

**PREFERRED PRACTICE PATTERN®**



# Bacterial Keratitis

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# CORNEA/EXTERNAL DISEASE PREFERRED PRACTICE PATTERN® DEVELOPMENT PROCESS AND PARTICIPANTS

The **Cornea/External Disease Preferred Practice Pattern® Panel** members wrote the Bacterial Keratitis Preferred Practice Pattern® guidelines (“PPP”). The PPP Panel members discussed and reviewed successive drafts of the document, meeting in person twice and conducting other review by e-mail discussion, to develop a consensus over the final version of the document.

## **Cornea/External Disease Preferred Practice Pattern Panel 2012–2013**

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The **Preferred Practice Patterns Committee** members reviewed and discussed the document during a meeting in March 2013. The document was edited in response to the discussion and comments.

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The Bacterial Keratitis PPP was then sent for review to additional internal and external groups and individuals in June 2013. All those returning comments were required to provide disclosure of relevant relationships with industry to have their comments considered. Members of the Cornea/External Disease Preferred Practice Pattern Panel reviewed and discussed these comments and determined revisions to the document.

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In compliance with the Council of Medical Specialty Societies' Code for Interactions with Companies (available at [www.cmss.org/codeforinteractions.aspx](http://www.cmss.org/codeforinteractions.aspx)), relevant relationships with industry are listed. The Academy has Relationship with Industry Procedures to comply with the Code (available at <http://one.aao.org/CE/PracticeGuidelines/PPP.aspx>). A majority (70%) of the members of the Cornea/External Disease Preferred Practice Pattern Panel 2012–2013 had no financial relationship to disclose.

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The disclosures of relevant relationships to industry of other reviewers of the document from January to August 2013 are available online at [www.aao.org/ppp](http://www.aao.org/ppp).



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## OBJECTIVES OF PREFERRED PRACTICE PATTERN® GUIDELINES

As a service to its members and the public, the American Academy of Ophthalmology has developed a series of Preferred Practice Pattern® guidelines that **identify characteristics and components of quality eye care**. Appendix 1 describes the core criteria of quality eye care.

The Preferred Practice Pattern® guidelines are based on the best available scientific data as interpreted by panels of knowledgeable health professionals. In some instances, such as when results of carefully conducted clinical trials are available, the data are particularly persuasive and provide clear guidance. In other instances, the panels have to rely on their collective judgment and evaluation of available evidence.

**These documents provide guidance for the pattern of practice, not for the care of a particular individual.** While they should generally meet the needs of most patients, they cannot possibly best meet the needs of all patients. Adherence to these PPPs will not ensure a successful outcome in every situation. These practice patterns should not be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the best results. It may be necessary to approach different patients' needs in different ways. The physician must make the ultimate judgment about the propriety of the care of a particular patient in light of all of the circumstances presented by that patient. The American Academy of Ophthalmology is available to assist members in resolving ethical dilemmas that arise in the course of ophthalmic practice.

**Preferred Practice Pattern® guidelines are not medical standards to be adhered to in all individual situations.** The Academy specifically disclaims any and all liability for injury or other damages of any kind, from negligence or otherwise, for any and all claims that may arise out of the use of any recommendations or other information contained herein.

References to certain drugs, instruments, and other products are made for illustrative purposes only and are not intended to constitute an endorsement of such. Such material may include information on applications that are not considered community standard, that reflect indications not included in approved U.S. Food and Drug Administration (FDA) labeling, or that are approved for use only in restricted research settings. The FDA has stated that it is the responsibility of the physician to determine the FDA status of each drug or device he or she wishes to use, and to use them with appropriate patient consent in compliance with applicable law.

Innovation in medicine is essential to ensure the future health of the American public, and the Academy encourages the development of new diagnostic and therapeutic methods that will improve eye care. It is essential to recognize that true medical excellence is achieved only when the patients' needs are the foremost consideration.

All Preferred Practice Pattern® guidelines are reviewed by their parent panel annually or earlier if developments warrant and updated accordingly. To ensure that all PPPs are current, each is valid for 5 years from the "approved by" date unless superseded by a revision. Preferred Practice Pattern guidelines are funded by the Academy without commercial support. Authors and reviewers of PPPs are volunteers and do not receive any financial compensation for their contributions to the documents. The PPPs are externally reviewed by experts and stakeholders, including consumer representatives, before publication. The PPPs are developed in compliance with the Council of Medical Specialty Societies' Code for Interactions with Companies. The Academy has Relationship with Industry Procedures (available at <http://one.aao.org/CE/PracticeGuidelines/PPP.aspx>) to comply with the Code.

