The challenge of PERSISTANT EPITHELIAL DEFECT

***Mohamed Saad* , PhD, MD**

Prof. of ophthalmology

Assiut University hospital

No financial interest

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(PEDs or PCEDs):

Q.What is ment by PED?

Failure of rapid re-epithelialization and closure within 10-14 days after a corneal injury, even with standard supportive treatment .

If left untreated, PEDs can result in significant complications, including infection and vision loss

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Q.How can normal corneal epith.proliferate?

- The **limbus**, contains both **epithelial stem cells** and **basal cells**.
- **Epidermal growth factor (EGF)** ….. proliferation and migration process ….synthesis of nucleic acids in epithelial cells and extracellular matrix protein, fibronectin.
- As **basal cells migrate** towards the central surface of the cornea, they gradually **lose their proliferative** properties and eventually undergo **apoptosis** and are desquamated into the tear film .

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Q. What is the role of Inflammatory cytokines?

- **(TNF-α)** and **(IL-1),** are released in response to damage to the epithelium.
- Keratocytes respond to IL-1 and produce **(HGF)** and **(KGF),** which influence the migration and proliferation of epithelial cells.
- (**IGFs**) and **(TGF-β**) regulate differentiation and growth of stromal keratocytes and epithelial cells.
- **(PDGFs**) regulate migration and proliferation of keratocytes,
- **Thymosin-β4** promotes re-epithelialization and mediates epithelial migration during wound healing.
- **(NGF)** plays a vital role in trophic support, corneal sensation, and maintaining the tear film .

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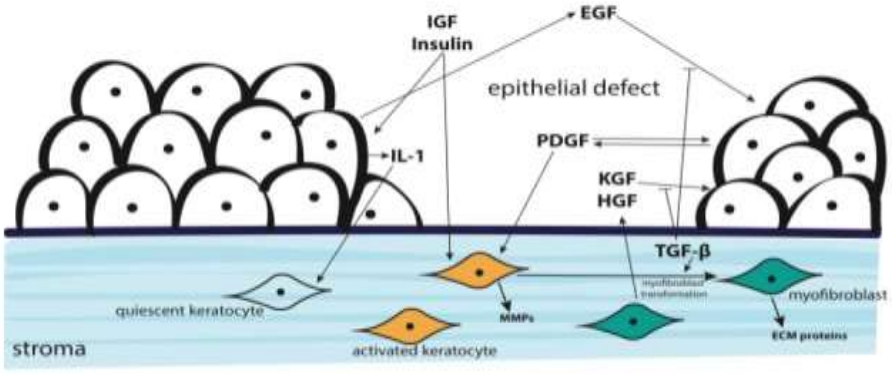

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- Injury to the cornea If the underlying **basement membrane is intact**, the epithelial layer undergoes an active **repair** process over **7-14 d.**
- Only after re-epithelialization can the stroma adhere to the regenerated epithelial layer via **hemidesmosomes** anchoring to fibrils.
- However, if the underlying **stromal layer is also affected** in addition to the basement membrane, the epithelial layer will regenerate over the lesion and attach to the recovering stromal layer after around **eight weeks.**
- PEDs commonly extend into the stromal layer, causing stromal melting, secondary ulceration, and stromal scarring .

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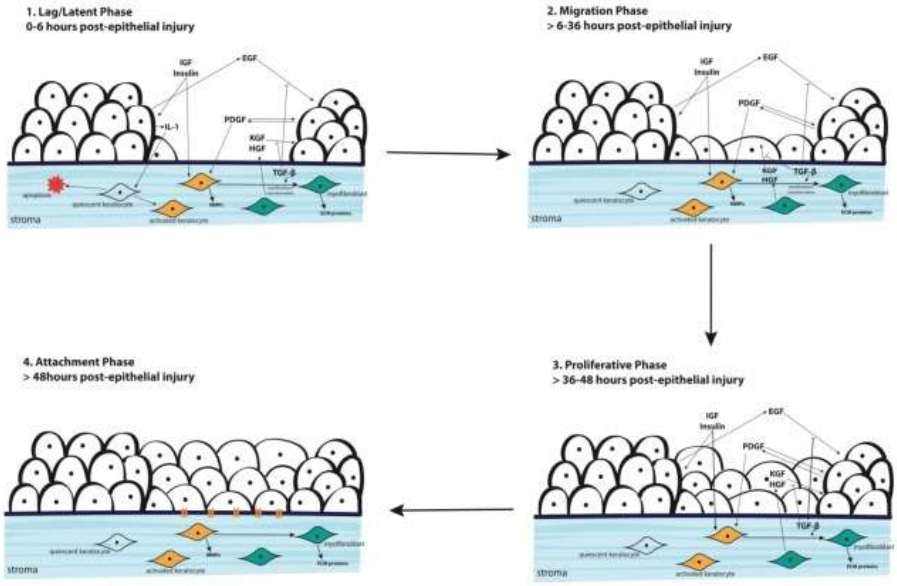
1. Lag/Latent Phase
0-6 hours post-epithelial injury
IGF
Insulin
EGF
IL-1
PDGF
KGF
HGF
TGF-β
stroma
2. Migration Phase
> 6-36 hours post-epithelial injury
3. Proliferative Phase
> 36-48 hours post-epithelial injury
4. Attachment Phase
> 48hours post-epithelial injury

