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An ophthalmic surgeon performing a corneal scraping procedure with the patient comfortably positioned at an operating microscope, assisted by an ophthalmic nurse ensuring the patient's comfort during the procedure. INDIA

Microbial keratitis: a practical guide

Prompt diagnosis and treatment are critical for achieving a good outcome for patients.

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Microbial keratitis is a sight-threatening ocular emergency which continues to affect several million people worldwide each year, resulting in loss of vision and negatively impacting people's quality of life. In some countries, up to 10% of patients will lose the infected eye; as a result, they may experience depression, anxiety, social stigma, and increased poverty due to reduced employment, as highlighted in the case study overleaf.

Leading risk factors vary geographically and include ocular trauma, occupational exposure, contact lens wear, and pre-existing ocular surface disease. Corneal infections are challenging to manage, and good outcomes depend on prompt recognition, referral to a specialist eye unit for accurate diagnosis, and appropriate, intensive treatment.

The range of microorganisms responsible for microbial keratitis is diverse. Treatment is pathogen specific, so it is important to find out which microorganism is responsible and to test for susceptibility to different antimicrobial medications, to inform prescribing. However, the facilities, equipment, and personnel needed for diagnostic and susceptibility testing are often not available in places where the magnitude of disease is greatest. Many settings also lack evidence-based national treatment guidelines.

In this issue, we provide diagnostic and treatment guidance for all eye health workers, including specific recommendations for those working in settings where diagnostic laboratory support is either limited or not available. We also offer resources in the form of posters which can be adapted and reused to raise awareness among communities in settings where agriculture-related corneal abrasions are prevalent, and to provide advice for pharmacists, who are often a patient's first point of contact.

About this issue

Microbial keratitis is a sight-threatening ocular emergency which affects several million people worldwide each year, resulting in loss of vision and negatively impacting people's quality of life. In this issue, we provide diagnostic and treatment guidance for all eye health workers, including specific recommendations for those working in settings where diagnostic laboratory support is either limited or not available. We also offer resources in the form of posters which can be used to raise awareness amongst community pharmacists and the public.

Contents

CASE STUDY

Lemarti*, a Masaai student planning to study medicine at university, was diagnosed with fungal keratitis shortly before starting his final year of school. Although the keratitis eventually resolved, the resulting corneal scar affected his physical appearance and left him blind in one eye (visual acuity < 3/60).

As a result, he faced significant stigma: "Even the group that I used to discuss with began to neglect me, so I had to start studying alone." This, together with the loss of income from farming – due to his need to wear spectacles – forced him to drop out of school. As Lemarti explained: "After I faced this problem and now that I use glasses, it means I can't go for grazing and dig. So that made me stop school because I couldn't raise enough money."

Lemarti expressed a profound sense of uncertainty about his future. "I am concerned for my present and future too. If I fail to manage my present, what about my future?" The vision loss also affected Lemarti's standing in the community. "Everyone is looking at me... I am supposed to look for money, and get married, I am a young man," he explained, adding that the condition left him unable to fulfill these responsibilities.

In addition to this feeling of exclusion, Lemarti described feeling uncomfortable in public places and lacking in confidence, explaining how this emotional burden was as debilitating as the physical effects of the condition.

Lemarti's case is just one of many patient stories that highlight the limitations of current medical counseling and treatment in settings where the magnitude of vision impairment is greatest. Ongoing support for patients who lose vision in one eye is critical for their welfare. Understanding the impact on patient's lives is also important in order to advocate for improved treatment options, including increased availability of appropriate and effective antimicrobial eye drops and corneal transplant services, which may provide better outcomes and hope for patients like Lemarti.

– **Zoha Mian**, MD Candidate: University of Louisville, USA

**Name has been changed*

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INTERNATIONAL CENTRE FOR EYE HEALTH

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IAPB

Diagnosing microbial keratitis in different settings

Microbial keratitis is an ocular emergency. Identifying the likely cause can help to save the eye and preserve vision.

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Microbial keratitis refers to severe corneal infection caused by a variety of microorganisms, including bacteria, fungi, viruses, and protozoa, such as *Acanthamoeba*; treatment depends on the type of microorganism involved.

Patients with microbial keratitis all present with a red, painful and light-sensitive eye. There may have been a history of trauma or contact lens wear. Clinical signs of microbial keratitis include a red eye with a white patch or infiltrate over the cornea. If fluorescein staining is available, the ulcer or epithelial defect will fluoresce green under a blue light. These signs are similar, regardless of the type of microorganism responsible, which makes diagnosis, and therefore management, a challenge. In an ideal setting, formal diagnosis is made following corneal scrapes for microscopy and culture. However, this is not always available, particularly in rural or low-resource settings.

It is therefore important to try to determine the type of infection with the resources that you have available, in order to give the patient the best possible outcome.

Epidemiology

Knowing which causes of microbial keratitis are common where you work is helpful if you need to diagnose and treat patients without the support of a diagnostic laboratory.

The incidence of microbial keratitis varies globally, influenced by factors such as occupational risk factors, climate, socioeconomic status, and other risk factors. In rural and low-resource settings, fungal keratitis following agriculture-related ocular trauma is common. In high-income, urban settings, contact lens wear-associated bacterial keratitis may be more prevalent; these would also be the only settings in which you are likely to see patients presenting with *Acanthamoeba* keratitis.

Diagnosis

Where there is no ophthalmic expertise or laboratory support

In the community, or at primary health care units where there is no ophthalmic expertise or diagnostic laboratory support, patients with suspected corneal infection should be prescribed broad-spectrum antibiotic eye drops and referred to an eye hospital urgently.

One of the challenges in getting patients the correct treatment, in time, is lack of awareness of the signs of corneal infection.

We therefore encourage you to share the poster on pages 14-15 with pharmacists and health workers in your local area. You may also wish to adapt the community education poster on page 16, which was used to educate farmers in Nepal about the importance of visiting an eye centre if something entered their eye.

Where there is ophthalmic expertise but no laboratory support

At health centres or hospitals where there is no laboratory support, but there is a trained eye care worker, optometrist, or ophthalmologist, it may be possible to differentiate between fungal and bacterial infection using a diagnostic algorithm based on clinical signs.

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Figure 1 Clinical features typical of fungal (a and c) and bacterial (b and d) infection.

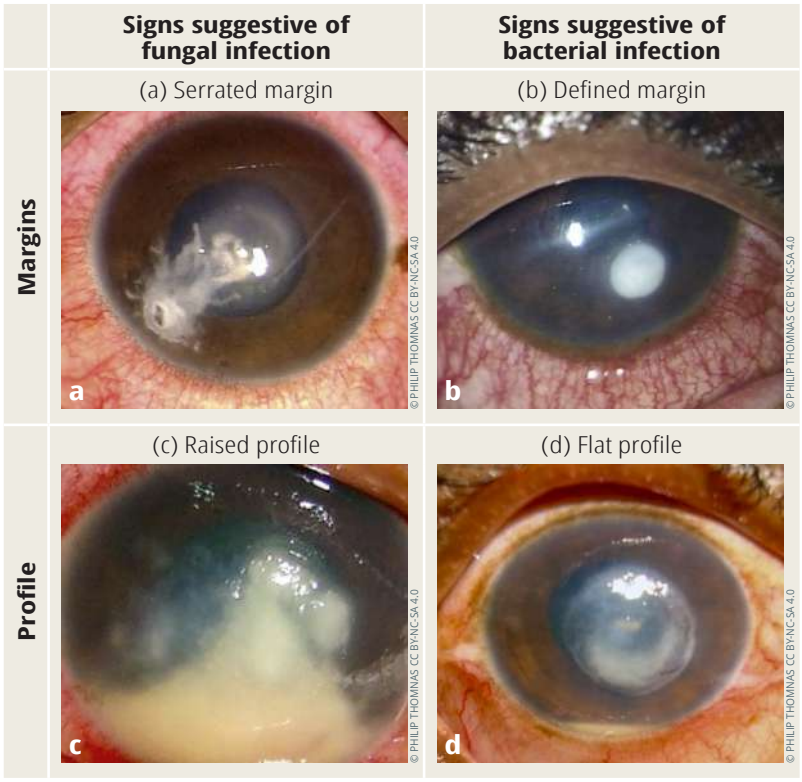
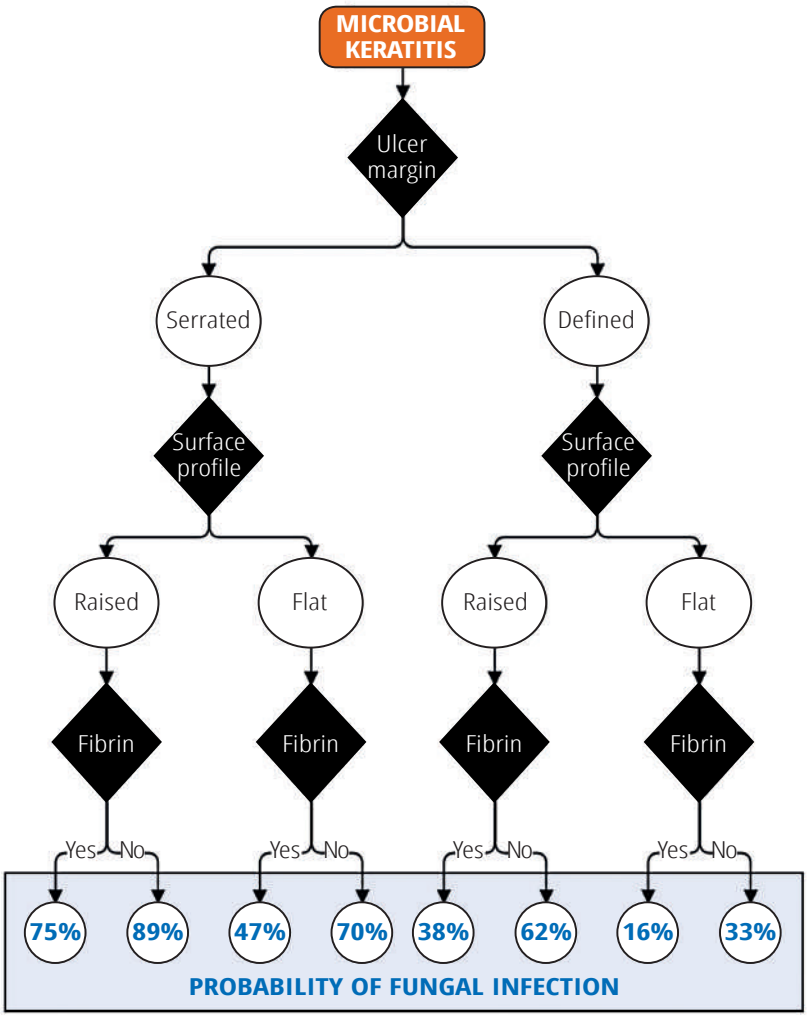