Appendix 2 contains the International Statistical Classification of Diseases and Related Health Problems (ICD) codes for the disease entities that this PPP covers. The intended users of the Bacterial Keratitis PPP are ophthalmologists.



## METHODS AND KEY TO RATINGS

Preferred Practice Pattern® guidelines should be clinically relevant and specific enough to provide useful information to practitioners. Where evidence exists to support a recommendation for care, the recommendation should be given an explicit rating that shows the strength of evidence. To accomplish these aims, methods from the Scottish Intercollegiate Guideline Network<sup>1</sup> (SIGN) and the Grading of Recommendations Assessment, Development and Evaluation<sup>2</sup> (GRADE) group are used. GRADE is a systematic approach to grading the strength of the total body of evidence that is available to support recommendations on a specific clinical management issue. Organizations that have adopted GRADE include SIGN, the World Health Organization, the Agency for Healthcare Research and Policy, and the American College of Physicians.<sup>3</sup>

- ◆ All studies used to form a recommendation for care are graded for strength of evidence individually, and that grade is listed with the study citation.
- ◆ To rate individual studies, a scale based on SIGN<sup>1</sup> is used. The definitions and levels of evidence to rate individual studies are as follows:

I++	High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias
I+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
I-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
II++	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
II+	Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
II-	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
III	Nonanalytic studies (e.g., case reports, case series)

- ◆ Recommendations for care are formed based on the body of the evidence. The body of evidence quality ratings are defined by GRADE<sup>2</sup> as follows:

Good quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Insufficient quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate Any estimate of effect is very uncertain

- ◆ Key recommendations for care are defined by GRADE<sup>2</sup> as follows:

Strong recommendation	Used when the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not
Discretionary recommendation	Used when the trade-offs are less certain—either because of low-quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced

- ◆ The Highlighted Findings and Recommendations for Care section lists points determined by the PPP Panel to be of particular importance to vision and quality of life outcomes.
- ◆ All recommendations for care in this PPP were rated using the system described above. To locate ratings for specific recommendations, see Appendix 3 for additional information.
- ◆ Literature searches to update the PPP were undertaken in June 2012 and January 2013 in PubMed and the Cochrane Library. Complete details of the literature search are available at [www.aao.org/ppp](http://www.aao.org/ppp).



## HIGHLIGHTED FINDINGS AND RECOMMENDATIONS FOR CARE

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The majority of community-acquired cases of bacterial keratitis resolve with empiric therapy and are managed without smears or cultures.<sup>4,5</sup> Smears and cultures are indicated, however, in cases that involve a corneal infiltrate that is central, large and extends to the middle to deep stroma; that are chronic in nature or unresponsive to broad spectrum antibiotic therapy; or that have atypical clinical features suggestive of fungal, amoebic, or mycobacterial keratitis.<sup>6,7</sup>

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Patching the eye of a contact-lens-wearing patient with a corneal abrasion is not advised because of the increased risk of bacterial keratitis.

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The use of a cycloplegic agent is an often overlooked adjunctive treatment and may decrease pain as well as synechia formation in bacterial keratitis. It is indicated when substantial anterior chamber inflammation is present.

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Corticosteroids may be considered after 48 hours when the causative organism is known. Corticosteroids should be avoided in cases of infection involving *Acanthamoeba*, *Nocardia*, and fungus.

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Due to the increasing resistance of methicillin-resistant *Staphylococcus aureas* (MRSA) to topical fluoroquinolones, combination therapy including vancomycin should be considered in a setting in which this etiological organism is likely to occur.

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Topical antibiotics should be prescribed to prevent ulceration in patients presenting to the emergency room within 24 hours of a corneal abrasion.

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# INTRODUCTION

## DISEASE DEFINITION

Bacterial keratitis is an infection of the cornea caused by bacteria.

## PATIENT POPULATION

The patient population includes individuals of all ages who present with symptoms and signs suggestive of bacterial keratitis such as pain, redness, blurred vision, discharge, corneal infiltrates, ulcerations, and anterior chamber inflammation.