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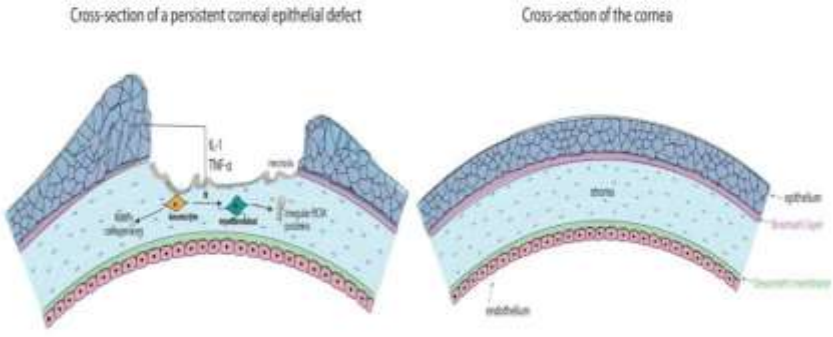
Cross-section of a persistent corneal epithelial defect
Cross-section of the cornea
IL-1
TNF-α
stroma
epithelium
endothelium

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Q.What are causes of PED?

Underlying Etiology	Examples of causative diseases	Mechanism
Defective epithelial adhesion	Recurrent corneal erosions Epithelial basement membrane dystrophies (EBMD) Toxic keratopathy Salzmann's nodular degeneration Band keratopathy Bullous keratopathy Vitamin A deficiency Scarring and trauma	Defective epithelial adhesion. Deficient or abnormal BM, Overproduction of matrix metalloproteinases (MMPs), Disruption of migration of epithelial cells

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Limbal stem cell deficiency	**Limbal stem cell deficiency (LSCD)** **Alkali-induced chemical injury** **Trauma**	**Deficiency of limbal stem cells**

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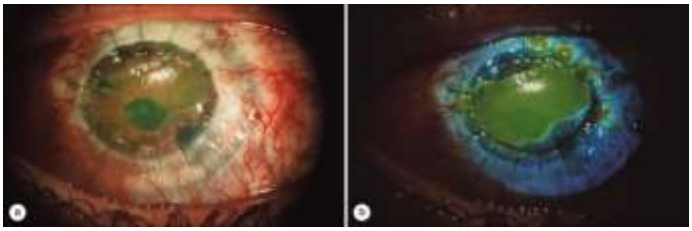

Inflammation	Keratoconjunctivitis sicca Rosacea Infectious keratitis Autoimmune diseases Sjögren's syndrome Mucous membrane pemphigoid Stevens-Johnson syndrome Graft vs. host disease Peripheral ulcerative keratitis Mooren's ulcer Rheumatoid arthritis	Over-activity of cytokines (TNF-α and IL-1), production of growth factors by keratocytes, proliferation and migration of epithelial cells, stromal remodeling

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Neurotrophic	Diabetes mellitus Severe dry eye syndrome Current or past herpetic keratitis Anesthetic abuse Traumatic or postoperative nerve damage	Local or systemic damage to trigeminal nerve, loss of corneal innervation

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Mechanical	Lagophthalmos Entropion or ectropion Trichiasis Blepharospasm Trachoma Severe dry eye disease Sjögren's syndrome Herpetic infection Chemical or thermal injuries	Recurrent abrasions can result in depletion of epithelial stem cells, dry or inflammatory ocular surface, corneal erosions from eyelid abnormalities

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Idiopathic and hereditary disorders	Aniridia Corneal, stromal and epithelial dystrophies	Deficiency in limbal stem cells Abnormal basement membrane adhesion

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Q. What are tips for diagnosis of PED?

