INFECTIOUS KERATITIS

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Introduction

- **Infectious keratitis** is a major global cause of visual impairment and blindness, often affecting marginalized populations.
- Approximately **71,000 cases** of microbial keratitis (including bacteria, fungus, and *Acanthamoeba*) occur annually in the United States, with an increasing incidence in recent years.
- The various microorganisms which can cause infectious keratitis can be classified into **eukaryotic** and **prokaryotic** organisms .
- The eukaryotic organisms include the relatively complex cells such as **protozoa** and the **fungi** .
- the prokaryotic organisms are more primitive cells, which include the filamentous bacteria**, true bacteria**, spirochaetes, mycoplasma and rickettsiae and chlamydiae

Bacterial keratitis :

- The **most important cause** of infectious keratitis .

- Rarely occurs in the normal eye because of the human cornea's natural resistance to infection .

Bacterial keratitis :

Risk Factors :

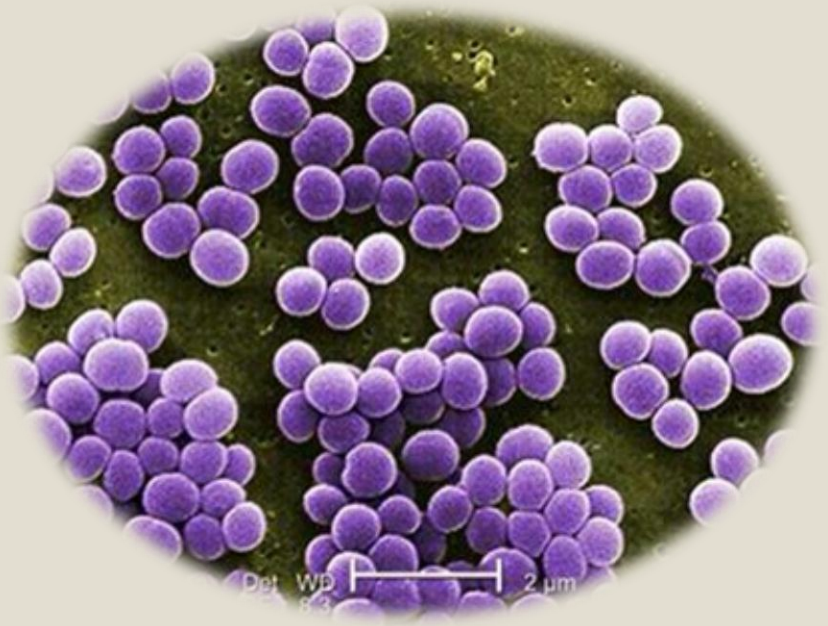
- predisposing factors, including: **contact lens wear**, **trauma**, **corneal surgery**, **ocular surface disease**, **systemic diseases**, and **immunosuppression**

- Some bacteria, including:

(***Neisseria gonorrhoeae***, ***Neisseria meningitidis***, ***Corynebacterium diphtheriae*** and ***Haemophilus influenzae)*** are able to penetrate a healthy corneal epithelium

Bacterial keratitis :

Pathogenesis :



- Remember that infections may be **polymicrobial**
- Common pathogens include :
  - ***Pseudomonas aeruginosa***
  - ***Staphylococcus aureus***
  - ***Streptococci :*** *S. pyogenes* - *S. pneumonia* (pneumococcus)
  - ***Enteric gram-negative rods*** : In particular, *Klebsiella, Enterobacter, Citrobacter, Serratia,* and *Proteus* are important causes of keratitis .
- ***others*** : *Mycobacterium* , Gonococci , *Corynebacterium diphtheriae* , *Haemophilus influenza*

Bacterial keratitis :

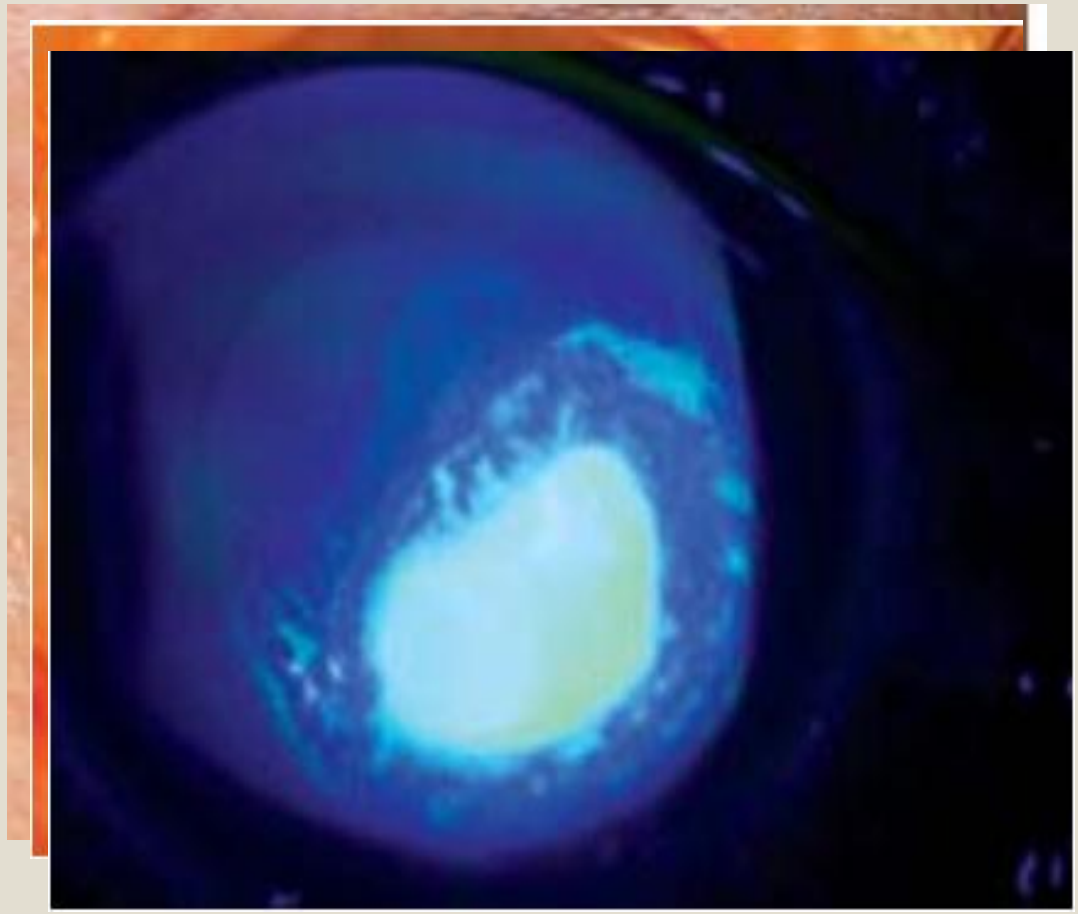
Symptoms :

- The classical ***symptoms*** of corneal ulceration include the presence of :

- **PAIN**
- **REDNESS & PHOTOPHOBIA**
- **DISCHARGE**
- **DICREASED VISUAL ACUITY**

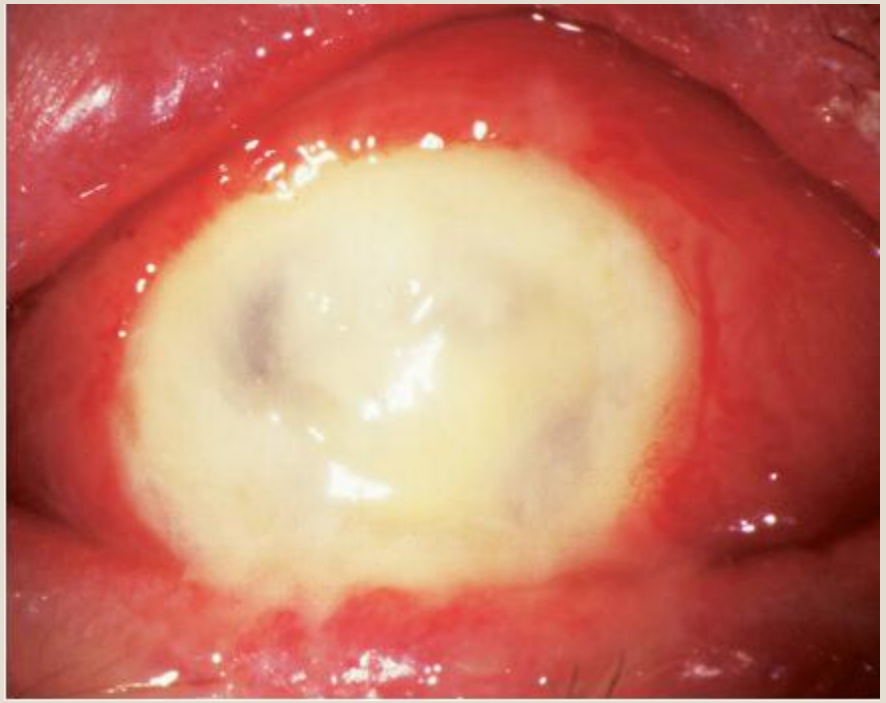
Bacterial keratitis :

