Guidelines for the Management of Corneal Ulcer at Primary, Secondary & Tertiary Care health facilities in the South-East Asia Region

World Health Organization
Regional Office for South-East Asia
2004
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Foreword

Launching of Vision 2020: The Right to Sight has given a new impetus to the existing programmes for prevention of blindness globally. Countries in the South-East Asia Region have been quick to respond to this call.

While cataract remains the major cause of reversible visual loss in the Region, diseases of the cornea are emerging as an important cause of visual impairment. Trachoma and vitamin A deficiency (xerophthalmia) have traditionally been the major cause of corneal blindness. With the introduction of the SAFE strategy for trachoma and mass distribution of vitamin A capsules, both these conditions have now been brought under control.

In the vast agrarian society of South-East Asia, particularly in countries where primary health care and referral systems are weak, minor eye injuries sustained in agricultural farms often lead to corneal ulceration, loss of vision and many a time result in loss of eyes. This is entirely avoidable if known public health measures are applied effectively.

WHO together with its Member States is currently dealing with this problem at two different levels. The first consists of developing a community model for prevention of post-traumatic corneal ulcer, and the second, providing a definitive guideline for effective management of established corneal ulcer.

The purpose of these guidelines is to provide a simple yet effective management strategy to rapidly reduce morbidity and visual loss due to corneal ulceration. I am confident that this will be found useful by all those involved in caring for these patients.

I would like to thank all our experts who have contributed to the development of these guidelines.

Samlee Plianbangchang, M.D., Dr. P.H.
Regional Director
Purpose

The purpose of this document is to provide guidance in the management of superficial ocular trauma and established suppurative keratitis in order to minimize morbidity and visual loss from bacterial and fungal corneal infections.

Need and Process of Development of Guidelines

Corneal ulcer is a major public health problem in the developing world causing prolonged morbidity, loss of vision and, many a time, loss of eyes. It has tremendous socioeconomic implications as sufferers are often the bread earners in the family.

Recognizing the public health importance of corneal ulcer, the WHO South-East Asia Regional office has taken several initiatives in the past, both for prevention of corneal ulcer as well as for its management, in the countries of South-East Asia at the request of the governments. Preventive interventions will be described in another publication. This document describes the management of corneal ulcer.

Treatment of corneal ulcers has at best remained unsatisfactory across the health systems of the developing world. The Regional Office commissioned a study in 1999 to prepare an epidemiological and microbiological profile of corneal ulcer in the Region. This study identified the magnitude of the problem, microbial pattern of infection, antibiotic/antifungal sensitivity of the microbes as well as modifiable risk factors. This greatly helped to fill in the information gap.

Subsequently these findings were reviewed at an intercountry meeting on corneal blindness held in 2002. The participating countries recommended to WHO to develop definitive guidelines for the treatment of corneal ulcer suitable for use at different levels of health system.

To respond to the above request, WHO entered into a contract with the Aravind Eye Care System (AECS) in Madurai, India, a WHO collaborating centre, for development of the guidelines. The first draft of the guidelines was prepared by Dr M Srinivasan and his colleagues based on the findings of the above cited study and review of the more recent literature.

This draft was circulated among over 200 clinical and public health experts. Their inputs were incorporated in the revised draft which was reviewed by selected experts from six WHO collaborating centres and corneal experts across the globe. The list of the collaborating centres is given in Annex 6. The document was further refined at Aravind Eye Care System and finally reviewed at WHO.
Guidelines for the Management of Superficial Corneal Trauma and Infections in Primary Health Facilities

History and examination
If there is a:
• history of superficial injury; and/or
• examination shows a corneal abrasion

Treat
with chloramphenicol, eye ointment (0.5 - 1%) three times per day for at least 3 days.
• Do not use any medicine containing steroids.
• Do not use traditional medicines.

Refer to an ophthalmologist
• if pain and redness persist for 3 days; or
• if there is a white mark on the cornea and a red eye (corneal ulcer).

Give the patient chloramphenicol ointment to use 3 times per day when you refer to an ophthalmologist or to the nearest eye care facility.

Do not delay the referral of a patient with corneal ulcer.

Clinical assessment and diagnosis
Primary level

Corneal abrasion
Inset abrasion without stain

Corneal ulcer
Guidelines for the Management of Suppurative Keratitis at the Secondary Level of Eye Care

History and examination
Confirm diagnosis of suppurative keratitis (refer to Table 1 and photographs)

Immediate referral to a tertiary ophthalmic centre is indicated if:
• the ulcer is in only eye
• the patient is a child
• there is impending or actual perforation
• a fungal ulcer is suspected on clinical examination, but KOH or other fungal stain is not available.

Take a corneal smear:
and stain with KOH (or other fungal stain) to look for fungal hyphae.

