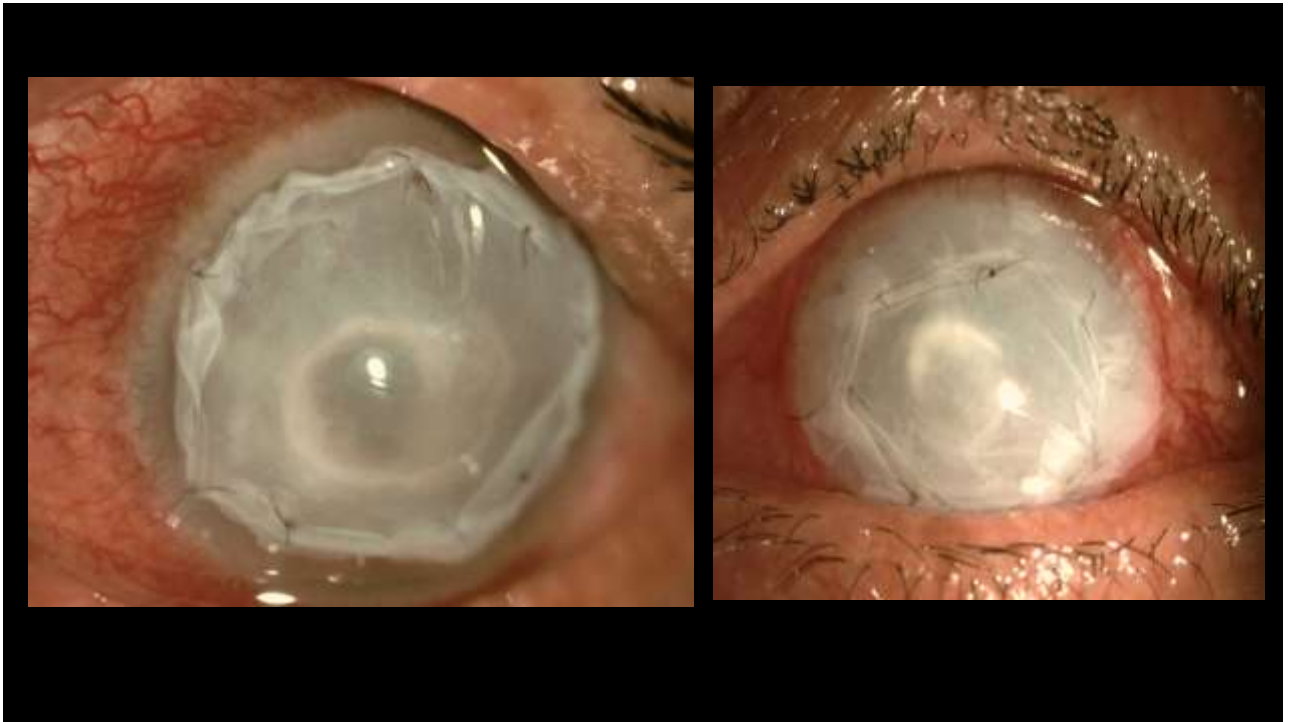


As a whole Graft

Eye drops and extracts

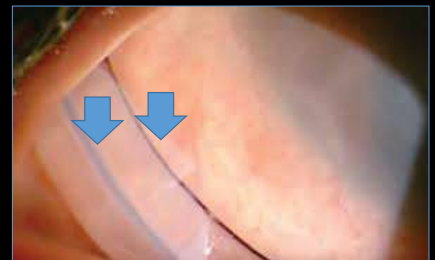
Amniotic Fluid

Umbilical cord serum



**AM**  
Contact Lens

**PROKERA**



Made by clipping a piece of Amniotic membrane between 2 rings of  
Clear flexible rings acting as contact lenses

# AM

## Eye drops

### Preparation

- 1- Wash with saline  
contains 5% penicillin and streptomycin
- 2- slicing the AM into small pieces
- 3- submerging in liquid nitrogen
- 4- this mixture is
  - Homogenized
  - Centrifuged
  - Sterilized



### Other method

- Pulverization
- Micronization
- Of the dried form

# Nerve Growth Factor

## Eye drops

## OXERVATE eye drops



# Oxervate ( Nerve growth factor Eye drops)

- First FDA approved NGF eye drops
- NGF is an endogenous protein involved in different ion and maintenance of neurons
- Recombinant form of human NGF contain **Cenergermin** produced in E Coli
- Acts through specific high and low affinity growth factors receptors
- 1 ml contains 20 microgram cenergermin
- Dose 6 times /day for 8 weeks