- **History** : trauma, herpetic infection, diabetes, immune disorders, pain, corneal ,refractive surgery or blurry vision.
- **Examination:** fluorescein… the size, location, and depth of the defect
  inflammation in the anterior chamber,
  eyelid abnormalities,
  decreased sensation of the cornea (neurotrophic PED).

Ant.segment OCT

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Tips for diagnosis of PED:

- Density of flouresceine staining….depth
- Filamentary keratitis….dry eye.
- Anaesthesia…..neurotrophic.
- Presence of infilteration….infection.
- Ulcer general pattern.

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Q.What is their prognosis?

- **Ulcer's general pattern:**

A **point-like corneal ulcer** …… mild…. early inflammation or when the corneal ulcers are almost cured.

A **flaky corneal ulcer** ….most serious … bright green color with clear boundaries. …. may induce scars of varying thicknesses on the ocular surface, which will significantly affect the patient's vision, and may even induce a loss of vision.

A point-flaky mixed corneal ulcer is irregularly distributed, containing both point-like and flaky ulcers .

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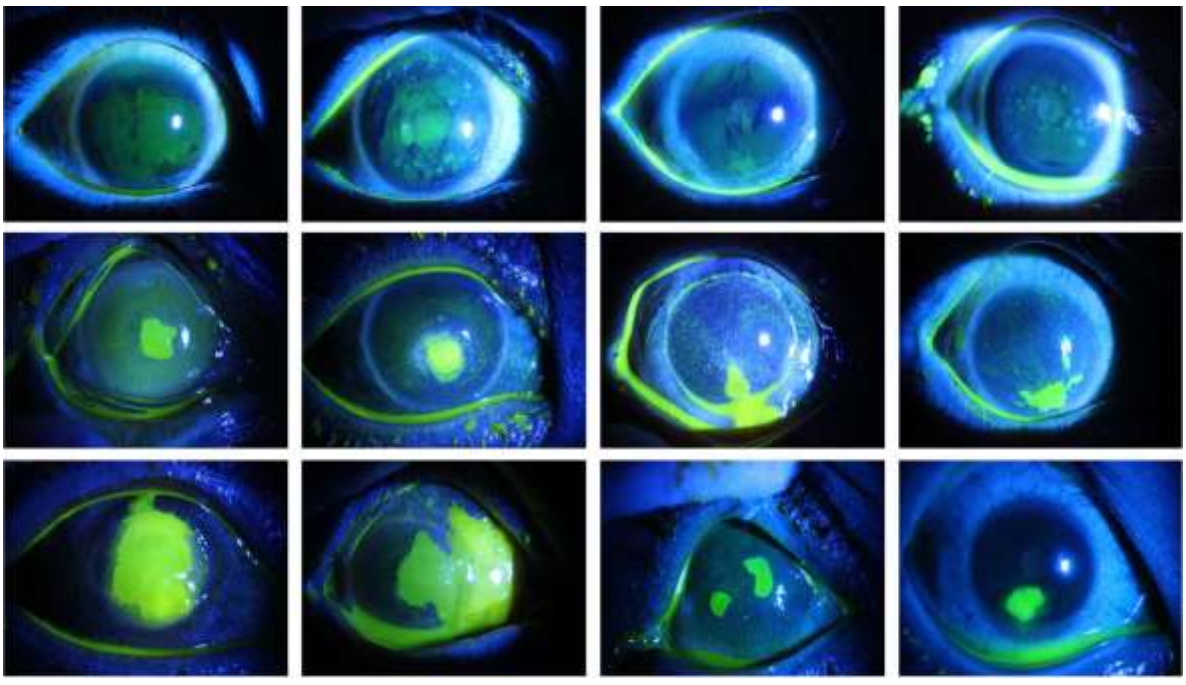