Admit the patient for in-patient treatment:
• if there is immediate threat to vision
• to ensure hourly treatment as below
• to ensure follow up as below
Treatment guidelines

<table>
<thead>
<tr>
<th>No fungal hyphae seen on smear</th>
<th>Fungal hyphae seen on smear</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cafazolin 5% and Gentamycin 1.4% drops hourly</strong></td>
<td><strong>Natamycin 5% drops hourly alone (no antibiotics)</strong></td>
</tr>
</tbody>
</table>
| Ciprofloxacin may be used instead of gentamycin.  
  - if hourly drops is not possible  
  - then a sub-conjunctival inj. can be considered. | or Amphotericin 0.15% drops hourly |

Treatment frequency, duration and followup:

<table>
<thead>
<tr>
<th>– Daily examination until the ulcer starts improving</th>
<th>– Examination every 2 days until the ulcer starts improving</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Then gradually reduce the frequency of drops and follow up over 2 weeks</td>
<td>– Then continue drops at least 3 hourly for at least 2 weeks after healing of the ulcer</td>
</tr>
</tbody>
</table>

Refer to tertiary ophthalmic centre if:

<table>
<thead>
<tr>
<th>Not improving after 3 days treatment</th>
<th>Not improving after 7 days treatment</th>
</tr>
</thead>
</table>

Adjunctive therapy:

- Includes cycloplegics; analgesics; anti-glaucoma medication if indicated.
- Do not use any preparation containing steroids.
- Investigate for diabetes mellitus as a possible risk factor for corneal ulceration.
Features of bacterial ulcer
1. History of trauma to the cornea, contact lens wear
2. Pain, redness, watering, decrease in vision
3. Lid oedema (marked in gonococcal ulcer), purulent discharge in gonococcal ulcer and bluish green discharge in pseudomonas corneal ulcer
4. Round or oval in shape involving central or para central part of the cornea. Rest of the cornea is clear. Hypopyon may or may not be present.
5. In pneumococcal ulcer the advancing border will have active infiltrate with undermined edges and the trailing edge may show signs of healing. Most of the pneumococcal ulcers will show leveled hypopyon associated with Dacryocystitis.
6. Pseudomonas ulcer will have short duration, marked stromal oedema adjacent to the ulcer with rapid progression. If untreated, will perforate within 2-3 days. Advanced ulcer may involve the sclera also.
7. Ulcers caused by Moraxella and Nocardia are slowly progressive in immunocompromised hosts.

Features of fungal ulcer
1. History of trauma with vegetable matter
2. Suspect fungal ulcer if patient reports agriculture as main occupation.
3. Pain and redness are similar to bacterial ulcer. But lid oedema is minimal even in severe cases unless patients have received native medicines or peri ocular injections.
4. Early fungal ulcer may appear like a dendritic ulcer of herpes simplex virus. The feathery borders are pathognomonic clinical features. Satellite lesions, immune ring, and unlevelled hypopyon may aid in diagnosis.
5. The surface is raised with greyish white creamy infiltrates, which may or may not appear dry.
6. Ulcer due to pigmented fungi will appear as brown or dark; raised, dry, rough, leathery plaque on the surface of the cornea.

Table-1: Typical clinical features

<table>
<thead>
<tr>
<th>Features of bacterial ulcer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. History of trauma to the cornea, contact lens wear</td>
</tr>
<tr>
<td>2. Pain, redness, watering, decrease in vision</td>
</tr>
<tr>
<td>3. Lid oedema (marked in gonococcal ulcer), purulent discharge in gonococcal ulcer and bluish green discharge in pseudomonas corneal ulcer</td>
</tr>
<tr>
<td>4. Round or oval in shape involving central or para central part of the cornea. Rest of the cornea is clear. Hypopyon may or may not be present.</td>
</tr>
<tr>
<td>5. In pneumococcal ulcer the advancing border will have active infiltrate with undermined edges and the trailing edge may show signs of healing. Most of the pneumococcal ulcers will show leveled hypopyon associated with Dacryocystitis.</td>
</tr>
<tr>
<td>6. Pseudomonas ulcer will have short duration, marked stromal oedema adjacent to the ulcer with rapid progression. If untreated, will perforate within 2-3 days. Advanced ulcer may involve the sclera also.</td>
</tr>
<tr>
<td>7. Ulcers caused by Moraxella and Nocardia are slowly progressive in immunocompromised hosts.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Features of fungal ulcer</th>
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<tbody>
<tr>
<td>1. History of trauma with vegetable matter</td>
</tr>
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<td>2. Suspect fungal ulcer if patient reports agriculture as main occupation.</td>
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</tr>
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<td>4. Early fungal ulcer may appear like a dendritic ulcer of herpes simplex virus. The feathery borders are pathognomonic clinical features. Satellite lesions, immune ring, and unlevelled hypopyon may aid in diagnosis.</td>
</tr>
<tr>
<td>5. The surface is raised with greyish white creamy infiltrates, which may or may not appear dry.</td>
</tr>
<tr>
<td>6. Ulcer due to pigmented fungi will appear as brown or dark; raised, dry, rough, leathery plaque on the surface of the cornea.</td>
</tr>
</tbody>
</table>
Early Bacterial ulcer