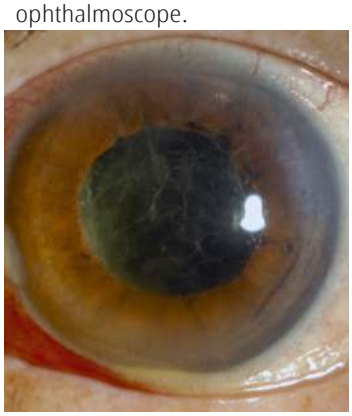
Figure 2 Algorithm for determining the probability of fungal keratitis. The black diamonds are decision points about three clinical features: ulcer or infiltrate margin, surface profile, and anterior chamber fibrin (see Figure 3). These probabilities are based on data presented in Thomas et al.[1]



Although it is difficult to distinguish bacterial from fungal keratitis on clinical examination alone, there are certain findings that can be suggestive of fungal infection, specifically if the margins have serrated or jagged edges (Figure 1a) and if the ulcer has a raised (or three-dimensional) profile (Figure 1c).[1-3]

If you are able to examine the anterior chamber, preferably with a slit lamp (to see if there is fibrin) you can use the recommended diagnostic algorithm in Figure 2 to differentiate between bacterial and fungal corneal infection. See Figure 3 for a photo of fibrin in the anterior chamber.

Figure 3 Fibrin seen in the anterior chamber using an ophthalmoscope.



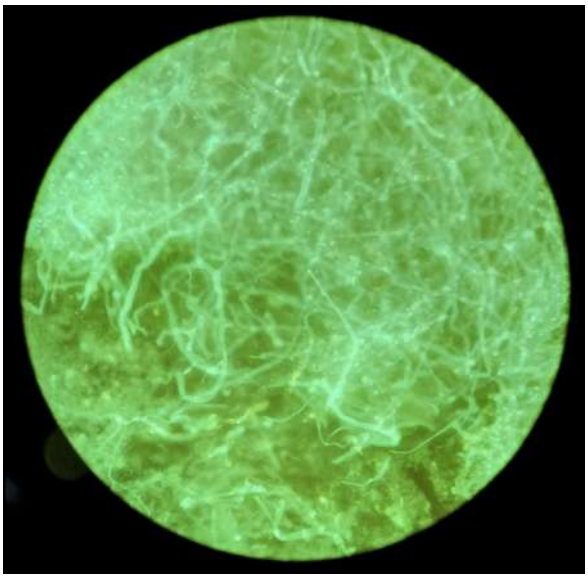
Where there are limited laboratory diagnostics

Microscopy provides a rapid presumptive diagnosis, even in the absence of culture facilities or the absence of microbial growth in culture.

In health care facilities with access to a diagnostic laboratory microscope and a health care professional who is competent in taking a corneal scrape specimen, corneal tissue can be examined using Gram stain and KOH reagents for the presence of bacteria, fungal hyphae, yeast cells, and *Acanthamoeba*. Details on how to perform a corneal scrape can be found here: **www.cehjournal.org/articles/583**

If microscopic examination of the smear reveals heavy bacterial infection (>30 cells per field of view) the clinician should be advised to begin antimicrobial therapy. If there are moderate numbers of Gram-negative bacilli observed (10–25 bacterial cells), this may also be significant.

Figure 4 Fungal hyphae in corneal tissue stained with calcofluor white, a fluorescent stain, seen using a UV microscope.



If the health centre/hospital has access to a UV microscope, as used in the laboratory diagnosis of tuberculosis (TB), it is possible to use a fluorescent stain to visualise fungal hyphae (Figure 4) and *Acanthamoeba* cysts.

Note: The presence of fungal hyphae in corneal tissue is always significant and the patient should be prescribed antifungal eye drops, even in the absence of culture results.

Where there is a full diagnostic laboratory service, including culture facilities

Tertiary-level centres should perform culture from corneal scrape material; this can confirm the type of infection and identify the causative microorganism, which helps to guide appropriate treatment. If culture is possible, antimicrobial susceptibility testing can also be performed to further inform antimicrobial prescribing and monitor antimicrobial drug resistance profiles.

To definitively confirm bacterial keratitis, the following criteria are applied:

- Growth of the same bacteria is demonstrated on two or more solid phase culture media
- There is semiconfluent bacterial growth at the site of inoculation (C-streak, Figure 5) or growth on one solid medium consistent with microscopy (that is, appropriate staining and morphology with Gram stain)
- Semi-confluent bacterial growth at the site of inoculation on one solid medium (if bacteria) or growth of the same organism on repeated scraping.

If culture results are negative, but microscopic examination of the smear reveals heavy bacterial infection (>30 cells per field of view, see Figure 6), the clinician should begin antimicrobial therapy.

If fungal hyphae are seen in any stained corneal material using light or UV microscopy, this is a definitive diagnosis for fungal infection. If microscopy is negative but there is fungal growth only at the site of C-streak inoculation on one or more solid culture media (agar plate or slope), the causative organism is reported as fungal.

Figure 5 Bacterial growth on C-streaks on chocolate (heated blood) agar.

Figure 6 Gram-stained corneal tissue showing a heavy inoculum of Gram-positive cocci (purple dots).

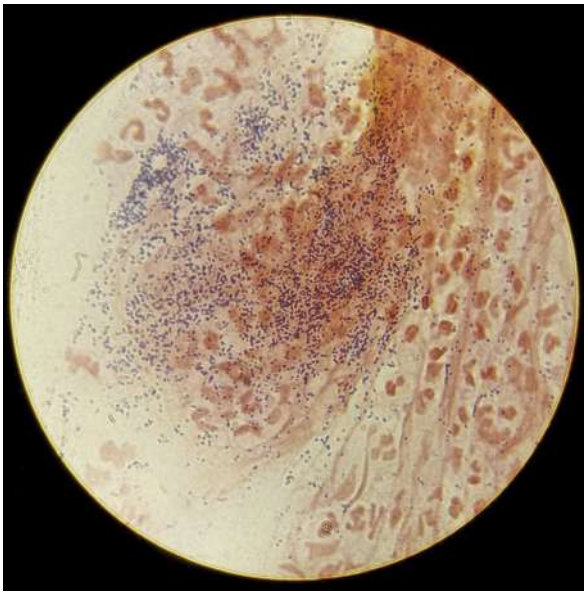
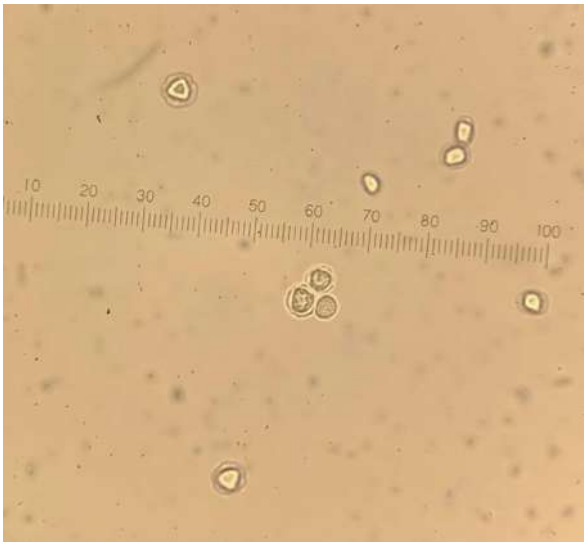


Figure 7 *Acanthamoeba* cysts – wet prep.