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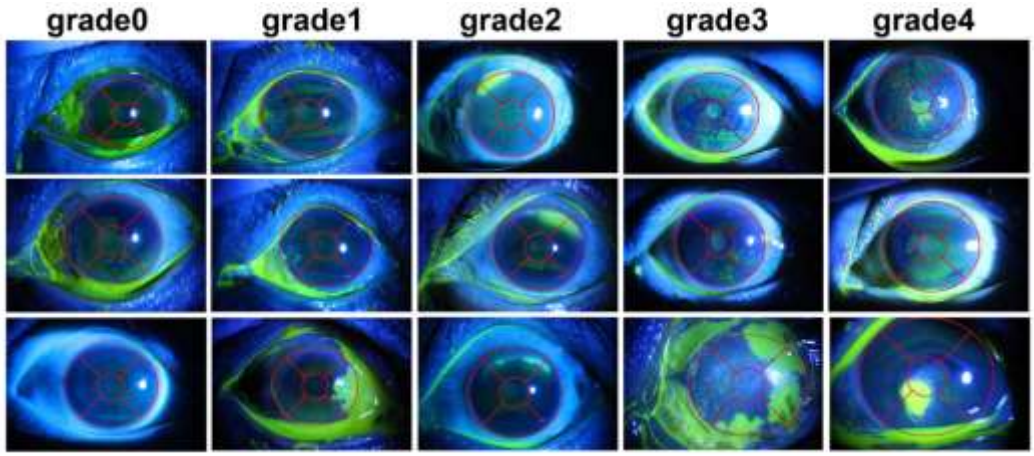

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Q. How to diagnose LSCD?

- **LSCD** commonly results in PED :

  early: late fluorescein staining
  corneal opacities,
  decreased vision,
  photophobia,
  unstable tear film.

  late: superficial vascularization.
  Scarring, ulceration,
  neovascularization
  perforation .

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Q. What are Complications of PED?

- If untreated PED include :
  - infection,
  - anterior stromal scarring,
  - melting,
  - neovascularization,
  - ulceration, perforation,
  - and significant vision loss

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Q. how to treat PED?

- 1.Treat underlying condition :.
  - Stevens-Johnson syndrome,
  - Graft vs. host disease,
  - Sjogren's syndrome.
  - Neurotrophic cornea …. topical nerve growth factor
  - Diabetic keratopathies…control;
  - Herpetic keratitis …..antiviral treatment
  - LSCD ……. limbal stem cell transplants

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2. Consider iatrogenic causes:

Benzalkonium chloride,

topical aminoglycosides and vancomycin drops.

3. Aggressive lubrication with preservative-free artificial tears

4. Punctal plug.

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- 5. **Oral tetracyclines** exhibit anticollagenolytic activity, inhibiting MMPs …. effective in healing PEDs within weeks
- Prophylactic **topical antibiotics**.
- **Topical corticosteroids** in Stevens-Johnson syndrome, and atopic keratoconjunctivitis .
- **Immunosuppression** Stevens-Johnson syndrome, graft vs. host disease, and Sjogren's syndrome

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- 6. Bandage soft contact lenses and/or pressure patching

7. Debridement,: removing inert, healing epithelial tissue from the edge of the PED to allow for migration of new epithelial cells to restore the corneal tissue.

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- 8. **Tarsorrhaphy** to decrease the area of exposed cornea.
- Temporary suture tarsorrhaphy is an option that may sustain the closed palpebral fissure for up to 6 weeks.
- administration of botulinum toxin A, cyanoacrylates glue.

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9.Autologous serum (PLATELET RICH PLASMA EYE DROPS): contains many growth factors, including vitamin A, vitamin E, EGF, TGF-β, PDGF, IGF, nerve growth factor, substance P, immunoglobulins, and fibronectin.

- 50 ml blood on anticoagulant-citrate-dextrose sol…..centrifuge at 200xg.
- Upper 2/3 diluted to 20% wrap in alumnium foil.
- Store at -20

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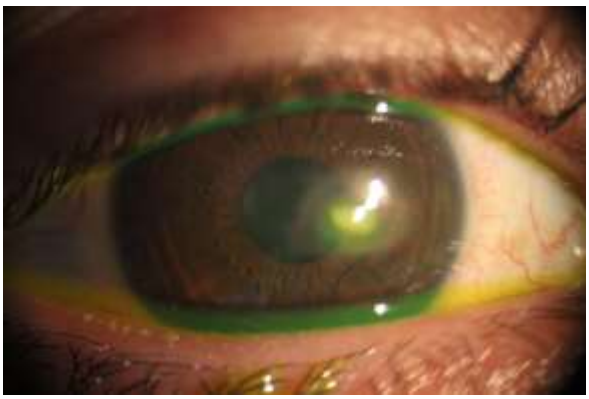