Late Bacterial ulcer

Early Fungal ulcer

Late Fungal ulcer
Fig. 1 Management of Supurative Keratitis at the Secondary Level of eye care

Suppurative keratitis

Ulcer in an only eye
The patient is a child
Impending or actual perforation
Suspected fungal ulcer

Yes

Refer to Tertiary centre immediately

No

Perform KOH smear or other fungal stain

Fungal hyphae seen

No

Yes

Cefazolin 5% & Gentamycin 1.4% drops hourly

Daily examination until improvement

Suspected fungal ulcer

No improvement after 7 days

Refer to tertiary ophthalmic centre

Natamycin 5% or Amphotericin 0.15% drops hourly

Examination every 2 days until improvement
**How to perform a Potassium hydroxide (KOH) & Lactophenol cotton blue (LPCB) stain to identify fungal hyphae**

<table>
<thead>
<tr>
<th>Equipment required</th>
<th>Preparing 10% KOH smear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential equipment</td>
<td>• Weigh approximately 10g (8 pellets) of KOH</td>
</tr>
<tr>
<td>Kimura spatula</td>
<td>• Dissolve in 10ml of distilled water</td>
</tr>
<tr>
<td>No 15 surgical blade</td>
<td>• Add 1 drop of 10% glycerol</td>
</tr>
<tr>
<td>Sterile glass slides</td>
<td>• Prepare fresh stock every week</td>
</tr>
<tr>
<td>Cover slips</td>
<td>Can be kept at room temperature in a dropper bottle</td>
</tr>
<tr>
<td>Binocular microscopes</td>
<td></td>
</tr>
<tr>
<td>10% KOH</td>
<td></td>
</tr>
<tr>
<td>Spirit Lamp</td>
<td></td>
</tr>
<tr>
<td>Topical anaesthetic</td>
<td></td>
</tr>
</tbody>
</table>

**Performing KOH smear**

1. Make the patient sit at the slit lamp or lie down over a bed. (need magnifiers, loupe or operating microscope), explain this simple procedure to the patient.
2. Instill one or two drops of tetracaine or 0.5% proparacaine. One can use 4% lignocaine if the above two are not available. Wait for a minute or two before scraping.
3. Keep two clean glass slides having 1cm circle made with glass pencil on the reverse side of the slide.
4. Scrape the base and edges of the corneal ulcer with flame sterilized kimura spatula or sterile 15# Bard Parker blade.
5. Streak the specimen over the glass slide within the circle; one for KOH and the other for Gram stain.
6. Apply KOH over the specimen. Cover the KOH smear with a cover slip and examine under light microscope immediately.
7. If the person is not trained to interpret the smear, send both slides immediately (within 2 hrs) to the microbiology laboratory.
Equipment required

<table>
<thead>
<tr>
<th>Essential equipment</th>
<th>Preparing LPCB smear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kimura spatula</td>
<td>Lacto phenol cotton blue can be obtained commercially and can be stored for a indefinite period.</td>
</tr>
<tr>
<td>No 15 surgical blade</td>
<td></td>
</tr>
<tr>
<td>Sterile glass slides</td>
<td></td>
</tr>
<tr>
<td>Cover slips</td>
<td></td>
</tr>
<tr>
<td>Binocular microscopes</td>
<td></td>
</tr>
<tr>
<td>LPCB stain</td>
<td></td>
</tr>
<tr>
<td>Spirit Lamp</td>
<td></td>
</tr>
<tr>
<td>Topical anaesthetic</td>
<td></td>
</tr>
</tbody>
</table>

How to perform a LPCB smear

1. Make the patient sit at the slit lamp or lie down over a bed. (need magnifiers, loupe or operating microscope), explain this simple procedure to the patient

2. Instill one or two drops of tetracaine or 0.5% proparacaine. One can use 4% lignocaine if the above two are not available. Wait for a minute or two before scraping.

3. Keep two clean glass slides having 1 cm circle made with glass pencil on the reverse side of the slide.

4. Scrape the base and edges of the corneal ulcer with flame sterilized kimura spatula or sterile 15 # Bard Parker blade and spread it on the glass slide within the circle.

5. Apply locto phenol cotton blue over the specimen.

6. Cover with a cover slip and examine under light microscope.
Guidelines for the Management of Suppurative Keratitis at Tertiary Ophthalmic Centres

History and Examination:
Use a standard form and classification of corneal ulceration. (see Annex 4)

Take a Corneal Smear:
Stain with KOH (or other fungal stain) and Gram stain.