If *Acanthamoeba* are suspected as the cause of an infection, a corneal tissue specimen is taken for microscopic examination. A second corneal tissue specimen is inoculated onto a non-nutrient agar (NNA) plate, a portion of which is transferred in the laboratory to a second non-nutrient agar plate overlaid with *E.coli* to determine viability (Figure 7).

Key points:

- It is important to consider fungal infection until proven otherwise in settings where fungal infection is prevalent.
- Microscopy is a very sensitive diagnostic tool and can help you to reach a definitive diagnosis for fungal infection.
- Microbial culture is important, particularly for the diagnosis of bacterial infection, and it also enables identification and antimicrobial susceptibility testing to be carried out, increasing our knowledge base of what causes corneal infection within a region and guiding appropriate treatment.

"It is important to consider fungal infection until proven otherwise in settings where fungal infection is prevalent."

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Types of microbial keratitis

Bacterial keratitis

The most common type of corneal infection worldwide is bacterial keratitis, associated with ocular trauma, contact lens wear, or pre-existing ocular surface disease. Common causative microorganisms include *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Streptococcus pneumoniae*. Bacterial keratitis typically presents with rapid onset of pain, redness, and tearing.

Figure 1 Corneal infection caused by *S.pneumoniae*

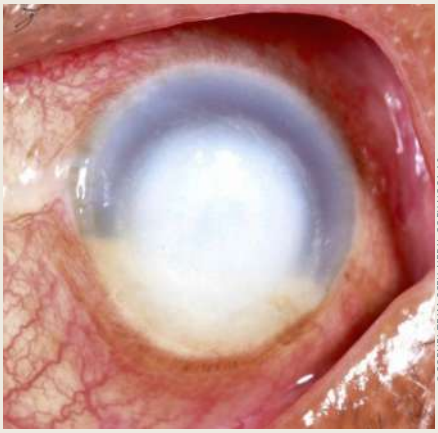


Figure 2 Corneal infection with *P. aeruginosa*

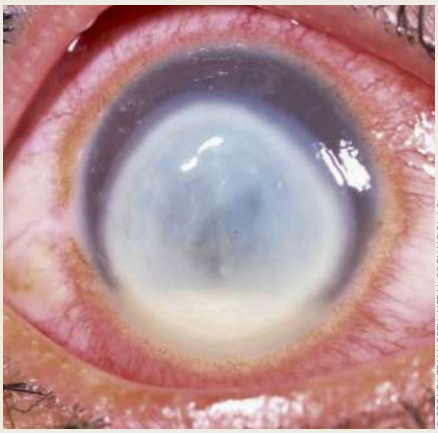
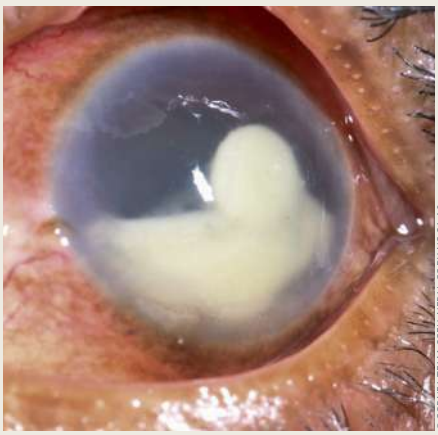


Figure 3 A cornea infected with *S. aureus*



Fungal keratitis

Predominantly seen in tropical and subtropical climatic regions, fungal keratitis is frequently associated with agriculture-related ocular trauma involving plant material. Pathogens such as *Fusarium*, *Aspergillus* and *Curvularia* species are frequently responsible. This type of infection often presents with a slower onset and more drawn-out course compared to bacterial keratitis, but the clinical signs can be similar similar to bacterial keratitis.

Figure 4 *Fusarium* keratitis

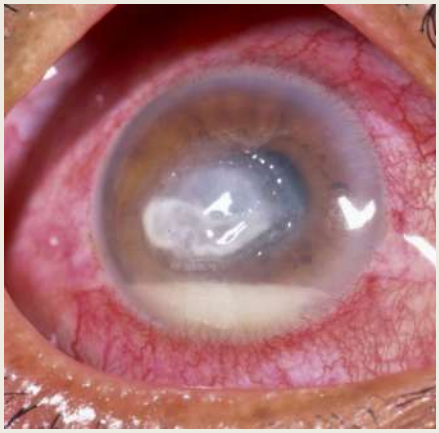


Figure 5 Corneal infection due to *Aspergillus sp.*

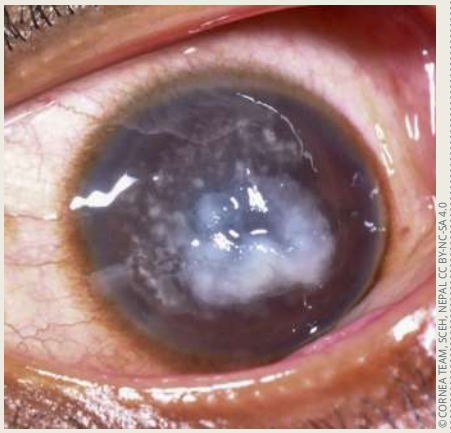
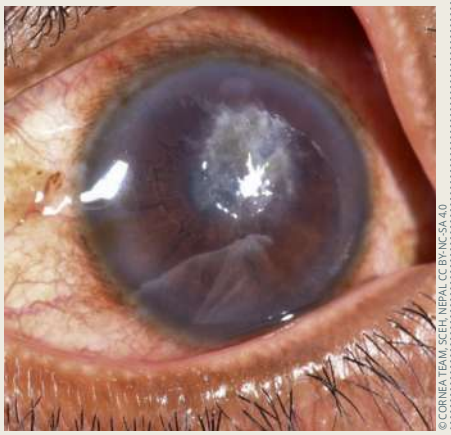


Figure 6 *Curvularia* keratitis



Viral keratitis

Primarily caused by herpes simplex virus (HSV) and, less frequently, by varicella-zoster virus (VZV), viral keratitis can lead to recurrent episodes and chronic complications. Herpetic keratitis is characterised by dendritic or geographic ulcers, stromal keratitis, and potential for chronic scarring. Viral keratitis can be diagnosed using blue light examination at a slit lamp – no laboratory investigations are needed.

Figure 7 Dendritic appearance of a viral corneal infection

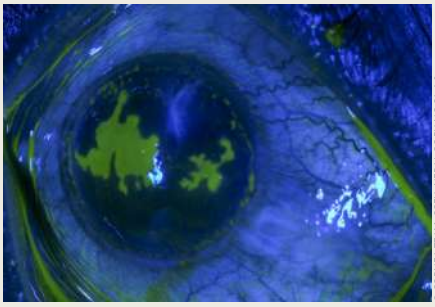
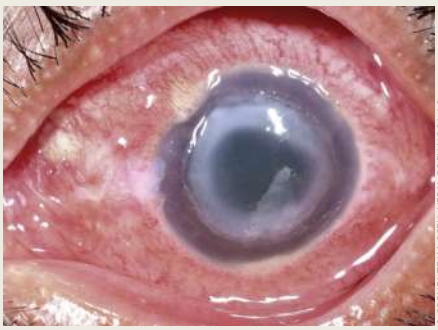


Figure 8 Geographical ulcer (viral)

Acanthamoeba keratitis

Although less common, keratitis caused by *Acanthamoeba* spp.is particularly severe and challenging to treat. It is typically associated with **improper contact lens hygiene,** or **exposure to fresh water sources containing the protozoa**. In early disease, patients can present with non-specific signs, but at a later stage they can develop severe pain due to the infiltration of corneal nerves.

Figure 9 *Acanthamoeba* keratitis



Pythium insidiosum: the organism that mimics fungal keratitis

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Microbial keratitis is commonly caused by bacteria and fungi, however, what may appear to be fungal keratitis is sometimes the result of infection with a different microorganism: *Pythium insidiosum*.