## CLINICAL OBJECTIVES

- ◆ Recognize and reduce risk factors that predispose patients to bacterial infection of the cornea
- ◆ Establish the diagnosis of bacterial keratitis and differentiate it from other causes of keratitis
- ◆ Utilize appropriate diagnostic tests
- ◆ Select appropriate therapy
- ◆ Relieve pain
- ◆ Establish appropriate follow-up
- ◆ Prevent complications such as medication toxicity, intraocular infection, cataract, corneal perforation, and loss of vision due to corneal scarring
- ◆ Educate patients and their families about treatment and ways to reduce risk factors in the future



# BACKGROUND

## PREVALENCE

It is estimated that 30,000 cases of microbial keratitis (including bacteria, fungus, and *Acanthamoeba*) occur annually in the United States,<sup>8</sup> with an increasing incidence in recent years.<sup>9</sup> Bacterial keratitis rarely occurs in the normal eye because of the human cornea's natural resistance to infection. However, predisposing factors, including contact lens wear, trauma, corneal surgery, ocular surface disease (e.g., tear deficiencies and corneal abnormalities), systemic diseases,<sup>10</sup> and immunosuppression, may alter the defense mechanisms of the ocular surface and permit bacteria to invade the cornea (see Risk Factors).

Causes of bacterial keratitis in the United States are listed in Table 1. Although the most common pathogenic organisms identified in bacterial keratitis include *Staphylococci* and gram-negative rods (*Pseudomonas* species), studies differ on the epidemiology of bacterial keratitis. A large review of insurance data showed that the most common cause of bacterial keratitis in a diverse population was *Staphylococcus aureus* and that contact lens wear, trauma, and HIV were the most common associated medical conditions.<sup>11</sup> In bacterial keratitis associated with the use of contact lenses, *Pseudomonas* has been identified as the most frequent etiologic agent, accounting for up to one-third of cases.<sup>12,13</sup> However, a review from Florida found that *Serratia marcescens* was isolated as frequently as *Pseudomonas aeruginosa* in contact-lens-associated keratitis<sup>14</sup> and a review from Melbourne, Australia, found that *Pseudomonas* was isolated in only 7% of contact-lens-associated keratitis.<sup>15</sup>

One study found that 78.2% of cultures grew a gram-positive organism, whereas 20.2% grew a gram-negative organism. Of the gram-positive organisms, 40.8% were coagulase-negative *Staphylococci* and 11.5% were *Staphylococcus aureus*. A review of the gram-negative organisms revealed *Moraxella* (8.0%) and *Pseudomonas aeruginosa* (3.4%) as the most common organisms.<sup>16</sup> Another 10-year review revealed that the most common isolated bacteria were *Staphylococci* (40.1%), followed by *Pseudomonas* species (28.5%), other gram-negative species (17.2%), *Streptococci* (7.1%), and *Corynebacteria* (6.0%).<sup>17</sup> Two retrospective analyses from the United Kingdom and Italy showed that contact lens use was the most common risk factor for bacterial keratitis. Gram-positive

## Bacterial Keratitis PPP: Risk Factors

organisms were the most common organisms in the UK study, whereas *Pseudomonas* was the most commonly identified organism in the study from Italy.<sup>18,19</sup> A Brazilian study of the elderly also identified gram-positive organisms as the most common pathogen (75.5%) and *Pseudomonas* as the most common among the gram-negative pathogens.<sup>20</sup> A preponderance of gram-positive organisms (63.4%) versus gram-negative organisms (36.6%) was also identified in another study where *Staphylococcus epidermidis* and *Corynebacterium* were the most commonly identified gram-positive organisms. In this study, *Pseudomonas* species were the most common gram-negative organisms.<sup>21</sup> Lastly, mixed microbial keratitis can occur. The most common causative organisms are *Staphylococcus epidermidis* and *Fusarium* species. In these patients, the most common etiology is trauma.<sup>22</sup>