Culture on
(a) Sheep blood agar; (b) Sabourauds; and if possible (c) Brain-heart infusion.
Other culture media may also be indicated in selected cases.

Admit the patient for in-patient treatment:
If there is immediate threat to vision
If the patient is a child
To ensure hourly treatment as below
To ensure follow-up as below

Treatment guidelines:

<table>
<thead>
<tr>
<th>Smear not possible</th>
<th>No organism seen on smear</th>
<th>Gram positive bacteria seen</th>
<th>Gram negative bacteria seen</th>
<th>Fungal hyphae seen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin 5% and Gentamycin 1.4% drops hourly</td>
<td>Natamycin 5% drops hourly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin may be used instead of gentamycin. If hourly drops is not possible then a sub-conjunctival injection can be considered.</td>
<td>or Amphotericin 0.15% drops hourly</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Treatment frequency, duration and follow-up:

| Daily examination until the ulcer is improving | Examination every 2 days until the ulcer starts improving |
| Then gradually reduce frequency of drops and follow up over 2 weeks | Then continue drops at least 3 hourly for at least 2 weeks after healing of the ulcer |
Adjunctive therapy includes cycloplegics; analgesics; anti-glaucoma medication, if indicated.

Figure 2 describes management if the ulcer does not respond to or worsens on above treatment.

**Fig. 2: Decision making algorithm in the management of therapeutic failures in presumed bacterial keratitis**

- **Culture performed**
  - No: Stop antibiotic for 24-48hr and reculture; corneal biopsy in severe progressive cases
  - Yes:
    - **Growth**
      - No: Change antibiotic to cover organism involved
      - Yes:
        - **Organisms susceptible to antibiotics used**
          - No: Add specific media for bacteria, fungi and parasite
          - Yes: 72 hours of therapy
            - No: Wait for 72 hrs of treatment
            - Yes:
              - **Growth of organism**
                - No: Consider Surgical Options
                - Yes: Treat specifically
              - Inadequate dosing
                - Increase to hourly dosing
              - Non-compliance
                - Repeat subconj. Injection and or hospitalize
              - Host immunocompromised
                - Supplement drops with subconj.inj & consider systemic antibiotics treat the cause
Role of Topical Steroids
Topical steroids are not recommended in any case of fungal keratitis.
The role of topical steroids in bacterial keratitis is controversial.
If steroids are used it should be with great caution and close observation.

Role of Systemic Antimicrobials
Systemic antifungals are recommended in fungal ulcers, which are:
- large and deep, or
- perforating, or
- have scleral involvement
Systemic antibiotics are recommended in bacterial ulcers if there is scleral involvement and may be used in perforated cases.

Role of Surgery
Surgical procedures may include:

Debridement/superficial keratectomy
Surgical removal of corneal epithelium without causing injury to the basement membrane.

Indication
- Epithelial herpes simplex virus keratitis
- Recurrent corneal erosion
- For diagnosing superficial infective keratitis
- Enhances penetration of topical antibiotics.

Techniques
This procedure is performed under topical anaesthesia on a slit lamp or operating microscope with sterile cotton tipped applicator, weckel sponge or surgical blade.

Superficial Keratectomy
Surgical removal of corneal epithelium including Bowman's membrane and anterior stroma of the diseased cornea.

Indication
- Biopsy in non-healing corneal ulcer
- Debulking of infective material

Technique
This procedure is performed under aseptic condition with topical or subconjunctival anaesthesia using 15# Bard Parker blade.
Tarsorrhaphy
Lateral
Central

Indication
Exposure keratitis (Bells palsy)
Neuroparalytic keratitis
Lateral tarsorraphy is frequently performed in an eye having Bell’s palsy with non-healing suppurative keratitis.

Technique
This procedure is performed at a minor operating theatre: Local infiltration with 2% lidocaine at the lid margins. About 1-2 mm of inter-marginal strip is shaved off deep upto dermis and apposed with 4 “0” silk suture and anchored with bolsters. The release of tarsorraphy depends upon the etiology of lagophthalmus and healing response of the ulcer.

Tissue Adhesive
This procedure is performed for:
- wounds with a small amount of tissue loss
- persistent aqueous leakage
- small lacerations
- puncture wounds
The tissue bed must be dry and free of epithelial cells.

Technique
A thin film of adhesive is applied using a small gauge disposable needle, a micro capillary applicator or the broken wooden end of a sterile cotton applicator. Following application, adhesives should be given several minutes to dry before any other manipulation.

Conjunctival flaps
This is rarely performed for suppurative keratitis.