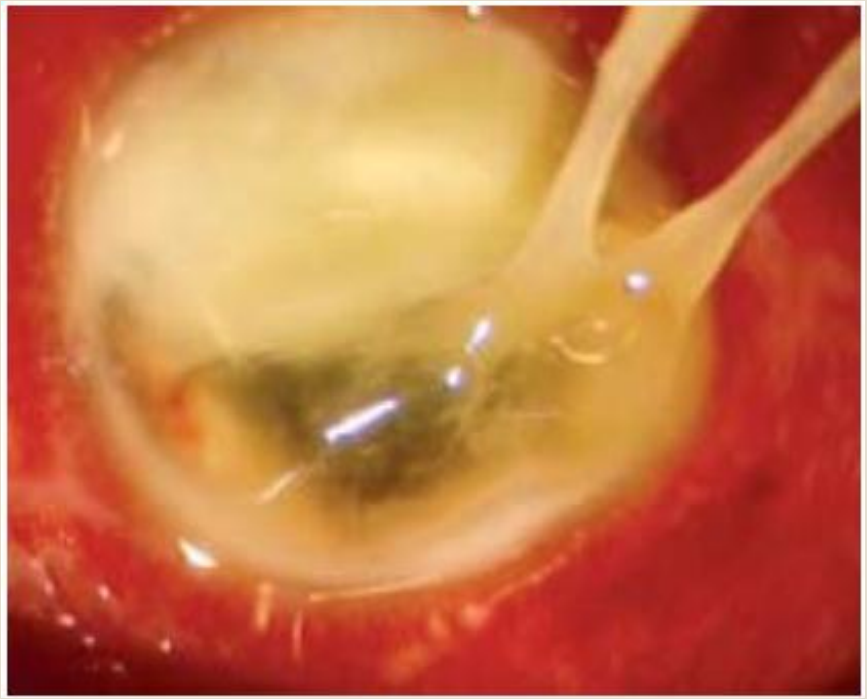
Signs :



Bacterial keratitis :

Signs :





Bacterial keratitis :

Work up :

- History taking and clinical examination are crucial for the diagnosis and management of microbial keratitis.
- A **meticulous history** helps to identify predisposing incidents, risk factors and can provide clues to etiological diagnosis of microbial keratitis .
- **Clinical examination** - ***corneal sensation*** which must be assessed prior to instillation of topical anesthetic .

Grading of corneal ulcer

Feature	*Mild*	*Moderate*	*Severe*
Size of ulcer (mm)	< 2	2-5	> 5
Depth of ulcer (%) Infiltrate	< 20	20-50	> 50
— Density	Dense	Dense	Dense
— Extent	Superficial	Extension upto mid-stroma	Deeper than mid stroma
Scleral involvement	Not involved	Not involved	May be involved

Ann Ophthalmol 1975;7(4):537-9

Bacterial keratitis :

Diagnostic tests :

Culture and smears :

- The majority of community-acquired cases of bacterial keratitis resolve with empiric therapy and are managed without smears or cultures.

- Smears and/or cultures are specifically indicated in the following circumstances :
  1. a corneal infiltrate is **central**, **large**, and/or is associated with **significant stromal involvement or melting** .
  2. the infection **is chronic or unresponsive** to broad-spectrum antibiotic therapy
  3. there is a history of **corneal surgeries**.
  4. **Atypical clinical features** are present that are suggestive of fungal, amoebic, or mycobacterial keratitis.
  5. infiltrates are in **multiple locations** on the cornea

- **Corneal scraping is a powerful diagnostic tool allowing definitive diagnosis of pathologic conditions**

Samples for diagnosis of corneal ulcer

Eyelid swab- Not of much use

Conjunctival swab - Not of much use

Corneal scraping- Most important

Contact lens, contact lens case and solution- Must in contact lens wear

AC paracentesis (Hypopyon)- Deep ulceration or when insufficient material is present

Bacterial keratitis :

Corneal scraping

The most important sample for microbiological examination

❖***Anesthesia*** :

- Topical 0.5% **proapracaine** in the lower fornix
- 0.5% proparacaine is least bactericidal as compared to other anesthetic agents.
- General anesthesia and sedation may be required in children, uncooperative adults or mentally impaired patients

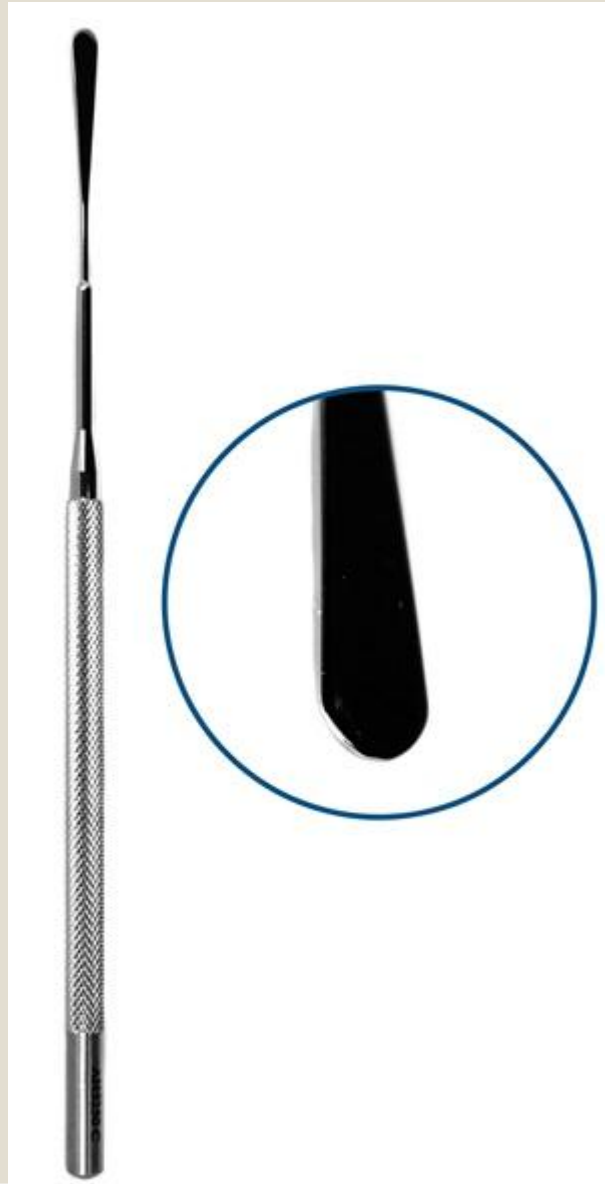
Bacterial keratitis :

Corneal scraping

The most important sample for microbiological examination

❖***Instruments:***

- Kimura' s spatula
- surgical blade no 15
- 23-gauge needle.
- calcium alginate swab



Bacterial keratitis :

Corneal scraping

The most important sample for microbiological examination

❖***Technique :***

- A lid speculum is applied gently to separate the lids
- done under a slit lamp or under an operating microscope.
- Any mucous or debris on and around the ulcer is carefully cleaned with a sterile swab stick .
- the leading edges and base of the ulcer are scraped
- it should be directly inoculated into the culture media rather than placing it first into the transport media. (broth culture medium)
- Multiple scrapings must be obtained to enhance the yield of the organism

Table 6.3 Stains for corneal and conjunctival scrapings

Stain	Organism
Gram	Bacteria, fungi, microsporidia
Giemsa	Bacteria, fungi, *Acanthamoeba*, microsporidia
Calcofluor white (fluorescent microscope)	*Acanthamoeba*, fungi, microsporidia
Acid-fast stain (AFB) e.g. Ziehl–Neelsen, auramine O (fluorescent)	*Mycobacterium*, *Nocardia* spp.
Grocott–Gömöri methenamine-silver	Fungi, *Acanthamoeba*, microsporidia
Periodic acid-Schiff (PAS)	Fungi, *Acanthamoeba*

Table 6.2 Culture media for corneal scrapings

Medium	Notes	Specificity
Blood agar	5–10% sheep or horse blood	Most bacteria and fungi except *Neisseria*, *Haemophilus* and *Moraxella*
Chocolate agar	Blood agar in which the cells have been lysed by heating. Does not contain chocolate!	Fastidious bacteria, particularly *H. influenzae*, *Neisseria* and *Moraxella*
Sabouraud dextrose agar	Low pH and antibiotic (e.g. chloramphenicol) to deter bacterial growth	Fungi
Non-nutrient agar seeded with *Escherichia coli*	*E. coli* is a food source for *Acanthamoeba*	*Acanthamoeba*
Brain–heart infusion	Rich lightly buffered medium providing a wide range of substrates	Difficult-to-culture organisms; particularly suitable for streptococci and meningococci. Supports yeast and fungal growth
Cooked meat broth	Developed during the First World War for the growth of battlefield anaerobes	Anaerobic (e.g. *Propionibacterium acnes*) as well as fastidious bacteria
Löwenstein–Jensen	Contains various nutrients together with bacterial growth inhibitors	Mycobacteria, *Nocardia*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How to Perform a Corneal Biopsy

A/Professor Graham A Lee

https://iop.vision

Bacterial keratitis :

Treatment :

- Ulcers and infiltrates are initially treated as bacterial unless there is a high index of suspicion of another form of infection.