TABLE 1 COMMON CAUSES OF BACTERIAL KERATITIS IN THE UNITED STATES

Class/Organism	Common Isolates*	Cases (%)
<b>Gram-Positive Isolates</b>		<b>29–75.1</b>
Gram-positive cocci	<i>Staphylococcus aureus</i>	4–27.6
	MRSA	1.3
	Coagulase negative <i>Staphylococci</i>	1–45.5
	MRSE	43.1
	<i>Streptococcus pneumoniae</i>	0–3.4
	<i>Streptococcus viridans</i> group	1–6.9
Gram-positive bacilli	<i>Propionibacterium</i> species	4–7
	<i>Mycobacterium</i> species	3
<b>Gram-Negative Isolates</b>		<b>31–50</b>
Gram-negative bacilli	<i>Pseudomonas aeruginosa</i>	3–33
	<i>Serratia marcescens</i>	3–13.5
	<i>Proteus mirabilis</i>	3.4–4
	<i>Moraxella</i> species and related species	1–20.7
	Enteric and other gram-negative bacilli	1–10
Gram-negative coccobacillary organisms	<i>Haemophilus influenzae</i> , other <i>Haemophilus</i> species	2.5

MRSA = methicillin-resistant *Staphylococcus aureus*; MRSE = methicillin-resistant *Staphylococcus epidermidis*

\* Regional differences may affect the order and percentage of pathogens.

Ranges are from the following sources:

Afshari NA, Ma JJK, Duncan SM, et al. Trends in resistance to ciprofloxacin, cefazolin, and gentamicin in the treatment of bacterial keratitis. *J Ocul Pharmacol Ther* 2008;24:217–23.

Alexandrakis G, Alfonso EC, Miller D. Shifting trends in bacterial keratitis in South Florida and emerging resistance to fluoroquinolones. *Ophthalmology* 2000;107:1497–1502.

Lichtinger A, Yeung SN, Kim P, et al. Shifting trends in bacterial keratitis in Toronto: an 11-year review. *Ophthalmology* 2012;119:1785–90.

Mah-Sadorra JH, Yavuz GA, Najjar DM, et al. Trends in contact lens-related corneal ulcers. *Cornea* 2005;24:51–8.

Marangon FB, Miller D, Alfonso EC. Impact of prior therapy on the recovery and frequency of corneal pathogens. *Cornea* 2004;23:158–64.

Yildiz EH, Airiani S, Hammersmith KM, et al. Trends in contact lens-related corneal ulcers at a tertiary referral center. *Cornea* 2012;31:1097–102.

## RISK FACTORS

Risk factors that predispose patients to bacterial keratitis can be divided into four categories.

### Extrinsic Factors

- ◆ Use of contact lenses, especially when associated with the following:
  - ◆ Overnight wear<sup>10,23-35</sup>
  - ◆ Overnight orthokeratology<sup>36-41</sup>
  - ◆ Misuse (overwear)
  - ◆ Inadequate disinfection of contact lenses
  - ◆ Contamination of the contact lens storage case<sup>34</sup>

- ◆ Ineffective or contaminated contact lens solution
- ◆ Inappropriate disposal of used contact lenses
- ◆ Storage or rinsing in tap water
- ◆ Sharing of decorative lenses
- ◆ Trauma, including chemical and thermal injuries, foreign bodies, and local irradiation
- ◆ Previous ocular and eyelid surgery, especially corneal surgery, and including refractive surgery and penetrating keratoplasty
- ◆ Loose corneal sutures<sup>42</sup>
- ◆ Medication-related factors (e.g., contaminated ocular medications, topical nonsteroidal anti-inflammatory drugs (NSAIDs), anesthetics, corticosteroids, preservatives, glaucoma medications)
- ◆ Immunosuppression (topical and systemic)
- ◆ Factitious disease, including anesthetic abuse
- ◆ Substance abuse (crack cocaine)

### **Ocular Surface Disease**

- ◆ Tear-film deficiencies
- ◆ Abnormalities of the eyelid anatomy and function (including exposure)
- ◆ Misdirection of eyelashes
- ◆ Adjacent infection/inflammation (including gonococcal conjunctivitis, blepharitis, canaliculitis, dacryocystitis)

### **Corneal Epithelial Abnormalities**

- ◆ Neurotrophic keratopathy (e.g., trigeminal neuropathy)
- ◆ Disorders predisposing to recurrent erosion of the cornea
- ◆ Corneal abrasion or epithelial defect
- ◆ Viral keratitis (herpes simplex virus [HSV] or varicella zoster virus [VZV] keratitis)
- ◆ Corneal epithelial edema, especially bullous keratopathy