Before treatment



6 weeks after Oxervate  
eye drops



**Cyclosporine 0.05%**

with or without Autologous serum

Can help corneal nerves regeneration after Lasik



## Omega 3 Fatty acids

Recently discovered to be  
Helpful for corneal regeneration  
Specially after  
Refractive surgery

## Serum eye drops

• Patient Autologous serum

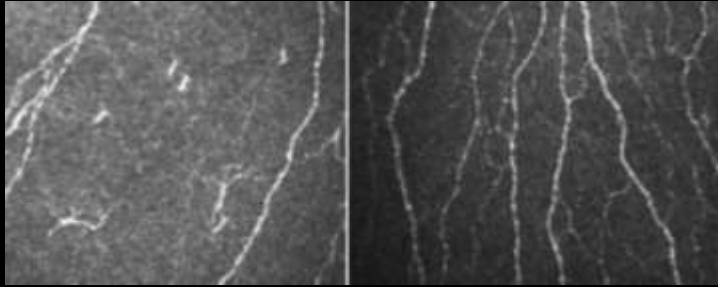
• Umbilical cord blood

+

Both together



## Umbilical cord serum eye drops



IN Vivo Confocal microscope  
Before  
treatment



IN Vivo Confocal microscope  
After  
treatment

# Drops prevent Melting

## Drugs prevent corneal Melting

- Systemic and local **Tetracycline**

- \* Patient **Autologous serum** {Contains }:

- \* Vitamin A
- # Neuromediators
- \* Antiprotinase
- \* Growth factors
- \* Fibronectin

- \* **Cyclosporine** 0.02 % drops

- **Re Genera Ting Agent**  
(**RGTA ORA 4120**)  
that is new matrix therapy agent  
1 drop/3 days for 3 months  
preventing stromal lysis

## Re Genera Ting Agent (RGTA ORA 4120) that is new matrix therapy agent Cacicol Eye Drops

- Group of **biopolymers** behave like **Keratan sulphate** mucopolysaccharide
- In NK and PED there is deficiency of [extra cellular Matrix} ECM specially Keratan Sulphate
- Can be used after CXL to enhance healing
- Dose / 1 drop /3 days for 3 monthes



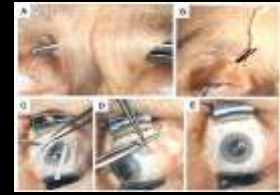
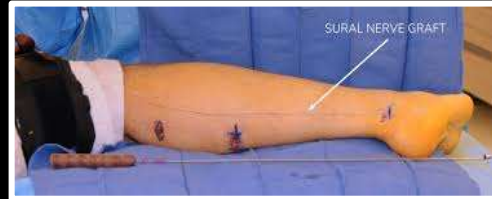
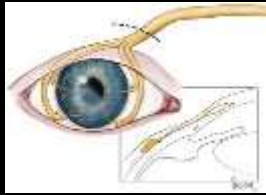


## Systemic Nicergoline

- **Nicergoline** 10 mgm/kg oral twice daily for 2 weeks
- Essentially for treatment of senile dementia
- found to enhance epithelial healing by increasing nerve growth factors in cornea and lacrimal glands

# Corneal Neurotization

- Sural nerve grafts
- Regional Contralateral supratrocheal nerve grafts



Take care → Four Drugs

## Corticosteroids

- \* Keratolysis
- \* Delay healing
- \* Enhance organism growth

## NSAID

- \* Toxic to cell wall Of epithelium
- \* Decrease sensory Flow

## Topical Anesthesia

Very dangerous  
Can lead to  
Factitious keratitis

## Decongestant

Contraindicated

# Home Message

- Don't be rush in prescribing antibiotics that may worsen the condition
- Testing of **corneal sensation** is an essential examination
- Corneal ulceration in the first year of life suspect **CCA**
- NK is a common disorder post refractive surgery
- NK is the second cause after viral infection after PKP
- NK is the most common corneal disorder after vitrectomy, **PRP**



# Thanks

**Vielen Dank**

**Mohamed Sameh ElShorbagy**

MD

Professor of Ophthalmology  
Fellow LMU Munich Germany