General tips :

- **Consider hospital admission** for severe keratitis – large> 1.5 mm , central involving the visual axis and patients who are not likely to comply or are unable to self-administer.
- **Discontinuation of contact lens wear**
- **Treatment strategies :** depend on severity of keratitis
- Empirical broad-spectrum treatment is usually initiated before microscopy results are available .

Fortified Antibiotic eye drops	Monotherapy
➢ **Combination Therapy** (+ , -) Provides Good Initial Broad-spectrum Antibiotic Coverage . ➢ **Disadvantages** ☹ : • Ocular Irritation • ↑ Cost • The Inconvenience Of Extemporaneously Preparing ➢ Their Chief **Advantage** Is : ☺ Their Potential To Save Vision In Aggressive Infections .	➢ **Fluoroquinolones** :alternative Tx in : ▪ Compliant Patients ▪ Less Severe Ulcers (e.g. <3 mm In Diameter) ▪ Mid-peripheral or Peripheral ▪ Not Associated With Significant Thinning. ➢ At least q.h.

Frequent → every(30- 60 minutes)

In Severe Cases → Every 5 minutes For 30 minutes as a loading Dose
- Oral Abx : scleral – impending perforation- endophthalmitis

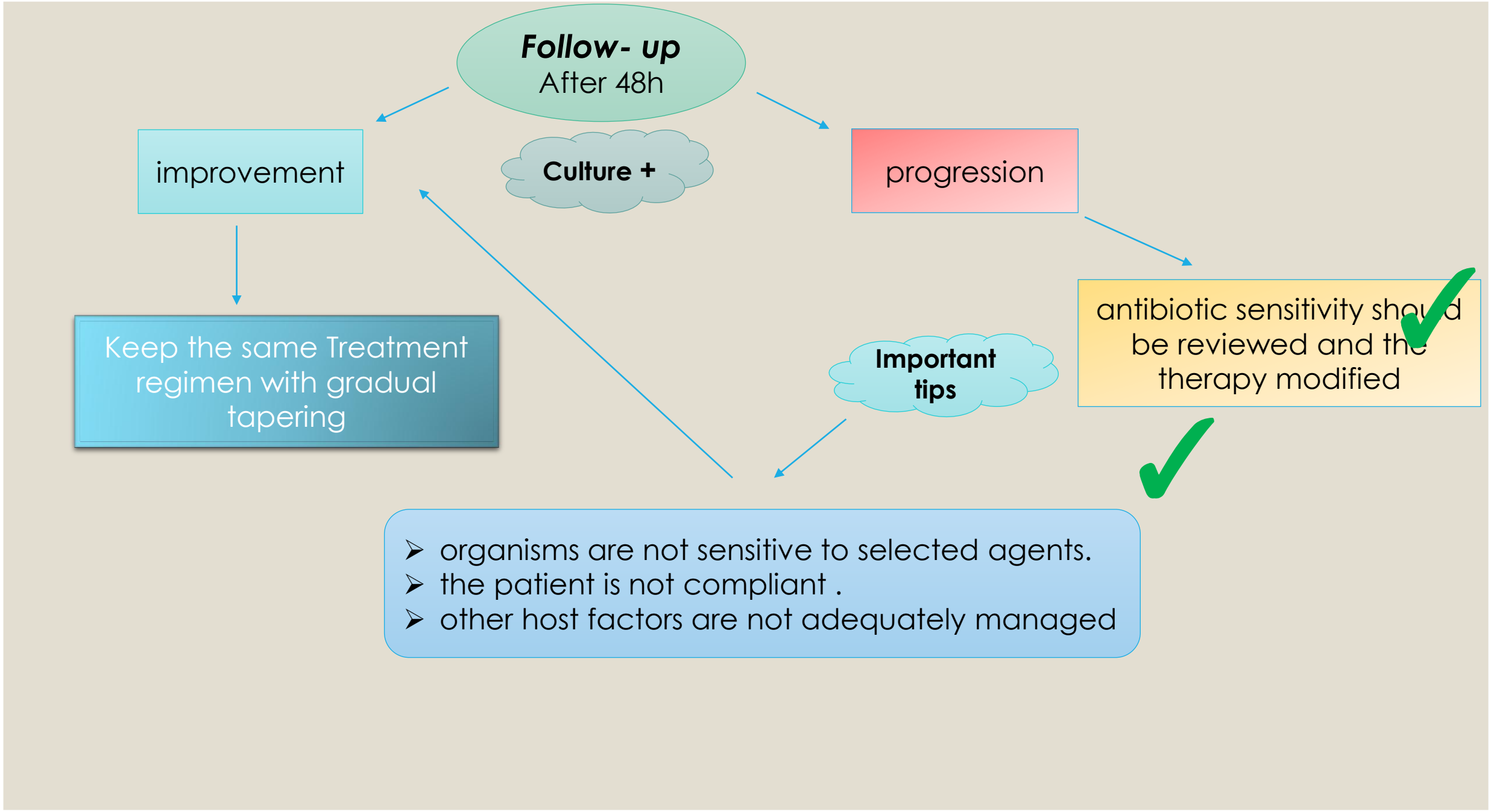
Organism	Antibiotic	Topical concentration	Subconjunctival dose
No organism identified or multiple types of organisms	Cefazolin with	50 mg/mL	100 mg in 0.5 mL
	Tobramycin or gentamicin	9–14 mg/mL	20 mg in 0.5 mL
	Fluoroquinolones	3–6 mg/mL	Not available
Gram-positive cocci	Cefazolin	50 mg/mL	100 mg in 0.5 mL
	Vancomycin‡	15–50 mg/mL	25 mg in 0.5 mL
	Moxifloxacin, gatifloxacin, besifloxacin, levofloxacin	5–6 mg/mL	Not available
Gram-negative rods	Tobramycin or gentamicin	9–14 mg/mL	20 mg in 0.5 mL
	Ceftazidime	50 mg/mL	100 mg in 0.5 mL
	Ciprofloxacin, ofloxacin Moxifloxacin, gatifloxacin, besifloxacin, levofloxacin	3–6 mg/mL	Not available
Gram-negative cocci§	Ceftriaxone	50 mg/mL	100 mg in 0.5 mL
	Ceftazidime	50 mg/mL	100 mg in 0.5 mL
	Ciprofloxacin, ofloxacin Moxifloxacin, gatifloxacin, besifloxacin, levofloxacin	3–6 mg/mL	Not available
Nontuberculous mycobacteria	Clarithromycin	10 mg/mL (0.03%)	20 mg in 0.5 mL
	Moxifloxacin, gatifloxacin, besifloxacin	3–6 mg/mL	Not available
	Amikacin	20–40 mg/mL	20 mg/0.5 mL
Nocardia	Sulfacetamide	100 mg/mL	
	Amikacin	20–40 mg/mL	20 mg/0.5 mL
	Trimethoprim/sulfamethoxazole	16 mg/mL	
		80 mg/mL	

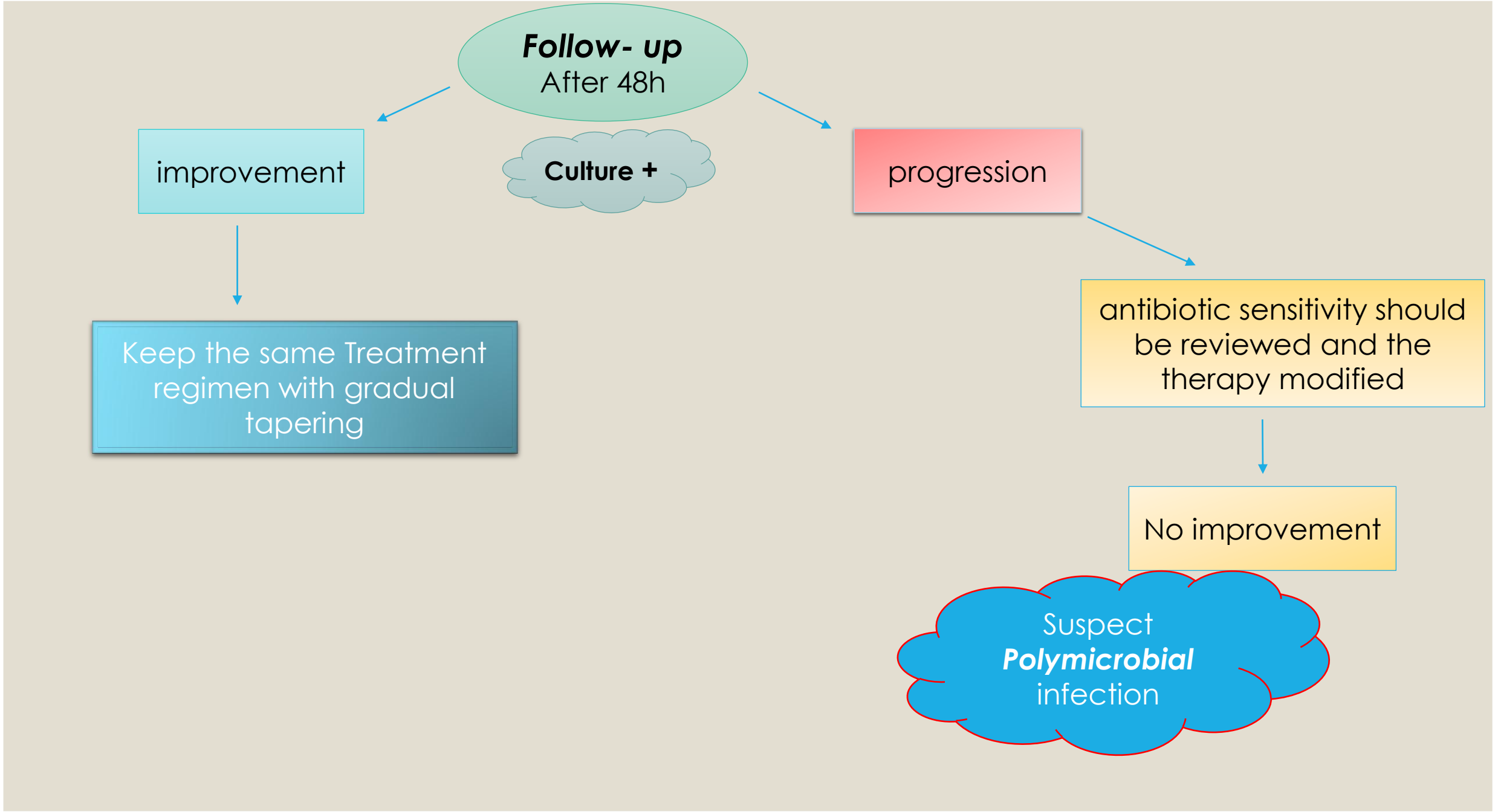
Bacterial keratitis :