### **Systemic Conditions**

- ◆ Diabetes mellitus
- ◆ Debilitating illness, especially malnourishment and/or respirator dependence
- ◆ Connective tissue disease
- ◆ Dermatological/mucous membrane disorders (e.g., Stevens-Johnson syndrome, ocular mucous membrane pemphigoid)
- ◆ Immunocompromised status
- ◆ Atopic dermatitis/blepharoconjunctivitis
- ◆ Gonococcal infection with conjunctivitis
- ◆ Vitamin A deficiency
- ◆ Acoustic neuroma or neurological surgery causing damage to the Vth and/or VIIth cranial nerves
- ◆ Graft-versus-host disease
- ◆ Diphtheria
- ◆ Chronic assisted ventilation<sup>43</sup>

## **NATURAL HISTORY**

While some forms of bacterial keratitis may not result in visual loss, many are associated with subsequent loss of vision due to corneal scarring or topographic irregularity. Untreated or severe bacterial keratitis may result in corneal perforation and has the potential to develop into endophthalmitis and result in loss of the eye. Because this process of destruction can take place rapidly (within 24 hours when the infection is caused by a virulent organism), optimal management requires rapid recognition, timely institution of therapy, and appropriate follow-up. Bacterial keratitis can occur in any part of the cornea, but infections involving the central or paracentral cornea are of

**Bacterial Keratitis PPP:  
Care Process**

paramount importance. Scarring in this location has the potential to cause substantial visual loss, even if the infecting organism is successfully eradicated. Although some bacteria (e.g., *Neisseria gonorrhoeae*) can invade an intact corneal epithelium, most cases of bacterial keratitis develop at the site of an abnormality or defect in the corneal surface.

The rate of disease progression is dependent on the virulence of the infecting organism and on host factors (see Risk Factors, and Prevention and Early Detection). For example, highly virulent organisms such as *Pseudomonas*, *Streptococcus pneumoniae*, or *Neisseria gonorrhoeae* cause rapid tissue destruction, whereas other organisms such as nontuberculous mycobacteria and *Streptococcus viridans* species are usually associated with a more indolent course. Some bacteria that are considered to be normal conjunctival flora (e.g., *Corynebacterium*) may become opportunistic pathogens in the compromised eye.



## CARE PROCESS

### PATIENT OUTCOME CRITERIA

Outcome criteria for treating bacterial keratitis include the following:

- ◆ Reducing pain
- ◆ Resolving discharge as well as corneal and anterior chamber inflammation
- ◆ Resolving epithelial defect
- ◆ Restoring corneal integrity and minimizing scarring and vascularization
- ◆ Restoring visual function

### DIAGNOSIS

Evaluation of the patient with presumed bacterial keratitis includes those features of the comprehensive medical eye evaluation<sup>44,45</sup> specifically relevant to bacterial keratitis, as listed below.

#### History

Obtaining a detailed history is important in evaluating patients with bacterial keratitis. Pertinent information includes the following:

- ◆ Ocular symptoms (e.g., degree of pain, redness, discharge, blurred vision, photophobia, duration of symptoms, circumstances surrounding the onset of symptoms)
- ◆ Contact lens history<sup>28,46</sup> (e.g., wearing schedule, overnight wear, type of contact lens, contact lens solution, contact lens hygiene protocol, tap-water rinsing of contact lenses, swimming, using a hot tub, or showering while wearing contact lenses)
- ◆ Review of other ocular history, including risk factors such as HSV keratitis, VZV keratitis, previous bacterial keratitis, trauma, dry eye, and previous ocular surgery, including refractive surgery
- ◆ Review of other medical problems including immune status, systemic medications, and history of methicillin-resistant *Staphylococcus aureus* (MRSA) or other multidrug resistant infections
- ◆ Current and recently used ocular medications
- ◆ Medication allergies

#### Physical Examination

The physical examination includes measurement of visual acuity, an external examination, and slit-lamp biomicroscopy.

##### Visual Acuity

In many cases, patient discomfort, tearing, and inflammation will compromise visual acuity. It is useful, however, to document baseline visual acuity and to ascertain that it is consistent with the anterior segment examination.

## **External Examination**

An external examination should be performed with particular attention to the following:

- ◆ General appearance of the patient, including skin conditions
- ◆ Facial examination
- ◆ Globe position
- ◆ Eyelids and eyelid closure
- ◆ Conjunctiva
- ◆ Nasolacrimal apparatus
- ◆ Corneal sensation

## **Slit-Lamp Biomicroscopy**

Clinical features suggestive of bacterial keratitis include suppurative stromal infiltrate (particularly those greater than 1 mm in size) with indistinct edges, edema, and white cell infiltration in surrounding stroma. An epithelial defect is typically present. An anterior chamber reaction is often seen.