Indications
Non-healing superficial ulcer
Peripheral corneal ulcers with descemetole or small perforation

Contraindication
Perforated central corneal ulcer

Advantages
Promotes healing providing better nourishment to the underlying cornea

Disadvantages
Monitoring the progress of ulcer is difficult
Delays or impedes the penetration of topical antibiotics
Visual outcome will be poor due to scarring and vascularisation
Technique
This procedure is performed under local anaesthesia as in cataract surgery. It is taken up under general anaesthesia if the patient is non-cooperative or in the paediatric age group. Specific drugs should be continued post-operatively.

Patch Graft

**Indication**
- Descemetocele
- Small perforation

Patchgraft is usually 5 mm or 6 mm in size. Recipient bed is cleared of debris and not trephined. Lamellar or full thickness donor button could be anchored. This procedure is performed in the operating room under surgical microscope. Interrupted suture (12-16) is applied using 10/o or 9/o nylon. Appropriate antibiotics are continued post-operatively.

Penetrating keratoplasty

- Maintains the integrity of the globe for future optical grafts
- Promotes healing of corneal ulcer by total removal of pathology
- As a diagnostic technique to form a good source for histopathological and microbiological examination
- 40-50% of these patients recover useful vision
- Carries better prognosis in bacterial corneal ulcers

The indications for surgical intervention include:

- Non-healing in spite of all medical therapy
- Impending or actual perforation

If the ulcer does not respond to treatment:

- Review with gram stain, culture and sensitivity results
- If the organism is unknown, consider stopping all treatment for 48 hours, take new smears, cultures, and if required a corneal biopsy.

Use culture media for viral and uncommon pathogens. (anaerobes, acanthamoeba, mycobacteria).

20. Medical Laboratory Manual for Tropical countries; Vol II Microbiology, Monica Cheesbrough, Tropical Health Technology/Butteys worth


25. Harris DJ Stulting RD, Waring GO. Late bacterial and fungal keratitis after corneal transplantation; spectrum of pathogens, graft survival and visual progress Ophthalmology 1988,95: 1450 - 7


Epidemiology & Management Corneal Blindness and Suppurative Keratitis

1. Epidemiology of Corneal Visual Loss
   (a) The magnitude of blindness (all causes) in the countries of the South-East Asia Region varies from 3,000 people per million population in communities with good economy and health care to over 10,000 per million in low-income settings.
   (b) Corneal scarring is a common cause of blindness in low-income settings being responsible for 5-20% of all blindness.
   (c) Important causes of bilateral corneal blindness include trachoma, vitamin A deficiency, ophthalmia neonatorum and bacterial/fungal infections.
   (d) The Andhra Pradesh Eye Disease Study (APEDS)\(^\text{48}\) in Andhra Pradesh (India) estimated that 1,200 people per million population are blind (<3/60) from corneal pathology.
   (e) The prevalence of unilateral blindness due to corneal opacity in low-income settings is estimated to be in the range of 5,000 to 20,000 people per million population.

2. Epidemiology of Suppurative Keratitis
   (a) Suppurative keratitis due to bacteria and fungi is the main cause of unilateral corneal scar.
   (b) A two-year prospective study of over 34,000 people from a rural setting in Nepal reported an incidence rate of corneal ulceration of 8,000 cases per million population per year (160 cases per million pop per week). The results of retrospective studies in the Region are summarized in Table 1. It is estimated that up to 12 million cases of suppurative keratitis occur each year in the Region. An unknown proportion of these cases go on to visual loss or blindness.
   (c) Within the SEA Region the causes of suppurative keratitis depend mainly on climatic factors.
   (d) In warm, humid areas the relative proportion of fungal to bacterial ulcers approaches 50:50, while in cool dry climates most ulcers are due to bacteria.
   (e) The major bacterial causes are streptococcus; pseudomonas and staphylococcus.
   (f) The major fungal isolates are fusarium and aspergillus species. Candida is relatively uncommon.
   (g) Acanthamoeba even in well-equipped tertiary facilities is responsible for less than 5% of ulcers.
Agricultural trauma is the main risk factor; seasonal variations in incidence can occur. Contact lens wear is not an important risk factor within the Region.

3. Management of Suppurative Keratitis

(a) The outcome of corneal injury with secondary infection can be markedly improved by early diagnosis and appropriate treatment with antibiotics at the primary level of health care.

(b) Inappropriate use of traditional medicines or topical steroids and delay in referral to an ophthalmologist for diagnosis and treatment all contribute to unnecessary visual loss from superficial corneal trauma and secondary infection.

(c) Identification of fungal hyphae in a corneal smear with KOH stain is a simple, inexpensive and sensitive test, which should routinely be performed by ophthalmologists in cases of suppurative keratitis, particularly in areas where fungi are known or expected to occur. Lactophenol cotton blue is a simple alternative fungal stain reported from some countries.