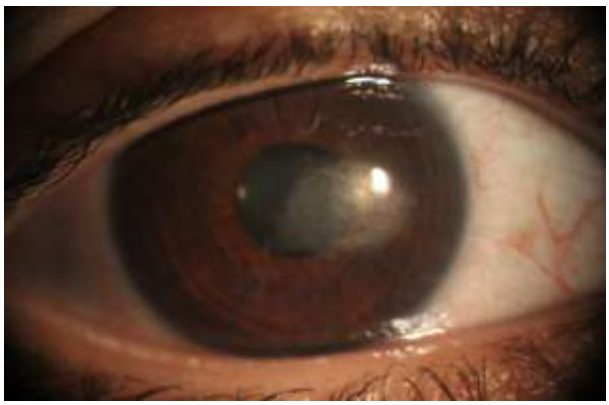

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10.Whole blood-derived products, such as **umbilical cord blood serum** and **platelet-rich fibrin tears**, can be used instead of autologous serum in patients with infection or systemic disease .

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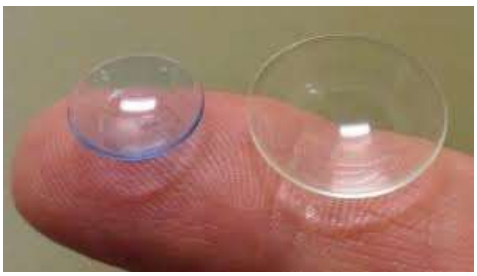
11.Scleral contact lenses are effective in treating PED due to their high oxygen permeability, lubricating properties, and protective effects on the corneal epithelium .



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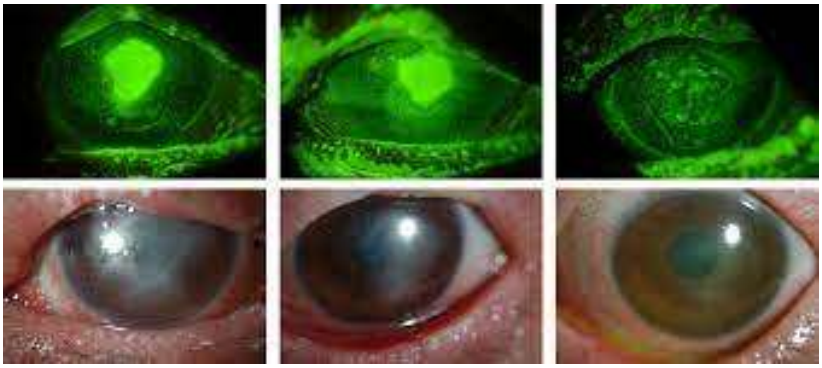
12. Temporary cyanoacrylate glue with patching has been shown to help with the re-epithelialization process, prevent stromal melting, and has bacteriostatic activity



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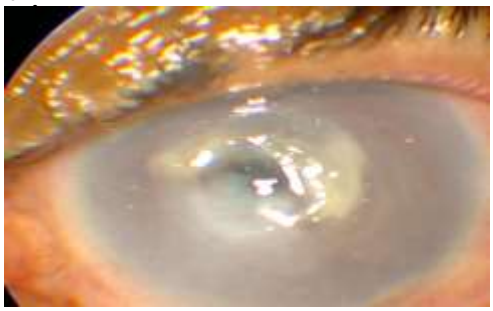

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Surgical:

- Amniotic membrane transplant (AMT) .
- Corneal epithelial stem cell transplantation.
- Phototherapeutic keratectomy (PTK).
- Corneal neurotization

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AMT

- **Advantages:**
- contain many of the growth factors (EGF, KGF, basic [FGF2]), proteinase inhibitors and proteins that faci healing.
- providing a scaffold for re-epithelialization,
- Decreasing vascularization,
- having anti-inflammatory properties
- reconstruction of surface ocular disorders, such as PED, limbal stem cell deficiency to prevent corneal perforations .
- Amniotic membranes are usually **fibrin-glued** or **sutured** underneath a bandage soft contact lens .

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- Prevention of tissue destruction by inhibition of various proteases.
- Structural support.
- Barrier against PNL from tear film.
- No immune rejection.
- Wound healing augmentation by fibroblast growth factor.

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- Long term drug delivery effect
- Antiviral effect (cystatin E).
- Inhibition of infection.
- Decease corneal haze.
- Pain reducing effect.