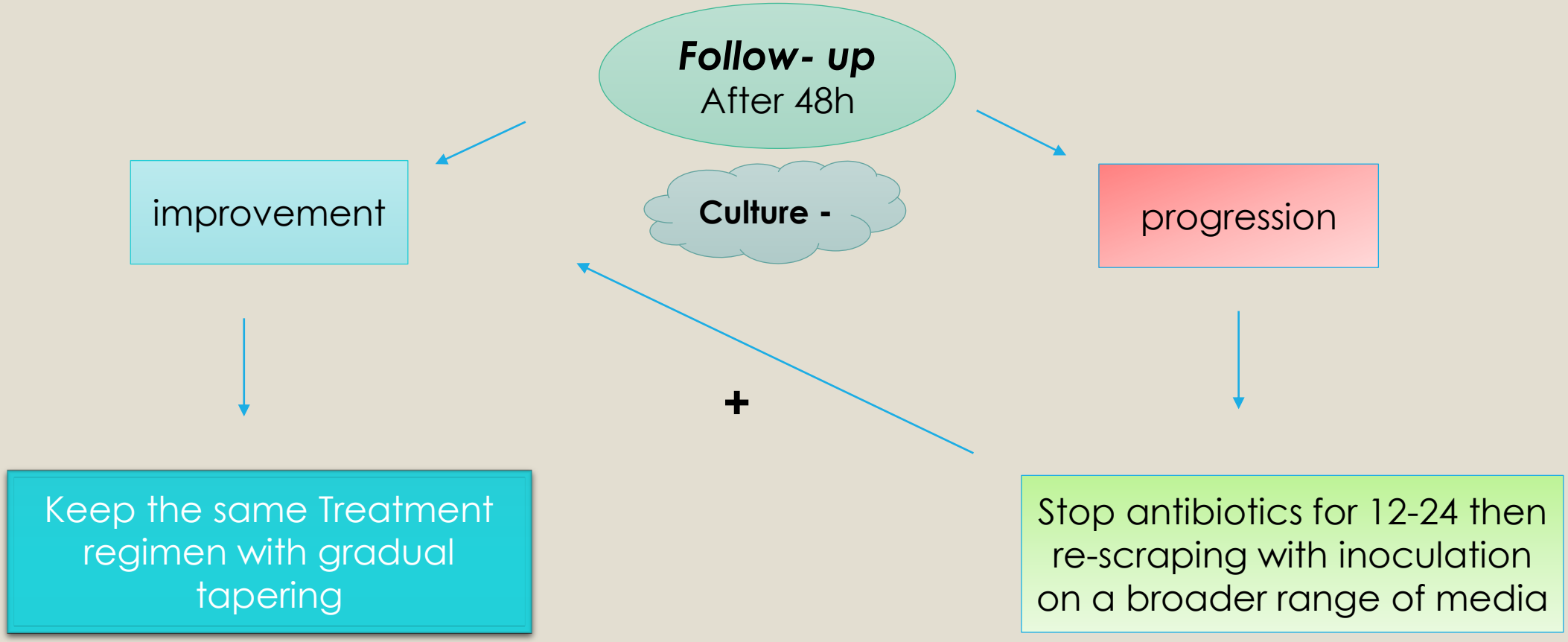
Follow-up :

- Daily evaluation at first, including repeated measurements of the size of the infiltrate and epithelial defect.
- The most important criteria in evaluating treatment response are the **amount of pain**, the **epithelial defect size**, the **size and depth of the infiltrate**, and the **anterior chamber reaction** .

- **Reduced pain** is often the first sign of a positive response to treatment


Follow- up
After 48h
improvement
Culture +
progression
Keep the same Treatment regimen with gradual tapering
Important tips
antibiotic sensitivity should be reviewed and the therapy modified
organisms are not sensitive to selected agents.
the patient is not compliant .
other host factors are not adequately managed


Follow- up
After 48h
improvement
Culture +
progression
Keep the same Treatment regimen with gradual tapering
antibiotic sensitivity should be reviewed and the therapy modified
No improvement
Suspect
Polymicrobial
infection


Follow- up
After 48h
improvement
Culture -
progression
+
Keep the same Treatment regimen with gradual tapering
Stop antibiotics for 12-24 then re-scraping with inoculation on a broader range of media

Fungal keratitis :

- One of the most difficult forms of microbial keratitis for the ophthalmologist to diagnose and treat successfully .
- Rare in temperate countries but is a major cause of visual loss in tropical and developing countries .
- A major blinding eye disease in Asia.
- can elicit a severe inflammatory response – corneal perforation is common, and the outlook for vision is frequently poor .

Risk factors for the development of fungal keratitis

OCULAR FACTORS

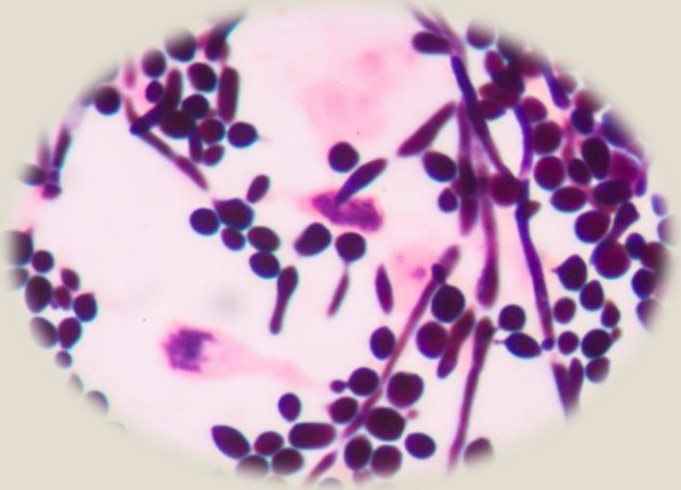
- Trauma
- Chronic corneal inflammation
  - Herpes simplex
  - Herpes zoster
  - Vernal allergic conjunctivitis
  - Ocular surface problems
  - Dry eye
  - Bullous keratopathy
  - Exposure Keratopathy
- Contact lens wear
- Drugs
  - Corticosteroids
  - Anesthetics
- Corneal surgery
  - Penetrating Keratoplasty
  - Refractive surgery

SYSTEMIC FACTORS

- Diabetes mellitus
- HIV positive patients
- Leprosy

Pathogenesis :

- Two main types of fungi cause keratitis:
- **Yeasts** (e.g. genus *Candida*), ovoid unicellular organisms that reproduce by budding, are responsible for most cases of fungal keratitis *in temperate climates*.
- **Filamentous fungi** (e.g. genera *Fusarium* and *Aspergillus*), multicellular organisms that produce tubular projections known as hyphae. They are the most common pathogens in *tropical climates*, but are not uncommon in cooler regions; the keratitis frequently follows an aggressive course