(d) Antifungal treatment is not recommended unless there is evidence of fungal infection by microscopy or culture. Natamycin is the drug of first choice in geographical areas where fusarium species predominate.

(e) The recommended first line antibiotic treatment is a combination of cephazolin and fortified gentamycin.
**Table 1: Reported incidence of corneal ulceration in the SEA Region**

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence / (million pop)</th>
<th>Reference</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nepal</td>
<td>7990</td>
<td>BJO⁴¹</td>
<td>Prospective 2 yr study</td>
</tr>
<tr>
<td>India</td>
<td>1130</td>
<td>BJO⁵</td>
<td>Retrospective study</td>
</tr>
<tr>
<td>Myanmar</td>
<td>7100</td>
<td>*Country report</td>
<td>Retrospective study</td>
</tr>
<tr>
<td>Bhutan</td>
<td>3390</td>
<td>*Country report</td>
<td>Retrospective study</td>
</tr>
</tbody>
</table>

**Table 2: Proportion of suppurative keratitis with fungal organisms in the SEA Region**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Sri Lanka</th>
<th>India</th>
<th>Nepal</th>
<th>Bangladesh</th>
<th>Thailand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any fungus</td>
<td>33</td>
<td>19-45</td>
<td>17-44</td>
<td>21-36</td>
<td>25</td>
</tr>
</tbody>
</table>

**Table 3: Microbiological profile of fungal Keratitis in the SEA Region**

(Percentages)

<table>
<thead>
<tr>
<th>Organism</th>
<th>Sri Lanka</th>
<th>India</th>
<th>Nepal</th>
<th>Bangladesh</th>
<th>Thailand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspergillus</td>
<td>18</td>
<td>16-53</td>
<td>46-60</td>
<td>29-29</td>
<td>34</td>
</tr>
<tr>
<td>Fusarium</td>
<td>80</td>
<td>10-47</td>
<td>13</td>
<td>14-28</td>
<td>26</td>
</tr>
</tbody>
</table>

**Table 4: Microbiological profile of bacterial keratitis in the SEA Region**

(Percentages)

<table>
<thead>
<tr>
<th>Organism</th>
<th>India</th>
<th>Nepal</th>
<th>Bangladesh</th>
<th>Thailand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steptococcus pneumoniae</td>
<td>44</td>
<td>31</td>
<td>22</td>
<td>3</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>10</td>
<td>12</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>14</td>
<td>11</td>
<td>20</td>
<td>45</td>
</tr>
<tr>
<td>Others or unknown bacteria</td>
<td>32</td>
<td>46</td>
<td>47</td>
<td>45</td>
</tr>
</tbody>
</table>

* (Figures as reported by Member Countries based on their hospital data projected to a captive population)
## Antimicrobial agents

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Sensitive organisms</th>
<th>Common resistance</th>
<th>Dose</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin</td>
<td>Strep pneumo, and most gram + bact.</td>
<td>Most gram – bacteria</td>
<td>5.0%</td>
<td>Not commercially available, must be prepared from injectable form as and when necessary</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>Most gram – and some gram + bact.</td>
<td>Strep pneumo</td>
<td>1.4%</td>
<td>Commercial drops need to be fortified</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Most gram – and many gram + bact.</td>
<td>Most Strep pneumo</td>
<td>0.3%</td>
<td>Commercially available</td>
</tr>
<tr>
<td>Chlormphenicol</td>
<td>Many gram + and gram – bact.</td>
<td>Good for pneumo</td>
<td>1.0%</td>
<td>Commercially available in drops and ointment</td>
</tr>
</tbody>
</table>