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COMPOSITION

- A single epithelial cell layer, a thick BM, and an avascular stroma
- Collagens IV and VII
- Fibroblast growth factor, hepatocyte growth factor, and transforming growth factor B
- Various protinase inhibitors.

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Preparation of AMT

From CS

Serological tests

Antibiotics

Dissection from chorion.

Storage;

-70 ° C /DMEM and glycerol

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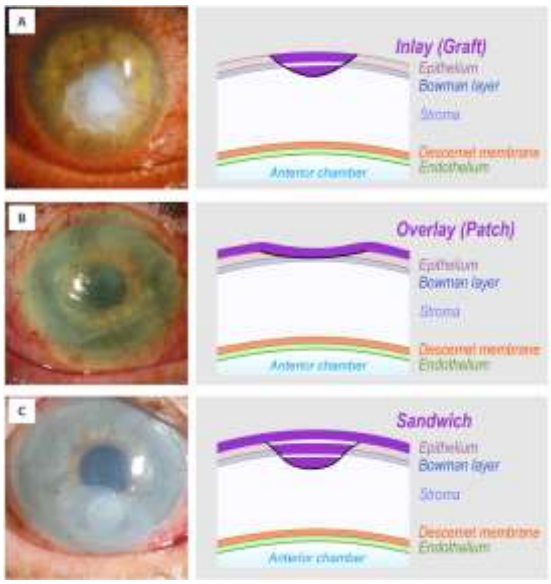

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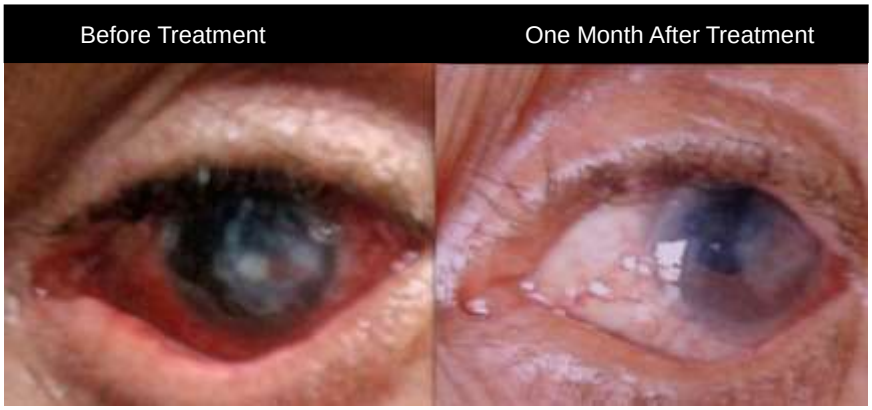

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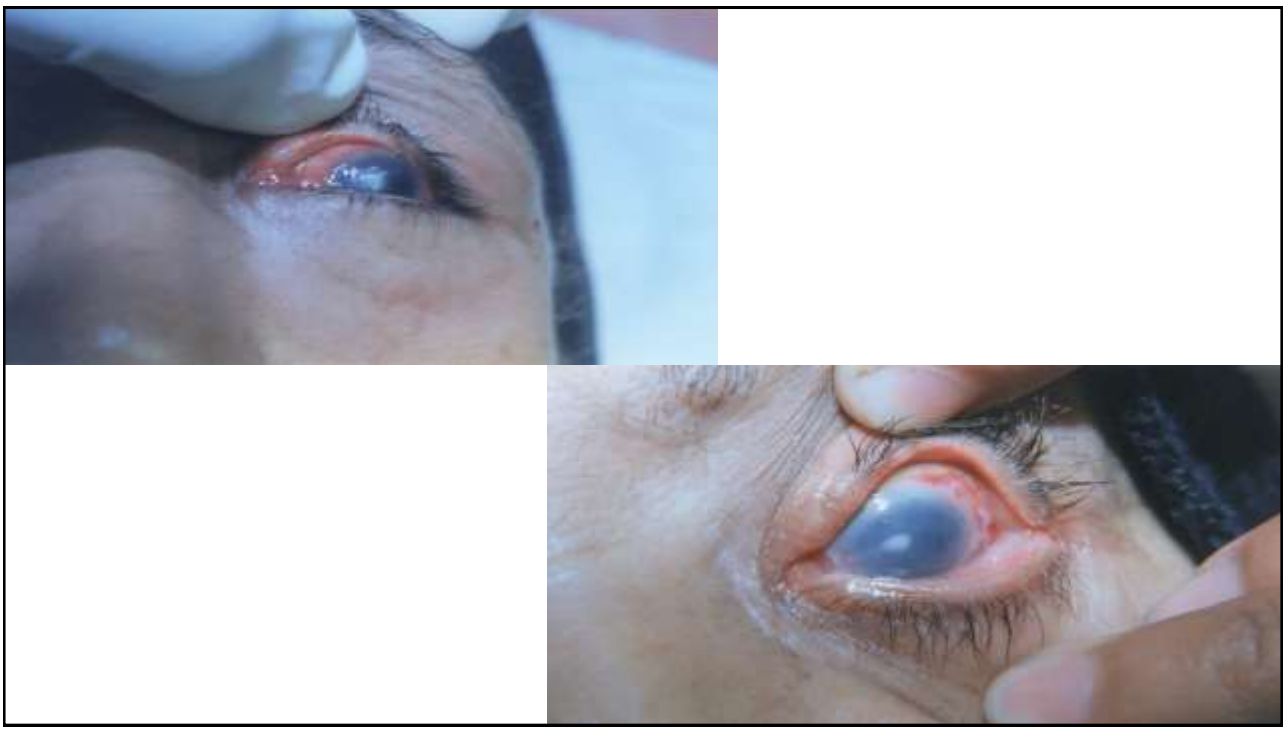