Slit-lamp biomicroscopy should include evaluation of the following:

- ◆ Eyelid margins
  - ◆ Inflammation
  - ◆ Ulceration
  - ◆ Eyelash abnormalities, including trichiasis/distichiasis
  - ◆ Irregularities
  - ◆ Lacrimal punctal anomalies
  - ◆ Ectropion/entropion
- ◆ Conjunctiva
  - ◆ Discharge
  - ◆ Inflammation
  - ◆ Morphologic alterations (e.g., follicles, papillae, cicatrization, keratinization, membrane, pseudomembrane, ulceration, prior surgery)
  - ◆ Ischemia
  - ◆ Foreign body
  - ◆ Filtering bleb, tube erosion
- ◆ Sclera
  - ◆ Inflammation (e.g., infectious versus immune)
  - ◆ Ulceration
  - ◆ Thinning
  - ◆ Nodule
  - ◆ Ischemia
- ◆ Cornea
  - ◆ Epithelium, including defects and punctate keratopathy, edema
  - ◆ Stroma, including ulceration, thinning, perforation, and infiltrate (location [central, peripheral, perineural, surgical, or traumatic wound], density, size, shape [ring], number [satellite], depth, character of infiltrate margin [suppuration, necrosis, feathery, soft, crystalline], color), edema
  - ◆ Endothelium
  - ◆ Foreign body, including sutures<sup>47</sup>
  - ◆ Signs of corneal dystrophies (e.g., epithelial basement membrane dystrophy)
  - ◆ Previous corneal inflammation (thinning, scarring, or neovascularization)
  - ◆ Signs of previous corneal or refractive surgery

## Bacterial Keratitis PPP: Diagnostic Tests

Fluorescein (or, occasionally, rose bengal staining) of the cornea is usually performed and may provide additional information about other factors, such as the presence of dendrites, pseudodendrites, loose or exposed sutures, foreign body, and any epithelial defect.

- ◆ Anterior chamber for depth and the presence of inflammation, including cell and flare, hypopyon, fibrin, hyphema
- ◆ Anterior vitreous for the presence of inflammation
- ◆ Contralateral eye for clues to etiology as well as possible similar underlying pathology

## Diagnostic Tests

### Cultures and Smears

The majority of community-acquired cases of bacterial keratitis resolve with empiric therapy and are managed without smears or cultures.<sup>4,5</sup> Smears and cultures are indicated, however, in cases that involve a corneal infiltrate that is central, large, and extends to the middle to deep stroma; that are chronic in nature or unresponsive to broad-spectrum antibiotic therapy; or that have atypical clinical features suggestive of fungal, amoebic, or mycobacterial keratitis.<sup>6,7</sup> Smears and cultures are often helpful for eyes that have an unusual history (e.g., if there has been trauma with vegetable matter or if the patient wore contact lenses while in a hot tub). Specialized studies may be indicated to identify atypical organisms. The hypopyon that occurs in eyes with bacterial keratitis is usually sterile, and aqueous or vitreous taps should not be performed unless there is a high suspicion of microbial endophthalmitis, such as following an intraocular surgery, perforating trauma, or sepsis. Before initiating antimicrobial therapy, cultures are indicated in sight-threatening or severe keratitis of suspected microbial origin. See Table 2 for additional details.

TABLE 2 RECOMMENDATIONS FOR DIAGNOSTIC TESTS: VITAL STAINS AND CULTURE

	Culture	Vital Stain Dyes
Small, peripheral, no stromal melting	Culture optional	Gram, Giemsa stain optional
Large, central, stromal melting, chronic, atypical appearance, sight threatening	Culture	Gram, Giemsa stain

A culture is a means of identifying the causative organism(s) and the only means of determining sensitivity to antibiotics. Cultures are helpful to guide modification of therapy in patients with a poor clinical response to treatment and to decrease toxicity by eliminating unnecessary medications. Microbial pathogens may be categorized by examining stained smears of corneal scrapings<sup>4</sup>; this may increase yield of identification of the pathogen, especially if the patient is on antibacterial therapy. The material for smear is applied to clean glass microscope slides in an even, thin layer (see Appendix 4 for specific diagnostic stains). Polymerase chain reaction and immunodiagnostic techniques may be useful,<sup>48-51</sup> but they are not widely available currently in the office setting.