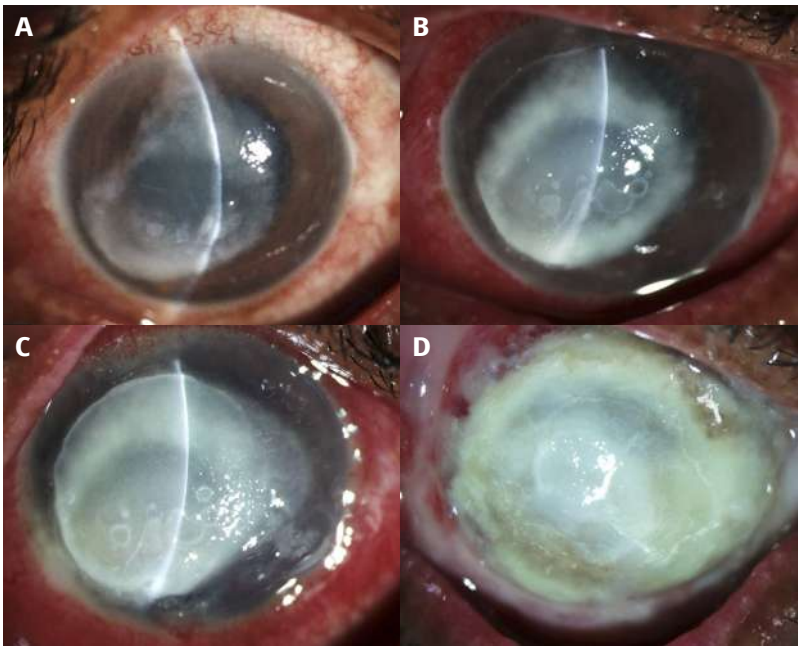


Figure 1 Progression in a patient with *Pythium* keratitis who received antifungals initially. The patient was given a large total penetrating keratoplasty, but this did not eradicate the infection and led to evisceration. **A:** Note the central greyish white ring infiltrate of 7 x 7 mm. **B and C:** Progressive worsening over 10 days. **D:** Total corneal infiltrate with adjacent scleral involvement after one month.

Pythium insidiosum belongs to a group of parasitic oomycetes, usually found in aquatic environments. Human infection is rare; however, a lack of awareness of *Pythium* spp. as a cause of microbial keratitis may lead to misdiagnosis as fungal keratitis and inappropriate treatment with antifungals. This has resulted in poor outcomes and the need to resort to therapeutic penetrating keratoplasty or evisceration (Figure 1).[1,2]

Pythium spp. produce spores and hyphal structures which led to them being misclassified as moulds until more recent genetic analysis proved otherwise.

The main reason it is important to differentiate *Pythium* infection from fungal infection is because the management is different – *P. insidiosum* is unresponsive to fungal treatment. Instead, it requires antibiotic treatment.

Microbial keratitis that looks like fungal keratitis (both clinically and on microscopy), but which does not respond to antifungal treatment, should be looked at again to rule out *Pythium* keratitis.

When to suspect *Pythium* keratitis

Although this type of corneal infection is more prevalent in subtropical and tropical climatic regions, the organism is widespread. Males are affected more frequently; this may be because they are more often exposed to ocular trauma during agricultural work. A significant proportion of patients affected have a history of dust or contaminated water in the eye(s), but there have also been reports of patients with a history of contact lens use and exposure to clay particles.

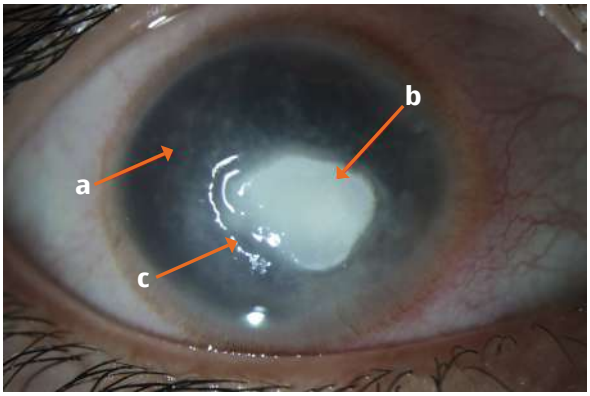
Signs, symptoms, and clinical findings

Affected patients usually complain of pain, redness, photophobia, and decreased vision on presentation.

The slit lamp findings[3] include lid oedema and conjunctival congestion, a central or peripheral grayish-white infiltrate with a raised profile (Figure 1), hyphal-like projections, pinhead lesions in the anterior mid-stroma, and peripheral furrowing or guttering around the infiltrate. These features are suggestive of *Pythium* but may be present in some patients with fungal keratitis. Detailed microbiological workup is therefore necessary for diagnosis.

There may be associated scleritis and, rarely, endophthalmitis. Intraocular spread is rare, suggesting that the corneal barrier prevents posterior extension of the organism. Peripheral guttering or furrowing around the infiltrate is typically seen as the ulcer heals and the infiltrate size decreases (Figure 2).[4,5] Significant, deep vascularisation is also seen in this phase.

Figure 2 Diffuse slit lamp image of the cornea in a patient recovering from *Pythium* keratitis infection. Hypal-like projections **(a)** and a raised central plaque **(b)** are typical of both fungal and *Pythium* keratitis. As the ulcer starts to heal, there is typically guttering around the infiltrate **(c)**.



Diagnosis

The diagnosis of *Pythium* keratitis requires a detailed microbiological workup by an experienced microbiologist.

Figure 3 The filaments of *P. insidiosum* are visible on direct microscopy in fluorescent light, on a potassium hydroxide and calcofluor white mount.

Pythium filaments can be observed by direct microscopy of a corneal scraping in Gram stain, or in 10% potassium hydroxide (KOH) with 0.1% calcofluor white, viewed under fluorescence (Figure 3). The filaments are classically aseptate or sparsely aseptate,[3] broad, and ribbon-like. However, this is also characteristic of some filamentous fungi or moulds, so further microbiological workup is needed to make a definitive diagnosis.

Figure 4 Flat, submerged translucent growth of *P. insidiosum* in blood agar.

Pythium keratitis can be differentiated from fungal keratitis (including filamentous fungi or moulds) by staining a corneal scraping smear using a mixture of potassium iodide and iodine with 65% sulphuric acid (IKI-H2SO4). The slide must be examined immediately under the microscope. The *P. insidiosum* filaments are stained bluish-black, whereas fungal filaments appear yellowish.[6] The growth on blood agar is feathery-edged and flat, and it is colourless or light brown (Figure 4). Further investigation includes growth of zoospores on carnation leaf pieces placed on non-nutrient agar and polymerase chain reaction (PCR).[7]

Treatment and management

Treatment is challenging as infection typically takes 2–3 months to resolve and patients may need to be admitted. Non-adherence could become an issue.

Patients presenting in the **early or moderate stages of *Pythium* keratitis** should be managed initially with a combination of antibiotics for a minimum of two weeks and observed closely. After the diagnosis is confirmed with a combined clinical and microbiological evaluation, start the patient on a combination of the following:

- Topical linezolid 0.2% (IV preparation) every hour during the day and every two hours at night
- Azithromycin 1% eye ointment twice a day
- Azithromycin 500 mg (orally) once a day for two weeks.

The combined topical medications are continued until a response is noted in the form of scarring or decrease in the size of infiltrate. With timely medical intervention, more than 70% cases can be successfully managed.[3]

Most patients can be seen as outpatients with regular follow-up. Patients who may have difficulty adhering with treatment, those who live far away, and those with only one functioning eye are admitted for 1–2 weeks.

Examine patients clinically every three days, followed by once a week, to assess the response. Check for thinning and deeper extension of infiltrate, including limbal infection, as this suggests the infection might be moving beyond the cornea, and could then spread more widely.

Good response to medical treatment is evident from the decrease in the size of hyphal-like extensions (Figure 5) and cellularity of the surrounding stroma.

Poor response to medical treatment includes:

- **Thinning.** Plan cyanoacrylate glue application in patients with significant corneal thinning to avoid corneal perforation.
- **Extension of the infiltrate and limbal infection.** Consider therapeutic penetrating keratoplasty.

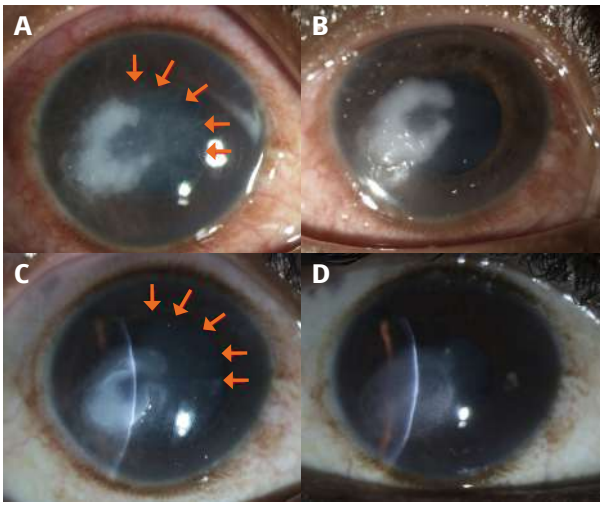
Patients presenting with **advanced** *Pythium* keratitis need close supervision and should be admitted and seen daily. Therapeutic penetrating keratoplasty with an extra 1.5 mm margin may be needed, as medical treatment alone may not be sufficient for the eradication of infection. Unfortunately, this modality is associated with a high risk of recurrence of infection, and evisceration may eventually be necessary.