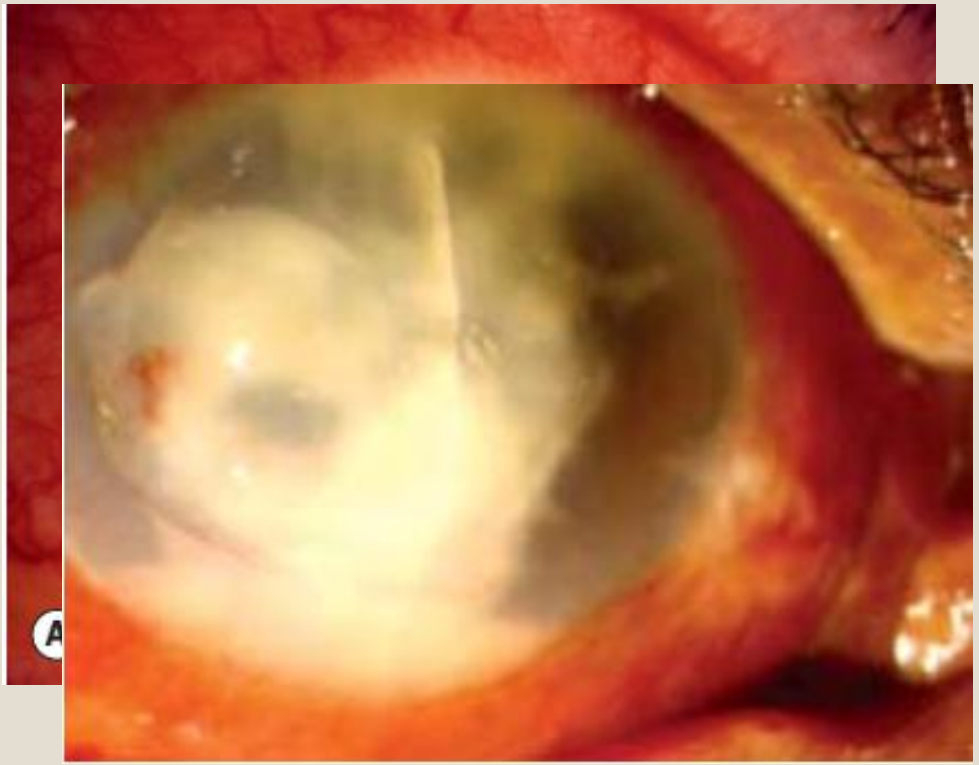


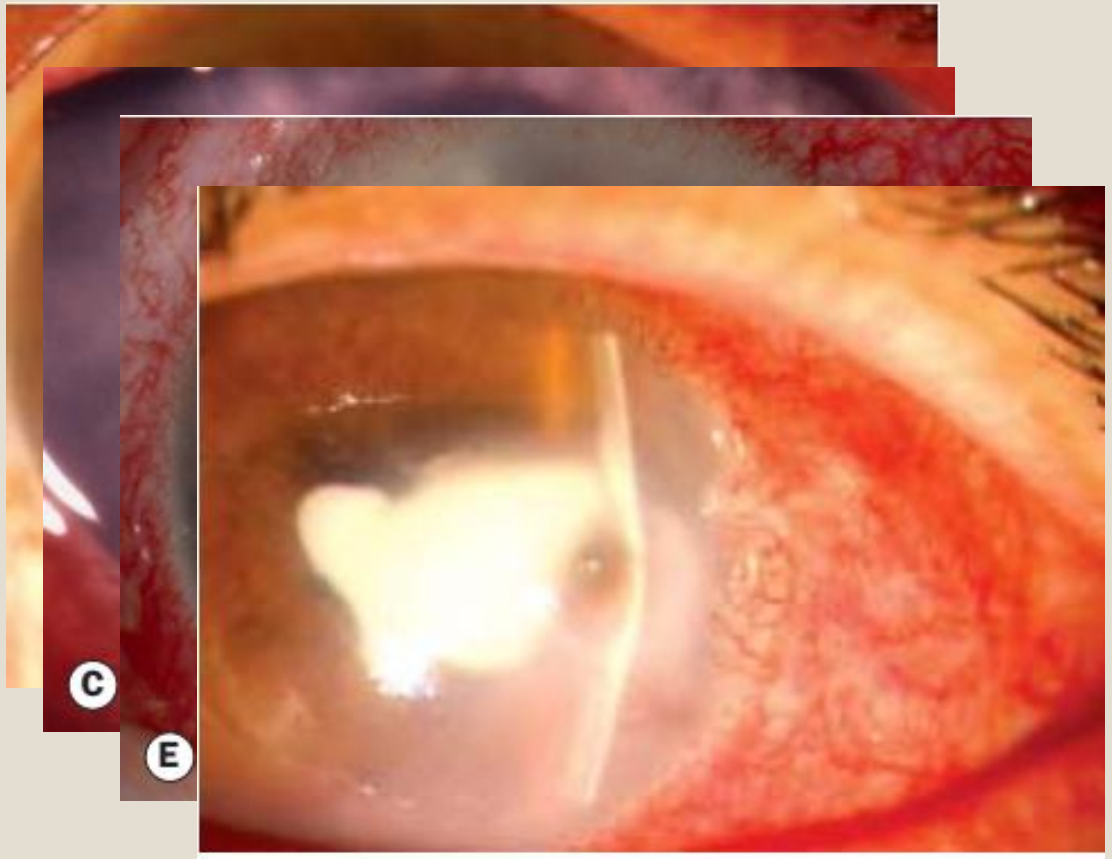
Clinical features :

- **Symptoms** : The onset of fungal keratitis is almost always insidious. Symptoms are usually non-specific, although possibly more prolonged duration (5 to 10 days)
- Patients generally complaint of a foreign body sensation for several days with a slow onset of increasing pain and diminution of vision especially if the keratitis involves the visual axis.

Clinical features :

- **Signs :**



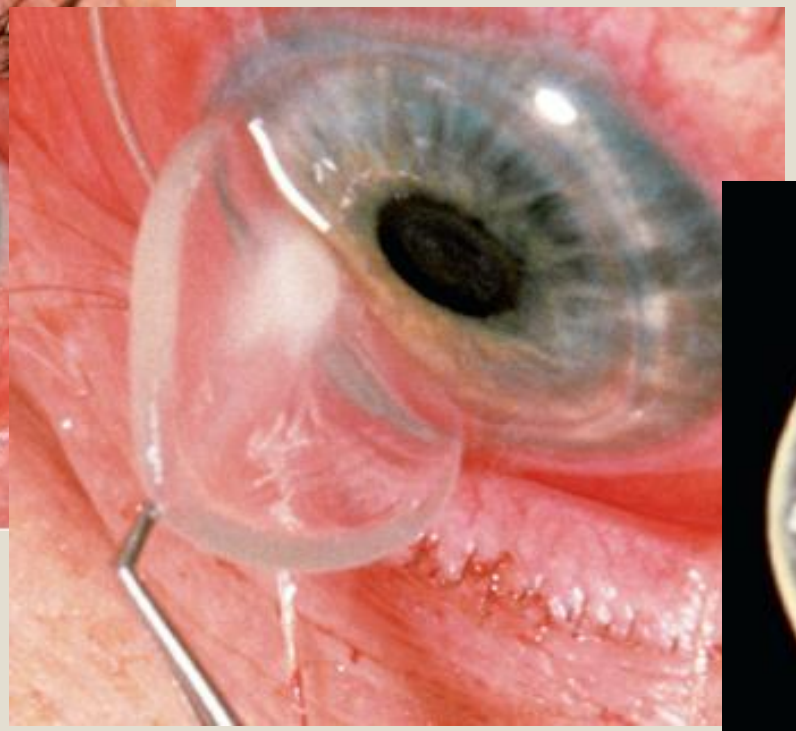


Diagnosis :

- **Staining** : **KOH** – highly sensitive
- **Culture** : Sabouraud dextrose agar
- **Polymerase chain reaction (PCR) analysis**
- **Corneal biopsy** is indicated in suspected fungal keratitis in the absence of clinical improvement after 3–4 days and if no growth develops from scrapings after **a week**
- **Anterior chamber tap** has been advocated in resistant cases with endothelial exudate
- **Confocal microscopy** frequently permits identification of organisms *in vivo*

Treatment :

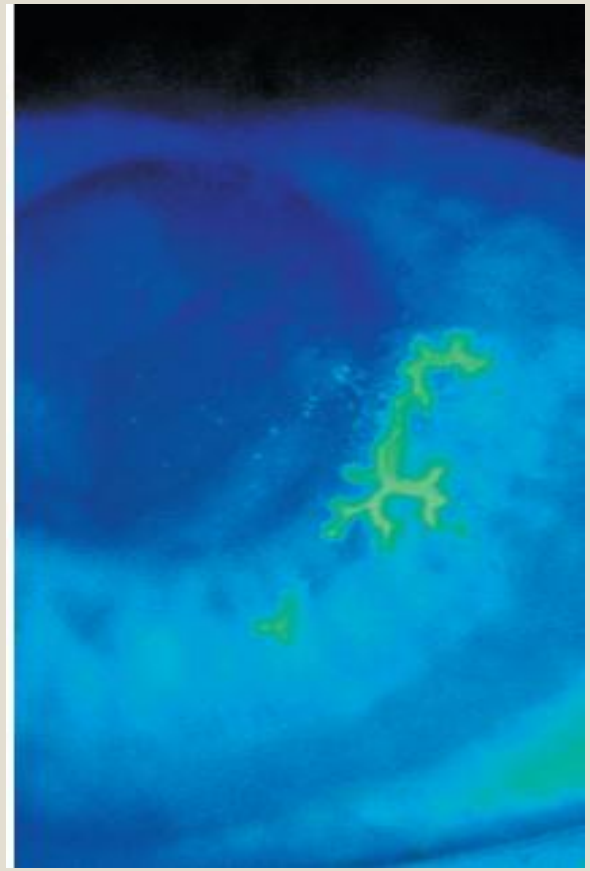
- **Hospital admission** is required
- **Topical Anti fungals** : q.h for 48h then tapering according to signs
  - Candida infection : amphotericin B 0.15% or econazole 1% alternatives include : natamycin 5% voriconazole 1 or 2% .
  - *Filamentous infection* : natamycin 5% or econazole 1% alternatives include : amphotericin B 0.15%
- **A broad-spectrum antibiotic**
- **Cycloplegia**
- **Systemic antifungals :** fluconazole 200 mg twice daily
- **Tetracycline** (e.g. doxycycline 100 mg twice daily) may be given for its anticollagenase effect when there is significant thinning .
- **Superfcial keratectomy**
- **Therapeutic keratoplasty**