Corneal material is obtained by instilling a topical anesthetic agent (tetracaine should be avoided due to antimicrobial effect) and using a heat-sterilized platinum (Kimura) spatula, blade, jeweler's forceps, or other similar sterile instrument to obtain scrapings of material from the advancing borders of the infected area of the cornea. Culture yield may be improved by avoiding anesthetics with preservatives.<sup>52</sup> Obtaining only purulent material usually results in inadequate yield. A thiol or thioglycollate broth-moistened dacron/calcium alginate or sterile cotton swab may also be used to obtain material. This is most easily performed with slit-lamp biomicroscope magnification. If using transport media, similar methods of obtaining corneal material are used. The material is then transferred to the cotton or calcium alginate swab, which is then placed in the tube.

Corneal scrapings for culture should be inoculated directly onto appropriate culture media to maximize culture yield (see Appendix 5).<sup>53</sup> If this is not feasible, specimens should be placed in transport media.<sup>54,55</sup> In either case, cultures should be immediately incubated or taken promptly to the laboratory. Cultures of contact lenses, the lens case, and contact lens solution may provide additional information to guide therapy.

It may be helpful to obtain cultures from eyes treated empirically that were not first cultured and in which the clinical response is poor; however, a delay in pathogen recovery may occur, so keeping cultures for longer may be helpful.<sup>56-58</sup> If the cultures are negative, the ophthalmologist may consider stopping antibiotic treatment for 12 to 24 hours and then reculturing.

### **Corneal Biopsy and Deep Stromal Culture Techniques**

Corneal biopsy may be indicated if the response to treatment is poor, or if repeated cultures have been negative and the clinical picture continues to strongly suggest an infectious process. It may also be indicated if the infiltrate is located in the mid or deep stroma with overlying uninvolved tissue.<sup>59,60</sup> With a cooperative patient, corneal biopsy may be performed while at the slit-lamp biomicroscope or operating microscope. Using topical anesthesia, a small trephine (2 to 3 mm) or blade is used to excise a small piece of stromal tissue that is large enough to allow bisection so that one portion can be sent for culture and the other for histopathology.<sup>61</sup> A femtosecond laser can also be used to excise a lamellar disc of tissue, although this is a more costly alternative. The biopsy specimen should be delivered to the laboratory in a timely fashion.

An option for a deep corneal abscess may be to use a suture that can be passed through the abscess without disturbing the overlying intact corneal epithelium and stroma. A 7-0 or 8-0 vicryl or silk suture can be passed through the abscess. The pathogen may attach to the fibers of the suture, and the suture can then be cultured. Another option in cases of a deep corneal abscess with overlying clear cornea is to take the biopsy from below a lamellar flap. An additional set of smears and cultures can be obtained from the deep stroma after the biopsy is performed.

### **Corneal Imaging**

Scanning laser confocal microscopy is used to image the various levels of the cornea from epithelium through stroma to the endothelium in vivo. Initially, confocal microscopy had been used to examine endothelial cells to assist clinicians in the management of endothelial conditions, as well as ex vivo to examine the quality of potential corneal donor tissue. With the recent advances in confocal technology to enhance the resolution and microscopic power, its use as a diagnostic tool has broadened. Confocal technology has been shown to be of some use in the diagnosis of infectious keratitis, including bacterial, fungal, and, most notably, parasitic (i.e., *Acanthamoeba*).<sup>62-65</sup> Optical coherence tomography may also be helpful in determining depth of involvement.

### **Differential Diagnosis**

The differential diagnosis includes infectious and noninfectious causes of infiltrates. Nonbacterial corneal pathogens, including fungi (both yeast and mold), parasites (including protozoa such as *Acanthamoeba*), and nematodes (such as *Onchocerca*) may cause infiltrative keratitis. An increase in the incidence of *Acanthamoeba* and fungal keratitis since 2004 has been noted.<sup>9,66-75</sup> Viruses including HSV, VZV, and Epstein-Barr virus produce immunologically mediated corneal infiltrates that may resemble a bacterial, fungal, or acanthamoebal keratitis. Eyes with viral keratitis are also prone to microbial superinfection, but this generally occurs in patients with larger epithelial defects, more severe viral disease, or older age. When in doubt, it is often best initially to manage these cases as infected. Viruses can also cause a true suppurative keratitis without superinfection, as in necrotizing stromal disease.