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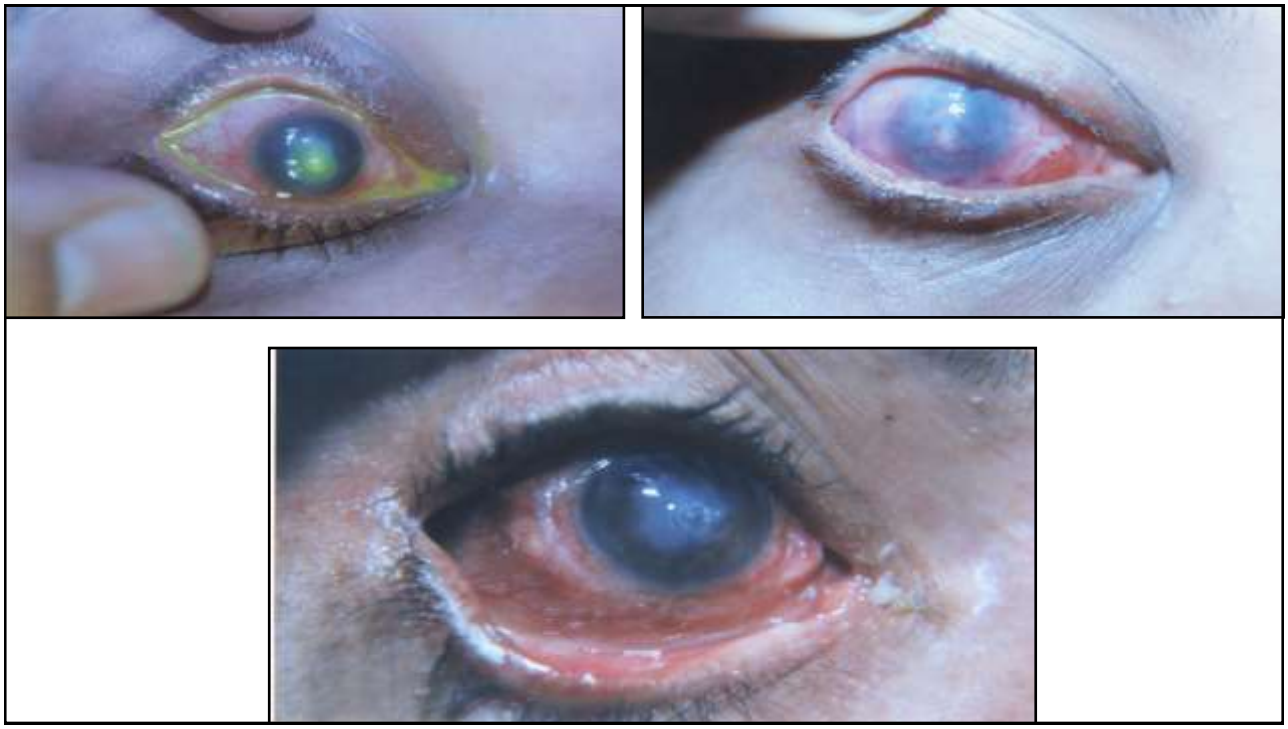