### Antifungal

<table>
<thead>
<tr>
<th>Antifungal</th>
<th>Filamentous fungi – Fusarium</th>
<th></th>
<th>5.0%</th>
<th>Commercial available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natamycin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amphotericin – B</td>
<td>Effective against most yeasts Aspergillus</td>
<td>Moderate response to Fusarium</td>
<td>0.15%</td>
<td>Not commercially available, must be prepared from an injectable preparation</td>
</tr>
</tbody>
</table>
### Classification, Dosage and Spectrum of useful Antifungal agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Topical</th>
<th>Systemic</th>
<th>Useful antifungal spectrum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyene Antifungals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetrenes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nystatin</td>
<td>3.3% ointment or 100 000 units/g every hr during day, every 2 hr at night</td>
<td>Poorly soluble, not absorbable from gastrointestinal tract. Not recommended for systemic use</td>
<td>Moderately effective against most Candida species. Slight effect against filamentous fungi.</td>
</tr>
<tr>
<td>Natamycin</td>
<td>5% suspension every hr during day, every 2 hr during night</td>
<td>Poorly soluble, not recommended for systemic use</td>
<td>Good effect against Candida, Aspergillus, Fusarium and some other fungi. Poorly soluble, difficult to treat deep mycotic corneal ulcer</td>
</tr>
<tr>
<td>Pentenes</td>
<td>0.5% solution too toxic; 0.1 to 0.2% solution effective every hr during day every 2 hr at night</td>
<td>0.25mg/kg on day 1; increase by 0.25 to 1mg/kg/day. Total dosage 1000-1500mg. Use 50 mg diphenhydramine orally before dose. Give as intravenous drip in 5% dextrose and water with 1000 units heparin</td>
<td>Highly effective against Candida, moderately effective against some filamentous fungi. Excellent for systemic use against Candida. Synergistic with flucytosine and this combination is recommended</td>
</tr>
<tr>
<td>Drug</td>
<td>Topical</td>
<td>Systemic</td>
<td>Useful antifungal spectrum</td>
</tr>
<tr>
<td>------</td>
<td>---------</td>
<td>----------</td>
<td>---------------------------</td>
</tr>
<tr>
<td>Imidazole derivative antifungals</td>
<td>1% solution in arachis oil every 1hr until response occurs, then 4 times a day for 8 to 12 weeks</td>
<td>60mg-100mg/kg/day for 2 weeks</td>
<td>Highly effective against Aspergillus Candida species, and some filamentous fungi, including Paecilomyces, Dreschlera, Alternaria, &amp; Cladosporium species. Poor effect against Fusarium.</td>
</tr>
<tr>
<td>Clotrimazole</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenethylalcohol group Miconazole</td>
<td>1% solution in arachis oil every 1 hr during day, every 2hr at night</td>
<td>300 to 600 mg/day intravenously has been used for ocular infection</td>
<td>Active against a larger spectrum of filamentous fungi and Candida organisms, but less effective against Aspergillus and Fusarium species than other agents. It also has some antibacterial activity against gram positive organisms</td>
</tr>
<tr>
<td>Econazole</td>
<td>1% solution in arachis oil every hr during day, every 2hr during night</td>
<td>200mg/day systemically</td>
<td>More effective than Miconazole against Aspergillus, Fusarium, and Pencillium species but less effective against Candida species</td>
</tr>
<tr>
<td>Drug</td>
<td>Topical</td>
<td>Systemic</td>
<td>Useful antifungal spectrum</td>
</tr>
<tr>
<td>-------------------</td>
<td>---------------------------------------</td>
<td>-----------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>1% suspension and 1% ointment</td>
<td>Oral adult dose 200mg/day. It should be continued for 1-2 months</td>
<td>It has a wider spectrum of activity than Imidazoles. It has an excellent in vitro activity against Aspergillus and Candida. It has not been very effective against Fusarium. Oral administration of Itracanazole appears to have less penetration than other triazoles into the cornea, aqueous and vitreous.</td>
</tr>
<tr>
<td>Pyramidine 5-Flurocytisine</td>
<td>1% solution for topical use is well tolerated</td>
<td>150 mg/g/day by oral route. Can also be administered intravenously</td>
<td>Effective against Candida, Cryptococosis and related fungi. Resistant strains emerge rapidly on monotherapy, usually combined with Amphotericin-B for treatment of sensitive fungi.</td>
</tr>
</tbody>
</table>

Annex 4

Standard Clinical Examination Form for Tertiary Care Center: Corneal Ulcer Patient Proforma

Patient details

Name: Age: ______ Sex: M F
Address: ________________________________

Ophthalmic history

- Trauma
- Dacrocystitis
- Corneal exposure
- Contact lens wear
- Eye surgery
- Ocular surface disorder
- Trichiasis
- Diabetes mellitus

Does the patient have a history of diabetes? Y/N.
If yes, for how long ______
If other, give details:
Current topical antibiotic Y / N specify __________
Current topical antifungal Y / N specify __________
Current topical steroid Y / N specify __________
Traditional eye medicine Y / N specify __________
Presentation Date of primary presentation __/__/____
Eye RE / LE / Bilateral
Duration of symptoms ______ days
Visual Acuity (uncorrected) Right ______ Left ______

BASE - LINE EXAMINATION

Ulcer size
### Lid Oedema
- [ ] Mild
- [ ] Moderate
- [ ] Severe

### Depth of Ulcer
- [ ] Deep
- [ ] Superficial

### Depth of Infiltrate
- [ ] Anterior stroma
- [ ] Mid stroma
- [ ] Posterior stroma

### Hypopyon
- [ ] Absent
- [ ] Present

**Height __________mm**

**REVIEW**

**Date:** __/__/____

---

### MICROBIOLOGY RESULTS

<table>
<thead>
<tr>
<th>Test</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram stain</td>
<td><em><strong>/</strong></em>/___</td>
</tr>
<tr>
<td>KOH</td>
<td><em><strong>/</strong></em>/___</td>
</tr>
<tr>
<td>Locto phenol</td>
<td><em><strong>/</strong></em>/___</td>
</tr>
<tr>
<td>Cotton Blue</td>
<td><em><strong>/</strong></em>/___</td>
</tr>
<tr>
<td>Culture (BA)</td>
<td><em><strong>/</strong></em>/___</td>
</tr>
<tr>
<td>Culture (SDA)</td>
<td><em><strong>/</strong></em>/___</td>
</tr>
<tr>
<td>Others (specify)</td>
<td><em><strong>/</strong></em>/___</td>
</tr>
</tbody>
</table>