The combined topical medications are continued until a response is noted in the form of scarring or decrease in the size of infiltrate. With timely medical intervention, more than 70% of patients can be successfully managed.[3]

Follow-up care

On the resolution of keratitis, there are increased chances of the development of cataract and glaucoma, which can significantly delay visual recovery, in addition to causing corneal scarring to develop. The development of cataract can be secondary to severe inflammatory reactions due to long-standing infection. Many of these patients need optical keratoplasty and cataract surgery for visual rehabilitation. The outcomes of these grafts are similar to grafts done for other indications.

Figure 5 A patient with *Pythium* keratitis. **A:** White mid-stromal infiltrate (5 mm x 6 mm) with tentacular extension (orange arrows) in the surrounding deeper stroma. **B to D:** stages of resolution showing tentacles (orange arrows) disappearing with medical treatment.



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Managing microbial keratitis in resource-limited settings

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In resource-limited settings, the management of corneal infections (microbial keratitis) is challenging. Patients often delay seeking medical help, arriving in clinic with advanced disease, and diagnostic laboratory support may be unavailable.

An ophthalmologist examining the patient with suspected corneal infection and performing corneal scrapping. INDIA

PART 1 General management principles

In this section, we discuss the general principles of managing a patient with microbial keratitis.

Patients with microbial keratitis need:

1 Early and appropriate diagnosis and treatment, ideally based on microbiology results
2 Good pain management
3 Good adherence with treatment during the first few days (usually achieved by admitting the patient)
4 Regular clinical review.

Early diagnosis and treatment

If there are clinical signs or symptoms to suggest microbial keratitis or corneal infection (see poster on pages 13-14), start patients on a broad-spectrum topical antibiotic and refer them urgently to a specialist eye clinic.

Once reviewed in hospital, most patients can be effectively managed with intensive topical treatment alone, but there are some patients for whom supportive or adjunctive treatment may be needed.

Ideally, the treatment given should be based on microbiological identification of the microorganism involved. In the absence of microbiological services, we suggest you refer to the article on page 3 to guide your decision making. In settings where fungal keratitis is known to be more common than bacterial keratitis, first-line treatment should include antifungal eye drops. If there is any uncertainty about the pathogen responsible, it is advisable to treat empirically with both antifungal and antibiotic eye drops, until a definitive diagnosis can be made.

For most patients with microbial keratitis, treatment typically follows an intensive 'sterilisation' phase for up to a week, where drops are instilled every hour. This is followed by a 'healing' stage, where the intensity of the drops is reduced to allow the corneal epithelium to heal. The timings and antimicrobial eye drops vary depending on the causative microorganisms.

For more information on the different medical treatment needed for bacterial, fungal and *Acanthamoeba* keratitis, see Part 2.

2. Pain management

Microbial keratitis causes severe pain. It is therefore important to manage patients' pain, as pain is often one of the reasons a patient may start using traditional eye medications or inappropriate conventional medicines, such as topical steroids. We recommend cycloplegia (with topical cyclopentolate or atropine), along with oral painkillers such as paracetamol, codeine, or NSAIDs such as ibuprofen.

3. Adherence and counselling

Management of microbial keratitis requires a multi-disciplinary approach. It is vital to counsel the patient about the disease, its management, the expected outcome, and the need for long-term follow-up.

Many patients do not get adequate information about how to continue their treatment after being discharged, such as how often to instil their eye drops and how to position themselves to ensure the drops go into the eye. This contributes to inadequate adherence with medication.

Long-term follow-up (of about 2–3 months) is often needed; if patients do not realise the importance of this from the outset, they frequently miss future appointments, which can lead to adverse clinical outcomes.

4. Monitoring and follow-up

Follow-up is essential to evaluate the effectiveness of prescribed medication in patients with microbial keratitis.

Follow-up frequency depends on disease severity; for most patients a review at 48–72 hours is recommended when initial symptomatic improvement (typically a reduction in pain and discharge) can be observed, along with reviewing any initial microbiology results. Patients with severe microbial keratitis may require admission (if available) and daily monitoring until stable, due to the risk of corneal perforation. If patients have to travel from far away, they should be admitted for as long as possible, ideally for the first few days of treatment at a minimum.

Signs that the patient is getting better include reduced pain, reduced redness and anterior chamber activity, and a reduction in the size of the epithelial defect. However, in fungal keratitis (and in certain forms of bacterial keratitis, such as *Pseudomonas* keratitis), there can be an initial worsening of clinical signs due to the inflammatory response to dead or dying pathogens. Drug toxicity may also delay the healing process, which requires close monitoring. A reduction in pain and eyelid swelling may be the only initial positive findings.

If patients are not improving, then there are several questions to consider. First, what is their treatment adherence like? Are they using the drops as prescribed? Second, do they have an underlying (often unknown) systemic condition that is responsible, such as uncontrolled diabetes or HIV? Third, is this a mixed bacterial and fungal infection? Finally, are they using traditional eye medicine that is making things worse?

PART 2 Medical treatment

Treatment can be broadly categorised into medical and surgical options. Medical management typically involves the use of topical antimicrobial medication. When medical management is insufficient, or when there are complications, surgical interventions such as corneal debridement, therapeutic keratoplasty, or conjunctival flaps may be needed to preserve vision and the structural integrity of the eye.

In this section, we discuss the medical management of bacterial, fungal, and *Acanthamoeba* microbial keratitis in a low-resource setting.

A note about corticosteroids

The adjunctive use of topical corticosteroid therapy in microbial keratitis remains hotly debated. While corticosteroids may suppress inflammation and reduce scarring and associated visual loss, potential disadvantages include infection recurrence, local immunosuppression, corneal melting risk, and increased intraocular pressure. Patients already on corticosteroids should reduce or stop them until the infection is under control.

Topical corticosteroids may be considered for patients with severe bacterial keratitis with signs of significant acute inflammation, and if there is clinical improvement following at least 48 hours of intensive topical antibiotics. The dosing frequency should be the minimum amount to control the inflammation.

Steroids should **not** be prescribed for fungal, *Acanthamoeba* or *Nocardia* corneal infections.

Other adjunctive therapy

Oral antibiotics are not usually required unless there is a corneal perforation, when an oral fluroquinolone can be used, e.g. moxifloxacin. There may be a role for oral doxycycline 100 mg once daily to help limit corneal melting and scar formation, particularly in patients with more severe disease.

For patients with deep fungal keratitis, or where there is failure to respond to initial natamycin 5% treatment, oral antifungals such as voriconazole or itraconazole may be given. However, these drugs have dangerous side effects including liver toxicity and therefore should only be given where liver function testing can be performed. Additional treatment for these more challenging, deeper fungal infections includes injections of amphotericin B or voriconazole into the anterior chamber (intracameral injections), or intrastromal around the infiltrate. However, there is little convincing evidence to support the use of intrastromal injections.

Bacterial keratitis

It is always important to base antibiotic choice on local antimicrobial susceptibility profiles if such data are available.

Table 1 Bacterial keratitis: treatment summary

Indication	Drugs	Intensity and duration
Initial or first-line treatment	Moxifloxacin, ofloxacin, **or** ciprofloxacin eye drops	Hourly drops, day and night, for 48 hours, then hourly during the day for 3–5 days, then four times a day until the epithelial defect has healed
Patients with central or severe keratitis	Cefuroxime **and** gentamicin eye drops	As above
Patients with deep or large ulcers	Oral doxycycline 100 mg once a day for deep/large ulcers. After 48 hours, consider adding chloramphenicol 1% ointment at bedtime	

Ideally, admit the patient initially to ensure that the eye drops are administered as planned and to allow regular follow-up. Give treatment as per the frequency in Table 1.

Single-drug therapy with topical fluoroquinolones is as effective as combination therapy (see below). Fluoroquinolone options include ciprofloxacin, ofloxacin, levofloxacin, moxifloxacin and gatifloxacin.

Combination therapy – using a combination of topical cephalosporin (e.g., cefuroxime) and topical gentamicin – can be considered in patients with central or severe keratitis (generally defined as an infiltrate of greater than 2mm or more), particularly in patients with a hypopyon, or in patients who are unresponsive to initial single-drug therapy with fluoroquinolone.