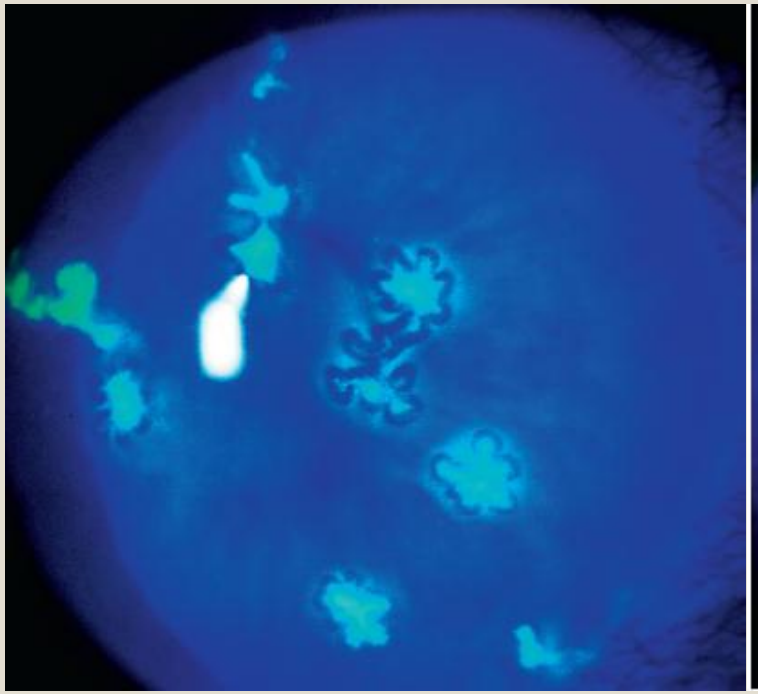



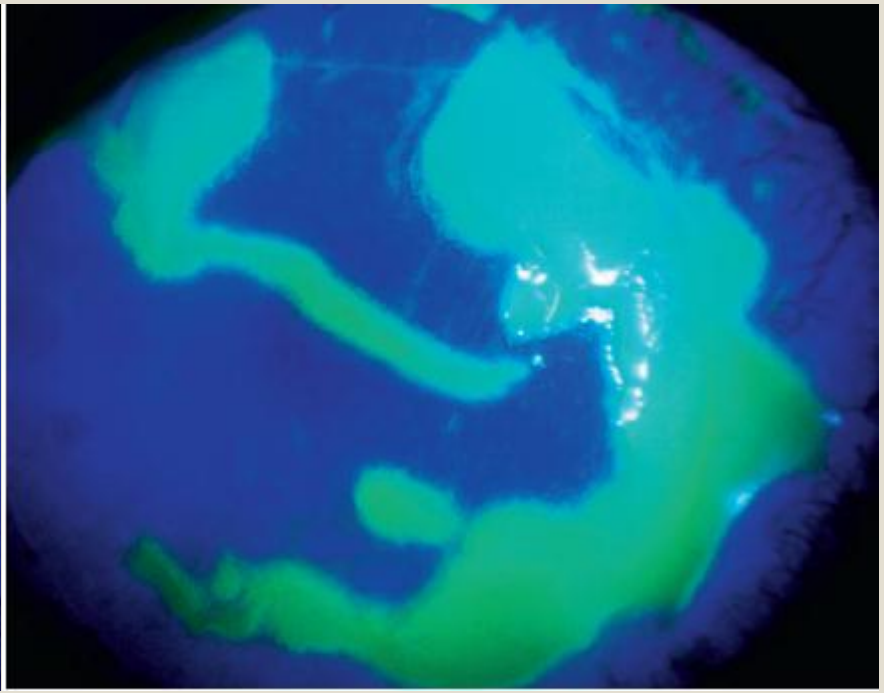

Viral keratitis : HSV

- Viral keratitis is the commonest cause of keratitis in the developed world .
- HSV – HZV – adenoviruses
- Herpes simplex keratitis is the most common infective cause of blindness in many developed countries
- The ocular disease affecting the cornea may be classified into **primary or recurrent**