**Eye**
- [ ] RE / LE / Bilateral

**Visual Acuity**
- Right ________  Left ________

**Ulcer size:**

- Depth of infiltrate
- Anterior stroma
- Mid stroma
- Posterior stroma
- Hypopyon
- Absent
- Present

**Height __________mm**

- Healing
- Working
- No Change
- Perforation
Classification of Corneal Ulcers

**Microbial ulcers**
These are caused by Staph or Strep species, present with pain, redness, lid oedema and discharge that varies according to the duration and severity of the ulcer. The ulcer is well circumscribed and may be central or at mid-periphery of the cornea. The borders of the ulcer are usually round or oval. Stromal infiltration may be present under the base of the ulcer with a yellowish white appearance. In severe ulcers, there may be folds in the deep stroma radiating from the ulcer bed; additionally a levelled hypopyon, 3 to 4 + cells and flare may be seen. Rarely posterior corneal abscess may be present with intact epithelium.

**Pneumococcal ulcer:**
- May be associated with chronic dacryocystitis in 55% of cases. 2, 18
- Haemorrhagic hypopyon may be associated with pneumococcal ulcer.
- Frequently seen in corneas having degeneration, epithelial problem and scars.
- The creeping edges and dense infiltrate at the leading edge of the ulcer are characteristic clinical features of pneumococcal ulcer.

**Gram positive bacterial ulcers**
The uninvolved portion of cornea will appear clear without oedema or infiltration.

**Gram negative bacterial ulcer**
Pseudomonas ulcer will have a short history.
- Signs and symptoms will be severe
- Diffuse ulceration with stromal infiltrate or oedema involving adjacent or whole cornea resulting in ground glass appearance is a distinguishing clinical feature from other ulcers. Mucopurulent discharge is seen frequently and it appears bluish green in untreated severe pseudomonas ulcers.
- Marked lid oedema and chemosis than seen in Gram positive bacterial ulcers.
- The ulcer perforates within few days if not managed properly.
- Pseudomonas ulcer may develop as ring abscess without epithelial defect.

**Ulcer caused by gram negative cocci**
- Marked lid oedema and copious purulent discharge;
- Pus will spurt out when the lids are separated.
- Ulcer is usually bilateral and perforates within short duration.
Lid abnormalities like ectropion, entropion, trichiasis, improper closure of lids as in leprosy, neurotrophic lesions due to herpes simplex, zoster or corneal degenerations, bullous keratopathy, and dry eyes predispose to bacterial ulcer in the SEA Region.
Satellite lesions, immune ring, endothelial plaques are present in both bacterial and fungal keratitis and do not help to differentiate between bacterial and fungal keratitis.

**Fungal Keratitis**
- The ulcer usually involves the central or exposed part of cornea.
- The edges are feathery with finger like projections, mimicking a herpetic dendritic ulcer in early stages.
- The fungal ulcer has raised creamy surface with greyish white infiltrate;
- The base of the ulcer is dry leathery (not in early fungal ulcer of about one week duration).
- The hypopyon is unlevelled and solid.
- There may be posterior corneal abscess with intact corneal epithelium.
- The remaining cornea appears clear.

**Pigmented fungal ulcer**
- The surface will show brown or dark pigmentation which is tough and leathery;
- Very difficult to scrape for diagnostic or therapeutic purposes.
- Untreated or improperly treated ulcer may progress to involve sclera also.

**Fungal ulcer caused by Candida**
- Usually involves an immunocompromised host and cornea;
- The ulcer appears as collar button and mimics staphylococcal ulcer.
Annex 6

List of WHO Collaborating Centres participating in the development of the Guidelines

1. Aravind Eye Hospitals and Aravind Eye Care System, Madurai, India
2. L V Prasad Eye Institute, Hyderabad, India
3. Dr R P Centre for Ophthalmic Sciences, New Delhi, India
4. London School of Hygiene and Tropical Medicine London, UK
5. Proctor Foundation for Research in Vision and Ophthalmology University of California, San Francisco, USA
6. Department of Ophthalmology, Juntendo University, Tokyo, Japan.

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Dr R. Pararajasegaram and Dr Madan P Upadhyay also participated at the expert group meeting on behalf of WHO.