Ointments are less effective, due to poor corneal penetration, but may be used adjunctively or at bedtime in patients with milder infection. Subconjunctival injections may be considered for patients with adherence difficulties or if there are delays in obtaining fortified antibiotic eye drops. Systemic therapy is reserved for patients with scleritis, endophthalmitis, microbial keratitis associated with systemic infections, or gonococcal keratitis.

Note: In patients with bacterial keratitis (particularly if caused by *Pseudomonas* spp.), the clinical signs can often be worse in the first few days after starting treatment; for example, the size of the hypopyon may increase. However, if the patient's pain is reducing significantly, this is a reassuring sign that the treatment is working. Treatment should then continue unchanged, and the patient be reviewed further in a few days' time.

Fungal keratitis

The standard treatment for fungal keratitis is natamycin 5% drops. The treatment schedule is given in Table 1.

Voriconazole 0.1% drops may be considered if natamycin is not available, although it may be prohibitively expensive. In the absence of commercially produced antifungal eye drops, 0.2% chlorhexidine drops can be considered an alternative treatment. Chlorhexidine has the advantage of being inexpensive and easy to formulate (see article in issue #118 **www.cehjournal.org/articles/285**).

Amphotericin B 0.15% eye drops have also been used in recalcitrant cases of filamentous fungal keratitis, and remains first-line treatment for patients with non-filamentous *Candida* keratitis. This could be made in a hospital, as per the instructions in the panel.

Amphotericin B 0.15% eye drop preparation

What you need:

- A 50 mg vial of liposomal amphotericin B parenteral powder for injection (the type used to constitute an IV drip; brands from India include Amfocare)
- Distilled, sterilised water
- Artificial tears (eye drops)
- Sterile eye drop bottle (minimum 10 ml).

Method

- Mix the 50 mg vial of liposomal amphotericin B parenteral powder with 10 ml of distilled, sterilised water. It should fully dissolve without any precipitates.
- Add 3 ml of this preparation to the eye drop bottle, followed by 7 ml of artificial tears (eye drops).
- Store the solution at 4 degrees Celsius; it can be used for 1 week.

While there is an epithelial defect, use a topical broad-spectrum quinolone antibiotic (such as moxifloxacin, ciprofloxacin, or ofloxacin, depending on local availability and resistance patterns) to prevent a secondary bacterial infection. This is administered four-times per day until the epithelium heals.

As with bacterial infections, the patient should be admitted initially to ensure the eye drops are administered as planned and to allow regular follow-up.

Table 2 Fungal keratitis: treatment summary

Indication	Drug	Intensity and duration
Initial or first-line treatment for filamentous fungal keratitis	Natamycin 5% eye drops	Hourly drops day and night for 48 hours, then hourly during the day for 5 days, then 2-hourly for 7 days, reducing to 4–6 times per day once there are signs of epithelium healing, followed by 4 times per day until the epithelium is fully healed
If natamycin is not available	Chlorhexidine 0.2% **or** voriconazole 1% eye drops	As above
First-line treatment for non-filamentous keratitis (e.g. yeast or *Candida* spp.). Adjunctive treatment for recalcitrant filamentous fungal keratitis	Amphotericin B 0.15% eye drops	As above
To prevent secondary bacterial infection while there is an epithelial defect	Quinolone antibiotic (such as moxifloxacin, ciprofloxacin, or ofloxacin eye drops)	Administer 4 times a day until the epithelium or ulcer has healed

Acanthamoeba keratitis

Acanthamoeba keratitis poses a challenge in treatment due to its resistant cyst stage, which is less responsive to therapeutic agents compared to the trophozoite stage. Biguanides, particularly chlorhexidine and polyhexamethylene biguanide (PHMB), are commonly used drugs, either alone or in combination with diamidines.

PHMB 0.06-0.08% monotherapy can be used as first-line treatment for *Acanthamoeba* keratitis. However, in resource-limited settings where fungal keratitis is also prevalent and PHMB may not be available, it is pragmatic to use chlorhexidine (typically 0.02%, but 0.2% can be used if that is all that is available), ideally in combination with a diamidine such as propamidine isethionate 0.1% and hexamidine 0.1%. However, prolonged use of propamidine isethionate may lead to toxic keratopathy, as well as iris atrophy, cataract, and peripheral ulcerative keratitis.[1]

Initial therapy for *Acanthamoeba* keratitis involves frequent administration (Table 1), gradually tapering based on response, with treatment durations ranging from 3 months to over a year.

Table 3 *Acanthamoeba* keratitis: treatment summary

Indication	Drug	Intensity and duration
Initial or first-line treatment	Polyhexamethylene biguanide (PHMB) 0.06–0.08%	Hourly drops during the day for 5 days, then 8 times a day for 7 days, then 6 times a day for 7 days, then 4 times a day until resolved (often for several months)
If PHMB is not available	Chlorhexidine 0.02% **and** propamidine 0.1%	As above. Monitor for possible side effects including epithelial toxicity and rarer side effects including peripheral ulcerative keratitis. Use minimum frequency possible.
To prevent secondary bacterial infection while there is an epithelial defect	Moxifloxacin, ciprofloxacin, or ofloxacin eye drops.	Administer 4 times a day until the epithelium or ulcer has healed

Management of complications secondary to microbial keratitis

Despite appropriate treatment, some patients with microbial keratitis develop complications including descemetoceles (exposure or protrusion of Descemet's membrane) and corneal perforations. For some patients, the cornea continues to melt. The recommended treatment for some of these complications would be to do an amniotic membrane transplantation, seal the perforation using tissue glue, use a bandage contact lens, or perform a therapeutic keratoplasty. These are, however, not available in many low-resource settings.

Figure 1 Conjunctival flap to address eccentric corneal ulcer perforation.

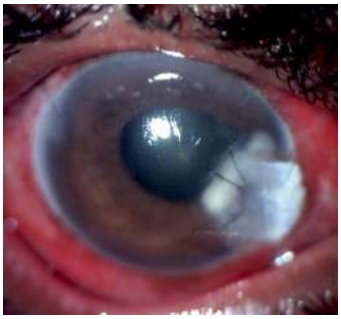


Figure 2 Temporary tarsorrhaphy using the drawstring method makes it possible to examine the eye without the need for repeat surgery.

In resource-limited facilities, small perforations and descemetoceles can be managed using procedures like conjunctival flaps (Figure 1) and temporary tarsorrhaphy, or surgical eyelid closure. The use of conjunctival flaps in patients with active corneal infection is not encouraged as it may aggravate the infection. We recommend that these patients first undergo a temporary tarsorrhaphy and, once there are no signs of infection (negative microscopy), the conjunctival flap is done. The drawstring procedure of temporary tarsorrhaphy (Figure 2) is recommended, because it enables us to loosen the sutures to examine the eye without the need for repeat surgery. See issue #89 for detailed guidance on how to perform drawstring tarsorrhaphy: **www.cehjournal.org.articles/584**.

Perforations can be sealed using **autologous Tenon grafts** for perforations of up to 5 mm or **scleral grafts** (preferably) for peripheral corneal perforations. Tenon grafts use tissue from the patient's own eye to treat corneal perforations. The tissue is harvested from the Tenon's capsule: a dense, elastic, fibrous connective tissue in the eye. Scleral grafts use the scleral rim from a corneal donor and can be stored on the shelf in 100% ethanol. They offer structural support and there is little chance of rejection.

Reference

1 Dart JKG, Papa V, Rama P, Knutsson KA, Ahmad S, Hau S, Sanchez S, et al. The Orphan Drug for Acanthamoeba Keratitis (ODAK) Trial: PHMB 0.08% (Polihexanide) and Placebo versus PHMB 0.02% and Propamidine 0.1. Ophthalmology. 2024;131(3):277-287. DOI: 10.1016/j.ophtha.2023.09.031.

PART 3 Fungal keratitis: two patients with different outcomes

Patient 1: Improvement with chlorhexidine 0.2% eye drops

An eighteen-year-old female patient presented with a chief complaint of eye pain, redness, and photophobia that had lasted for 15 days. There was no memorable history of ocular trauma. She had received one antibiotic in the form of eye drops for 6 days from the local pharmacy shop; however, no documents were available to confirm which treatment had been given.

On examination, she had paracentral stomal infiltration (2.8 x 2.2 mm in size) involving about 50% of the total stomal thickness, along with a hypopyon of 0.4 mm (Figure 3). On microbiological examination, septate fungal hyphae were seen on KOH mount and culture but the species could not be identified.

The patient was prescribed chlorhexidine 0.2% eye drops every hour, day and night, initially, then tapered as per the standard protocol. The patient was admitted to ensure compliance with the frequent drop application and to monitor response to treatment. This also ensures the patient can attend follow up, as they often have to travel considerable distances. The patient showed marked improvement on subsequent follow-up evaluation at 2 months (Figure 4) and 3 months (Figure 5), although there was ongoing scarring at 3 months.