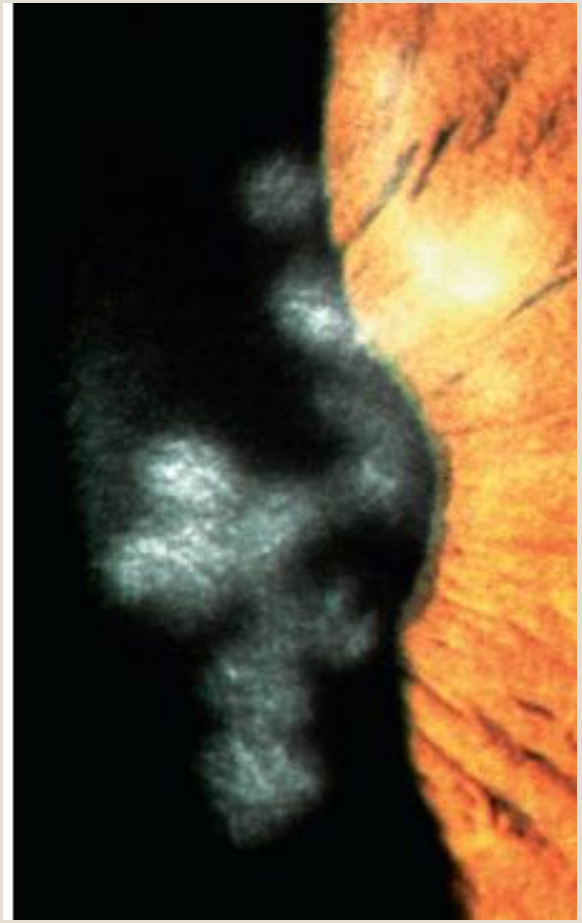
Signs : HSV

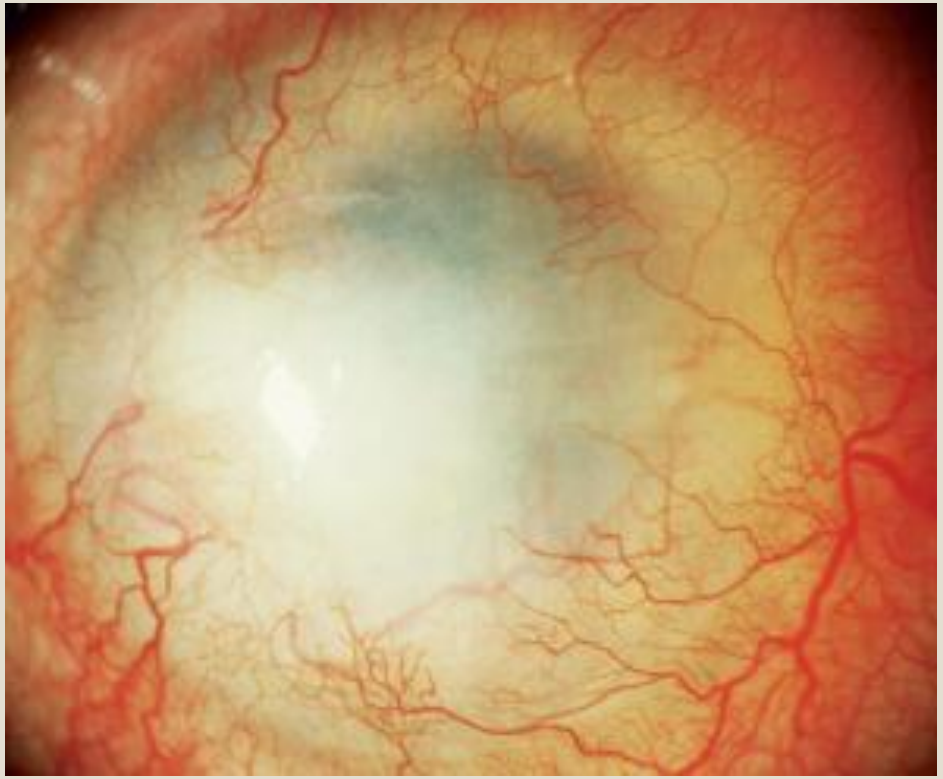


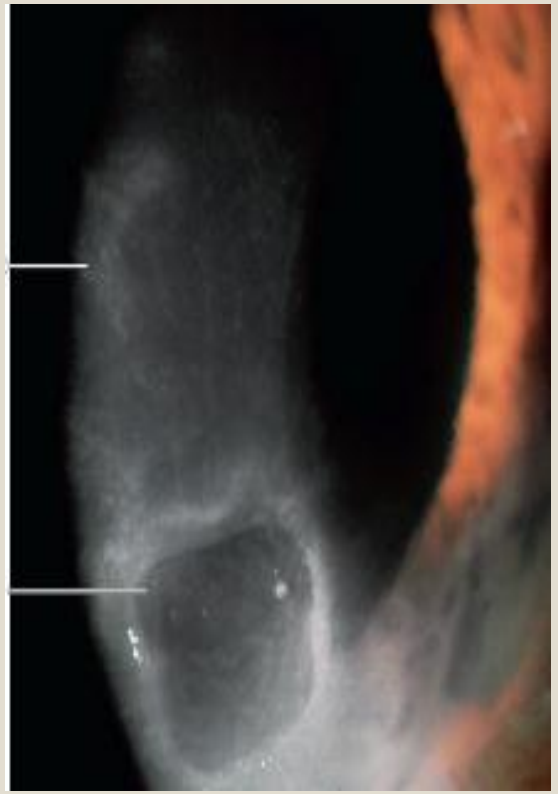




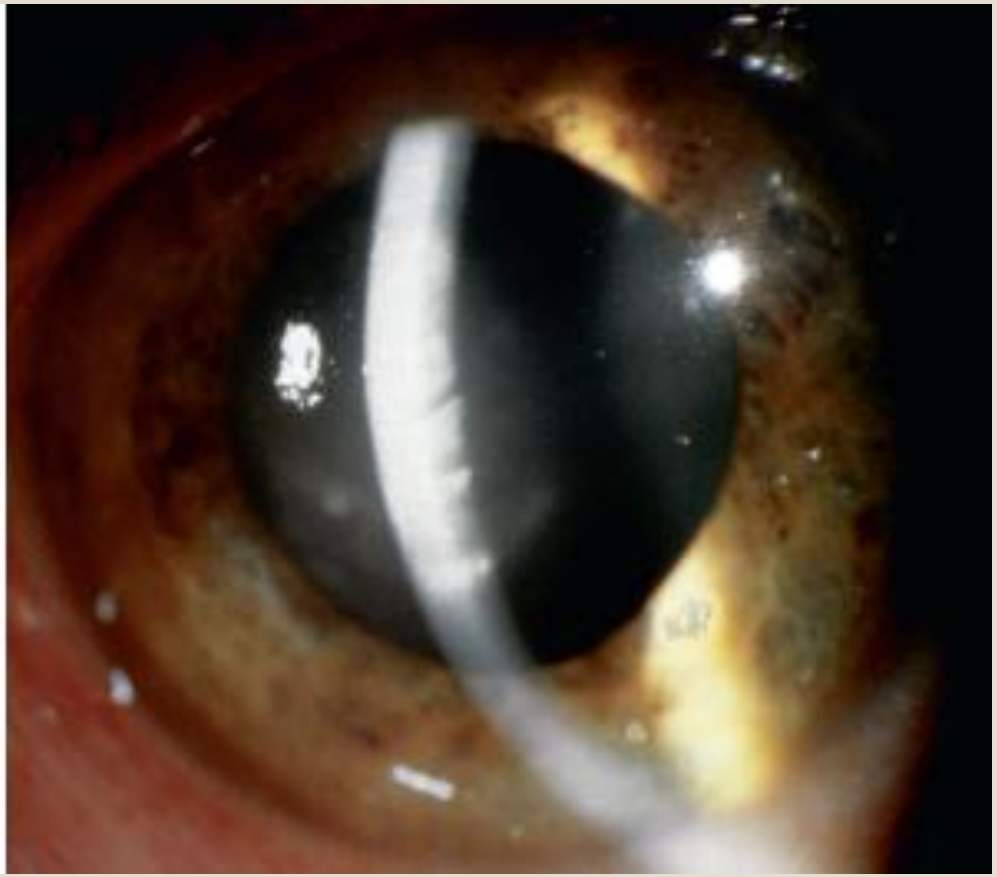
Signs : HSV

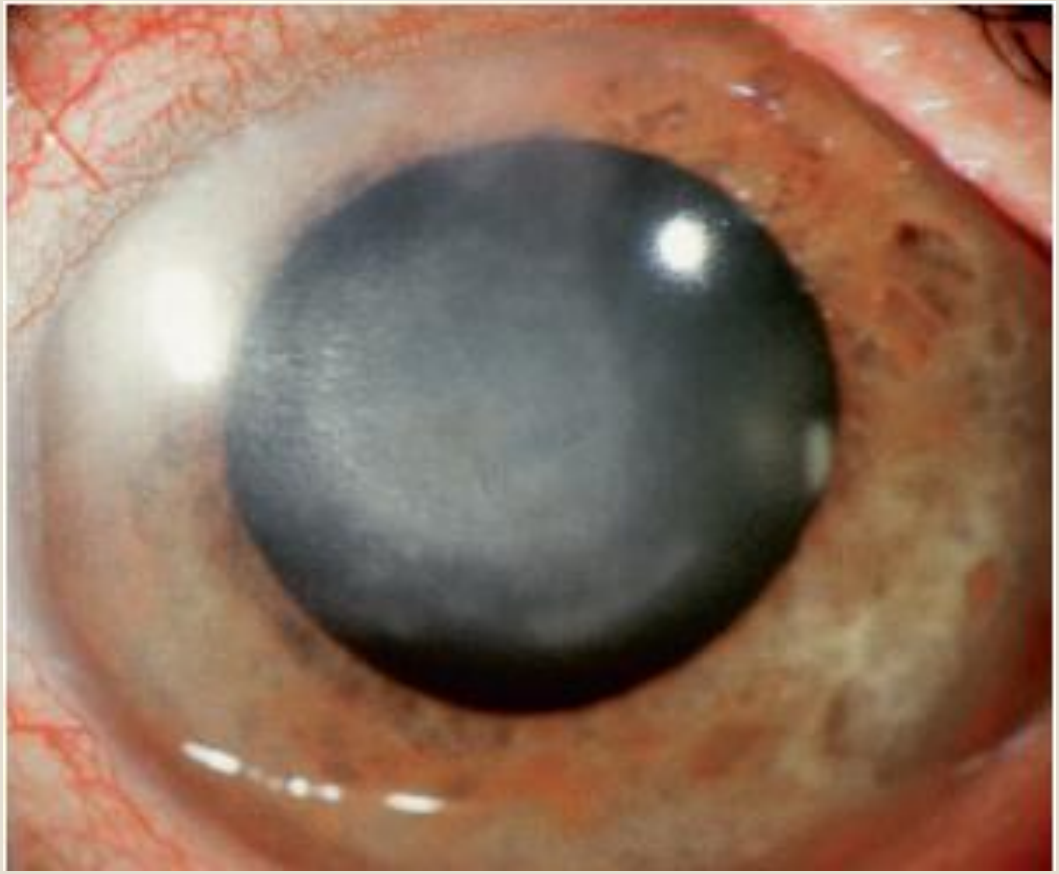




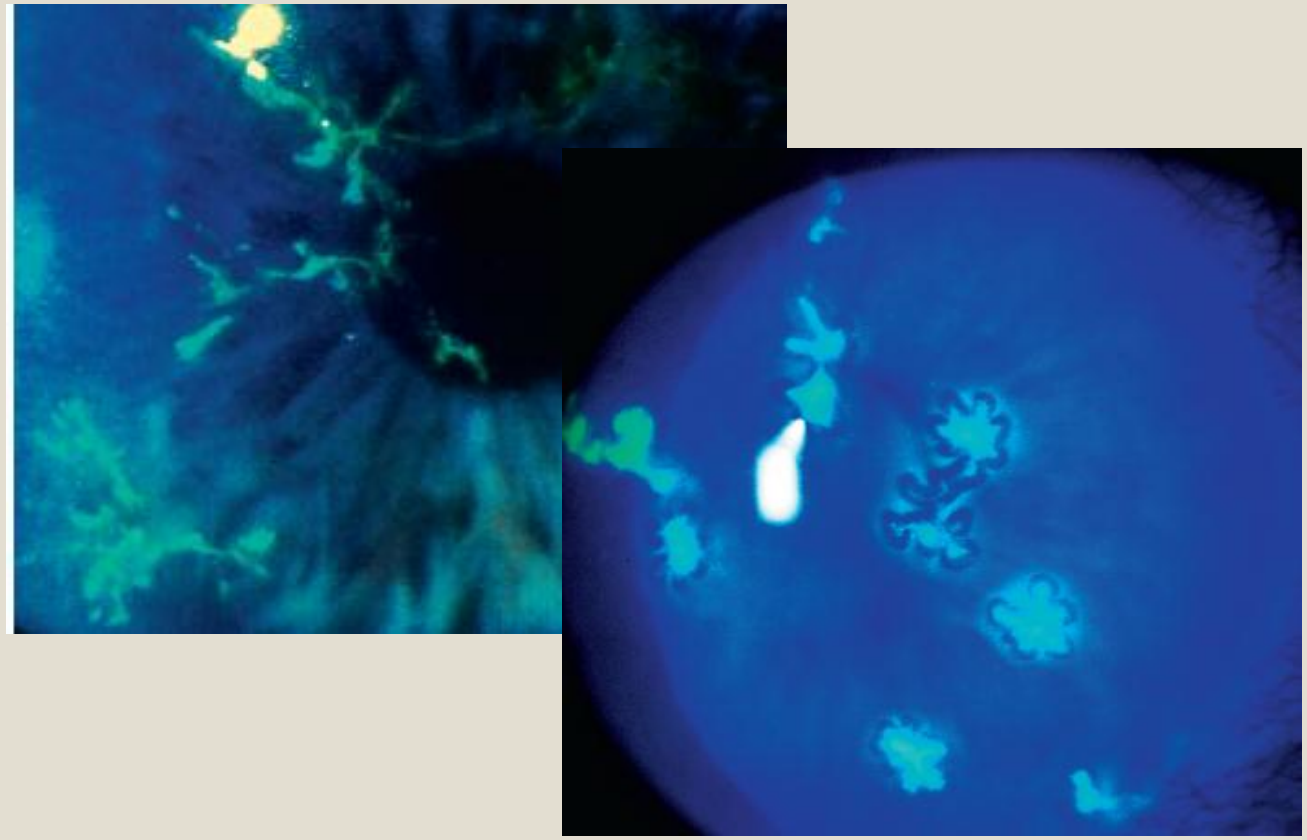


Signs : HSV

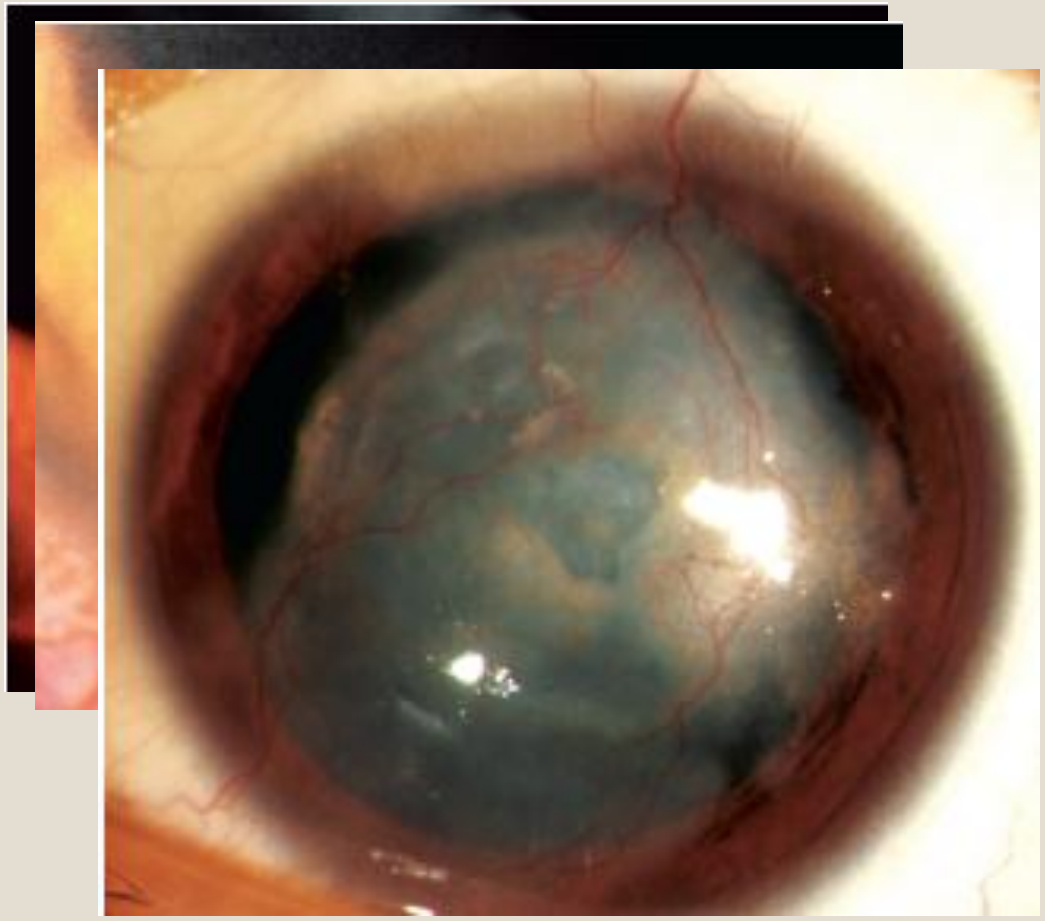


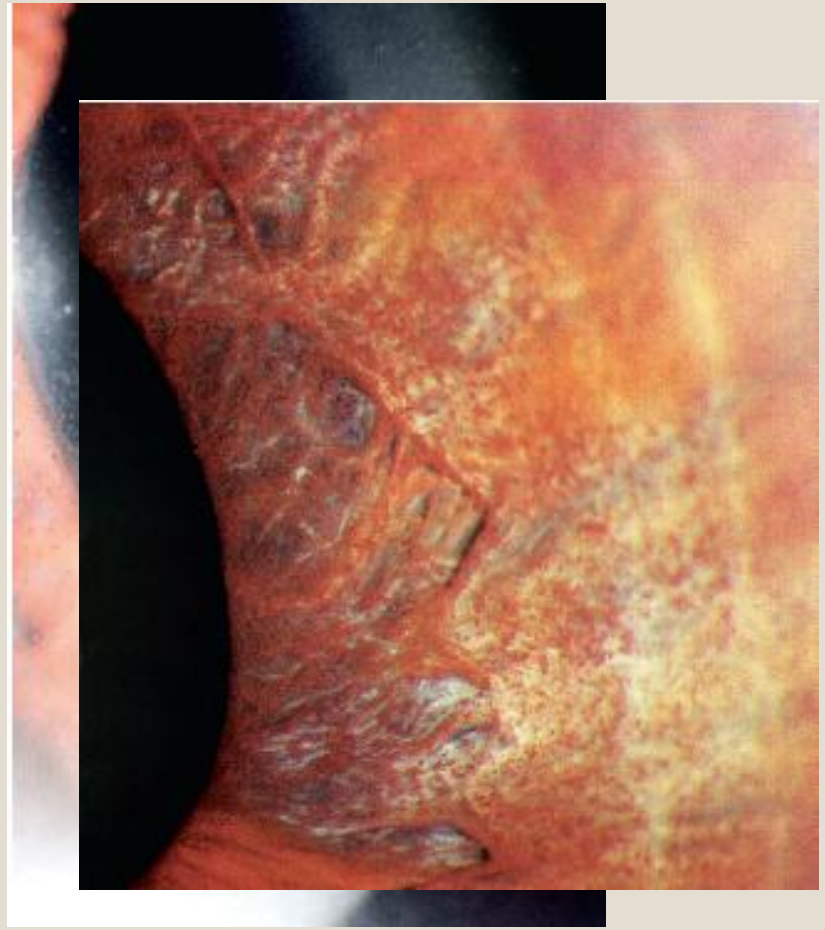


Signs : HZV

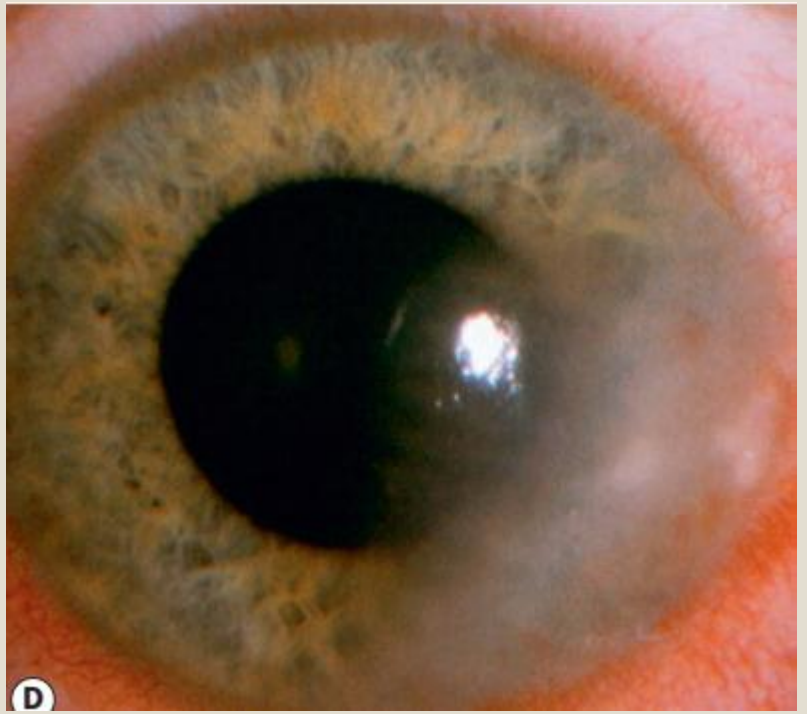


Signs : HZV





Signs : HZV



Acanthamoeba keratitis

- *Acanthamoeba* are ubiquitous free-living protozoa
- Isolated from soil, dust, sea, and fresh and chlorinated water
- Capable of encystment in unfavourable conditions .
- **Risk factors**
  • *CL wear*: especially with extended-wear CL, poor CL hygiene (e.g. rinsing in tap water), or after swimming with CL *in situ* (ponds, hot tubs, swimming pools).
  • *Corneal trauma*: notably in a rural or agricultural setting.
- **Clinical features**
  • *Variable*: ranges from asymptomatic, FB sensation, ↓VA, or tearing **to severe pain** (disproportionate to often relatively mild clinical fndings); may occasionally be bilateral.
  • Epithelial ridges, pseudo- and true dendrites; stromal infltrates (may progress circumferentially to form a ring); perineural infltrates; ↓corneal sensation.