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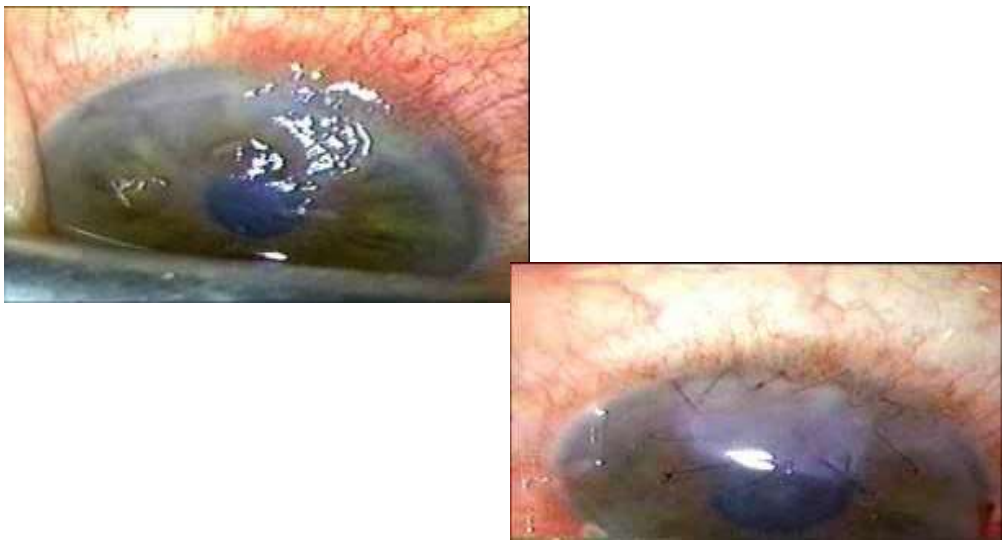

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- **Limbal stem cell transplantation** can aid in Stevens-Johnson syndrome, chemical or thermal burns, or stem cell deficiencies .
- Severe cases of PED, such as patients with extensive alkali burns, can be treated with **penetrating** or **lamellar keratoplasty** if there is a high risk for perforation .
- In patients with multiple failed corneal transplantations or grafts, the **Boston Keratoprosthesis** (KPro) implantation may help manage corneal LSCDs .

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LSCD




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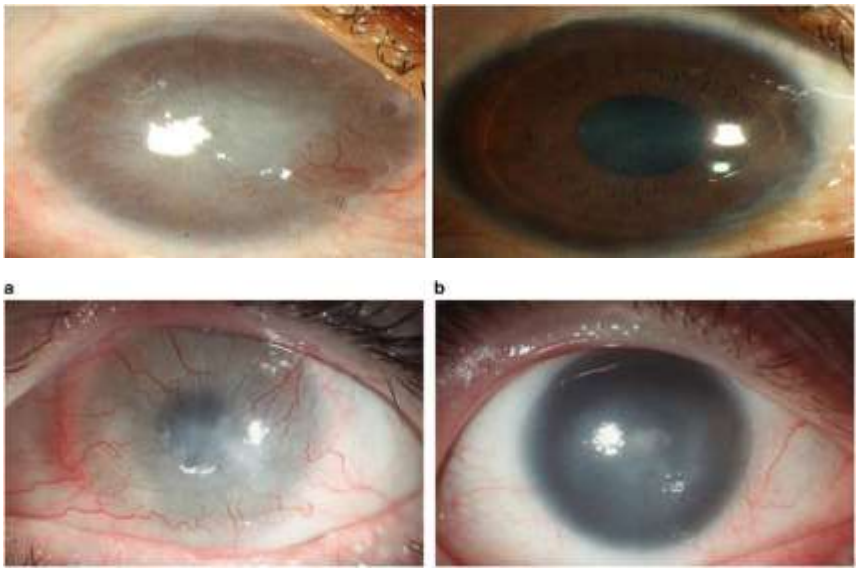

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(PTK)

- Applying a laser to the basement membrane and Bowman's layer to facilitate stronger adhesion mechanisms .
- PTK may be able to treat both refractive errors and epithelial defects

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Thank you

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