Figure 3 Stromal infiltration with hypopyon at presentation.

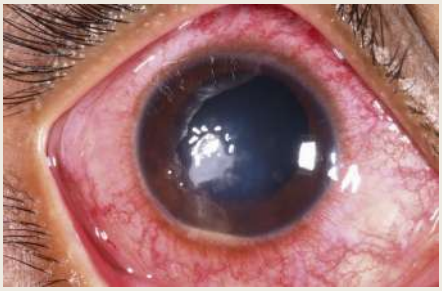


Figure 4 Resolving stromal infiltration on treatment with antifungal (chlorhexidine 0.2% eye drops) at 2-month follow-up.

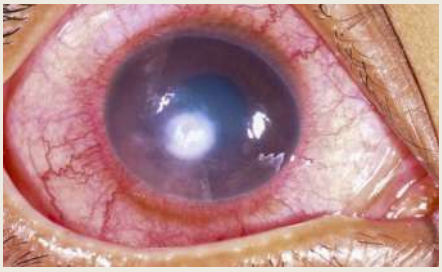
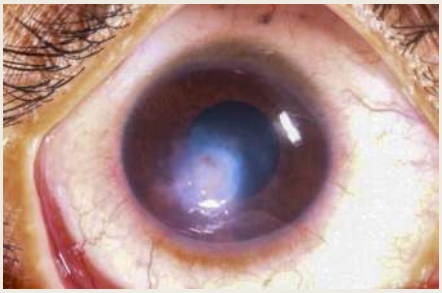


Figure 5 Ongoing scarring at 3-month follow-up.



Patient 2: Poor outcome despite treatment

A fifty-two-year-old female patient presented with reduced vision with perception of light in the affected eye. There was history of foreign body sensation, redness, and watering. These symptoms were present 22 days before she presented at the eye hospital. There was a history of the use of some eye drops for 10 days before presentation, although it was unclear which ones.

There was extensive corneal stromal involvement (5.5 mm x 7.0 mm) with the presence of an endothelial plaque (Figure 6). Microbiological tests revealed *Aspergillus* infection.

Figure 6 Late presenting subtotal stromal infiltration.

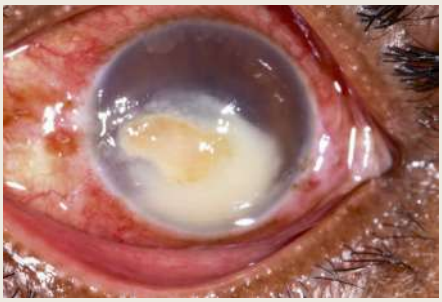
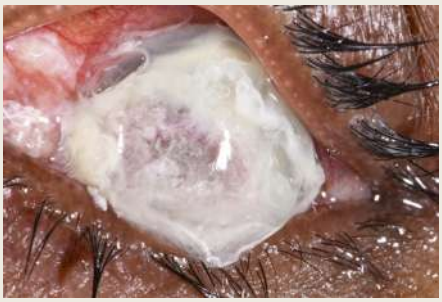


Figure 7 Perforated corneal ulcer.



The patient was admitted and topical natamycin 5% was started along with a systemic antifungal agent (oral voriconazole). Despite these medications, stromal infiltration worsened. Topical voriconazole 1% was added after a week. Unfortunately, 5 days later the affected eye had perforated (Figure 7) and an evisceration was performed.

These two patients highlight how fungal keratitis can lead to distinctly different clinical outcomes. There are several factors that can explain this: the delayed presentation for the second patient, the pathogen or microorganism involved (*Aspergillus* can be more challenging to treat and natamycin may be less effective), and the treatment given. The second patient may also have received topical steroid drops from a local pharmacy, which leads to worse outcomes.

INTERNATIONAL CENTRE FOR EYE HEALTH

Community Eye Health Journal
South Asia Edition

Corneal infection

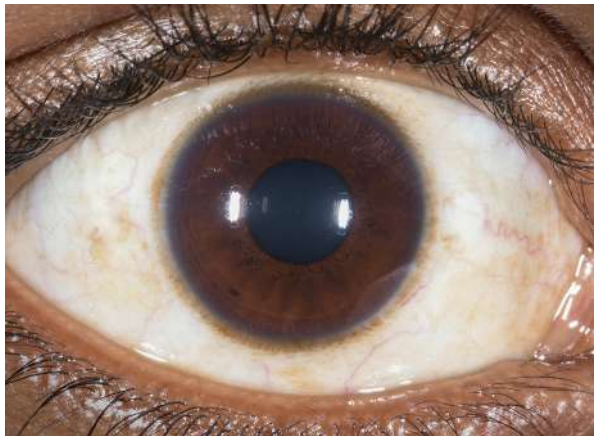
Act fast to prevent blindness!

Patients with painful red eyes often present to pharmacy staff and community health workers. If there is also a white spot on their cornea, they may have a corneal infection. If you act fast, you can prevent blindness and loss of the eye.

How to examine the eye

Look at the eye up close with a bright light and magnification (for example, a phone camera). Ask the patient to look up and down, and right and left.

If the eye is so painful that the patient cannot open their eye to be examined, refer them to an eye clinic or eye specialist immediately.



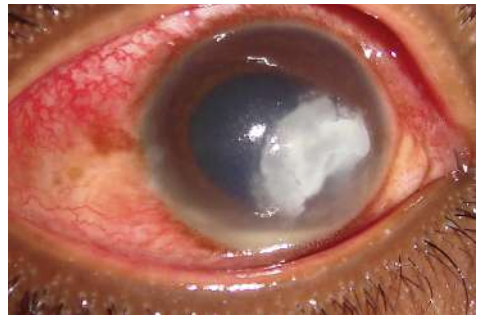
What is the cornea?

In a healthy eye, the cornea is the clear/see-through area in front of the pupil (black) and iris (brown).

How to recognise a corneal infection

Any **white patch on the cornea**, with **redness** and **pain**, suggests an infection.

Early-stage infection. Note the white patch on the cornea and the redness elsewhere.



Late-stage infection, with a larger white patch and a collection of pus at the base of the cornea.

What to do

If the patient has a white patch, redness, and pain:

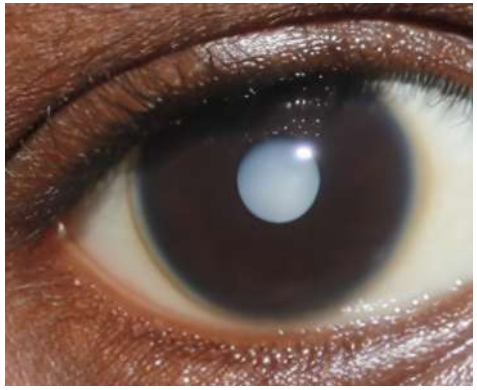
- ✓ **Urgently** refer the patient to an eye specialist. They must be seen **within 24 hours**. Give them the address and directions to get there.
- ✓ Start the patient on **broad-spectrum antibiotic eye drops**, which they must apply every 1 or 2 hours until they see the eye specialist.
- ✓ Explain to the patient how to instil the eye drops, without touching the eye.

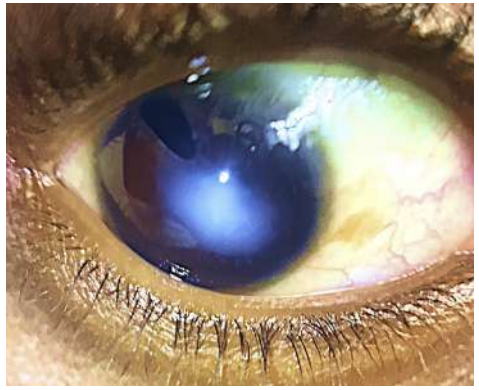
What to avoid

If the patient has a white patch, redness, and pain they must *not* use:

- ✗ Steroid eye drops, such as prednisolone or dexamethasone
- ✗ Non-sterile preparations

These will make the infection worse.





If you can see a white area but there is no redness or pain, this is probably not an infection. The patient may have **cataract** (left) or a **corneal scar** (right). Refer them to an eye specialist for advice.

Sandip Das Sanyam
Research Project Lead, Sagarmatha Choudhary Eye Hospital, Nepal.

Educating community members in Nepal about microbial keratitis

A poster about two farmers is encouraging agricultural workers in Nepal to seek urgent medical attention after eye injuries.

Microbial keratitis is an infection of the cornea: the clear, dome-shaped surface that covers the front of the eye. This condition is caused by various microorganisms, including bacteria, fungi, viruses, and protozoa. It is a serious eye condition that can lead to significant pain, vision loss, and even blindness if not treated promptly and effectively.

Nepal has a high incidence of corneal abrasions and infections. Farmers and agricultural workers are at increased risk as they are exposed on a daily basis to plant material, dust and debris. If farm workers do not use protective eyewear, they are at increased risk of eye injuries that introduce microorganisms directly into the cornea. Any delays in treatment will result in the infection becoming worse, increasing the risk of sight loss. To address this, Sagarmatha Choudhary Eye Hospital (SCEH), supported by the London School of Hygiene & Tropical Medicine and the International Centre of Eye Health, UK, have developed a poster to raise awareness about corneal ulcers amongst farm workers in Siraha District, Nepal, and encourage them to seek help urgently.

The poster describes the experience of two farmers: one who sought urgent treatment, and one who delayed seeking help. Using colourful, culturally appropriate images and storytelling, the poster makes it possible for all community members, including those unable to read, to learn about the connection between their health seeking behaviour and their future health and wellbeing.

Public health researchers and the SCEH team created the poster and ensured the information was scientifically accurate. Team members undertook four rounds of revision of the poster by asking patients attending SCEH hospital in Lahan to share their understanding of the illustrations; their feedback was incorporated in subsequent versions. This helped to ensure that the posters would be widely understood.

Canvas copies of the poster were displayed in 40 health centres, and in their surrounding vilages, in the district. For a few months after the posters were put up, the team noticed an increase in the number of patients coming to the health centres with red eyes or eye injuries, with patients saying they attended because of what they learnt from the posters. However, the posters degraded over time or were removed, which meant that these gains were not sustained. A more long-term or permanent display should be considered.

See overleaf for an English translation of the poster. Editable files are available if you would like to adapt it, e.g. by using names or images better suited to your local community. Email requests to **editor@cehjournal.org**.

A tale of two farmers: the story of Dukhiya and Sukhiya

Dukhiya (right), a hardworking farmer, sustained a minor injury to his eye while working in the field. Initially, he noticed redness and pain but chose to ignore it, believing it would heal on its own. As days passed, his symptoms worsened.

Instead of seeking professional medical help, Dukhiya tried home remedies. Unfortunately, this delay in seeking treatment made his condition much worse. The infection spread, causing significant damage to his cornea. Eventually, he lost vision in that eye. Dukhiya's story is a stark reminder of the dangers of neglecting eye injuries and the critical need for timely medical intervention.

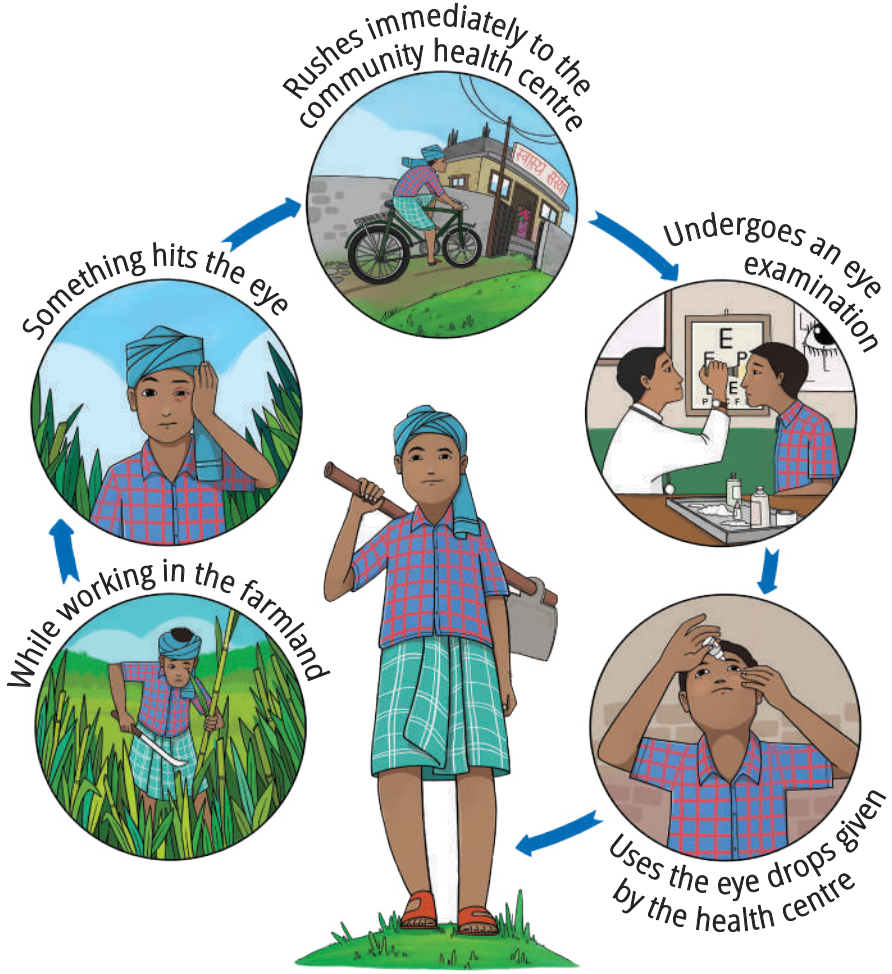
In contrast, **Sukhiya**, another farmer who faced a similar injury while working in the field, took immediate action. Noticing redness and pain in his eye, he promptly visited the nearby health centre in his community. The health care professionals evaluated his condition and prescribed eye drops, which Sukhiya used as directed. With timely and correct treatment, Sukhiya's eye healed quickly, and he was able to return to work without any lasting damage. Sukhiya's story highlights the importance of seeking professional medical help immediately after an eye injury to ensure a positive outcome.

"The poster underscores the significance of timely medical intervention and accessible healthcare facilities in preventing severe outcomes."

A Tale of Two Farmers

Sukhiya: a happy outcome

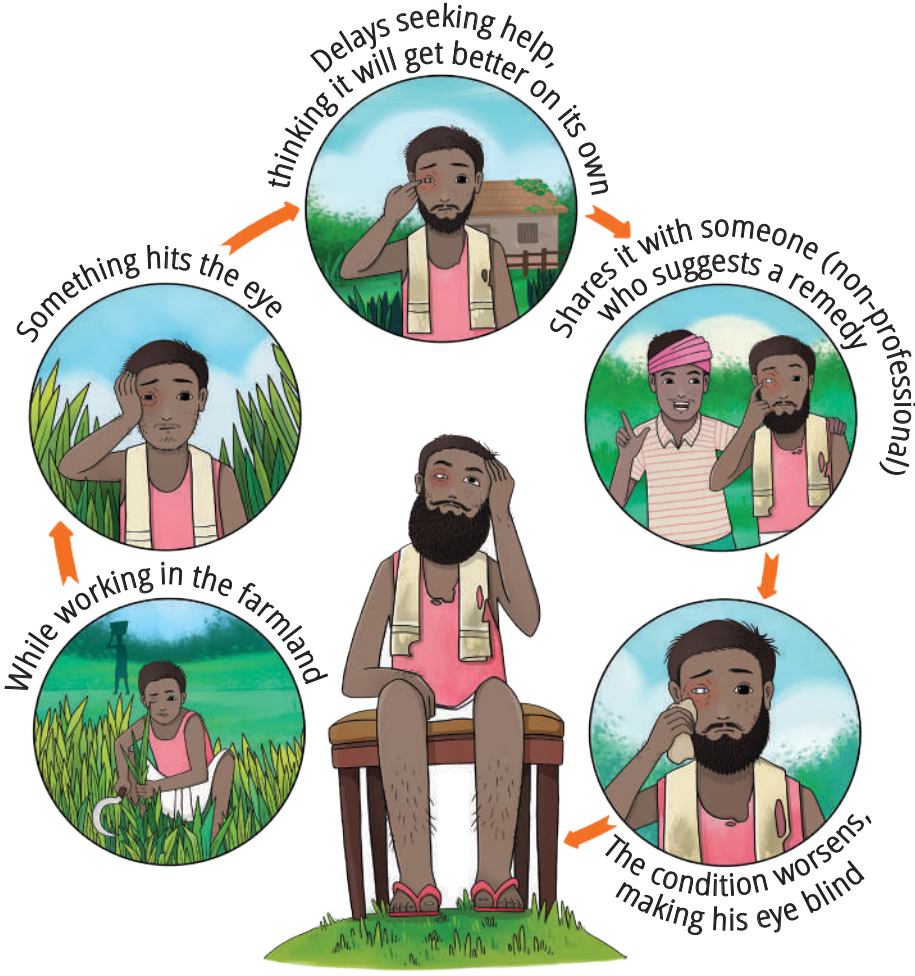
If you get injured and the eye gets red,
Make sure you stop and use your head,
Get to the nearest health centre quick,
And stop yourself from getting sick.



If we take care of our eyes when needed, we can return to a normal lifestyle soon.

Dukhiya: a sad outcome

If you get injured and the eye gets red,
Ignoring it makes it worse instead,
Staying at home, hoping it will go,
Leads to problems, don't you know?



Neglecting our eye problems could lead to difficulties in life.