Noninfectious stromal infiltration may be associated with contact lens wear (particularly extended-wear contact lenses) or antigens from local and systemic bacterial infections. Systemic diseases, such as connective tissue disease (e.g., rheumatoid arthritis, systemic

## **Bacterial Keratitis PPP: Management**

lupus erythematosus), vasculitic disorders (e.g., polyarteritis nodosa, granulomatosis with polyangiitis), and other inflammatory disorders such as sarcoidosis may produce infiltrative keratitis. Other causes include dermatologic disorders (e.g., severe ocular rosacea) and allergic conditions (e.g., vernal keratoconjunctivitis and atopic keratoconjunctivitis). Atopy is also a risk factor for HSV ocular disease.<sup>76</sup> Corneal trauma, including chemical and thermal injury, and corneal foreign bodies, including exposed or loose sutures, may also lead to infiltrative keratitis, which may be infectious or noninfectious.

## **MANAGEMENT**

### **Prevention**

Avoiding or correcting predisposing factors may reduce the risk of bacterial keratitis. For example, screening patients for predisposing factors and educating them about the risks of overnight wear of contact lenses<sup>32,41,46</sup> and proper contact lens care<sup>28,77</sup> may reduce the incidence of bacterial keratitis in those who wear contact lenses. (See Appendix 6 for recommendations for contact lens care.) For those patients who require a bandage contact lens for therapy for an ocular disease, many clinicians prefer to use topical antibiotic prophylaxis. Although studies have not been done to test or prove an optimal dose, nor are any topical antibiotics approved for bacterial keratitis prophylaxis, a recommended antibiotic dose is at least twice a day.<sup>78,79</sup> Some clinicians prefer not to use antibiotics in this setting because of the risks of bacterial resistance, drug or preservative toxicity, and cost. Most ocular trauma can be avoided by using protective eyewear for sports and other high-risk activities.<sup>80</sup>

Opinions vary on the use of a topical antibiotic when a bandage contact lens is employed and on how frequently such lenses should be changed. Patients should be informed of the risk of infectious keratitis when wearing a bandage contact lens, and of the need to contact their treating ophthalmologist if redness, pain, or increased photophobia develops. They should also be informed that they are still at risk for infection, despite the use of antibiotics. Ideally, bandage contact lenses should be used for a finite treatment period; however, in many cases, their use may be protracted. In this situation, periodic exchange of the contact lens is advised. Regular follow-up is necessary under these circumstances to reassess the contact lens, to look for evidence of a change in the patient's ocular status, and to re-emphasize the need for vigilance on the part of the patient.

Early detection and appropriate treatment are important to minimize permanent visual loss.<sup>10,81</sup> Patients with risk factors predisposing them to bacterial keratitis should be educated about their relative risk, be acquainted with the signs and symptoms of infection, and be informed that they should consult an ophthalmologist promptly if they experience such warning signs or symptoms. Ocular surface disease such as corneal epithelial defects, severe tear deficiency, or lagophthalmos should be treated. Prophylactic antibiotics can be considered for patients with chronic epithelial defects; however, the routine use of prophylactic topical antibiotics in this setting is controversial, because their efficacy has not been established and chronic use may promote growth of resistant organisms. Prophylactic topical antibiotics following corneal abrasion may prevent ulceration when treatment is started within 24 hours of the abrasion,<sup>82</sup> and for those contact-lens-wearing patients who develop a traumatic abrasion, it is advisable to avoid pressure patching, even if the patch might increase the patient's comfort.

### **Treatment**

#### **Initial Treatment**

Topical antibiotic eye drops are capable of achieving high tissue levels and are the preferred method of treatment in most cases.<sup>7</sup> Ocular ointments may be useful at bedtime in less severe cases and also may be useful for adjunctive therapy.

Subconjunctival antibiotics may be helpful where there is imminent scleral spread or perforation or in cases where adherence to the treatment regimen is questionable. Systemic therapy may be useful in cases of scleral or intraocular extension of infection or systemic



infection such as gonorrhea. Collagen shields or soft contact lenses soaked in antibiotics are sometimes used and may enhance drug delivery. They may also be useful in cases where there is an anticipated delay in initiating appropriate therapy, but these modalities have not been fully evaluated in terms of efficacy and the potential risk for inducing drug toxicity.<sup>83-85</sup> In addition, collagen shields and soft contact lenses can become displaced or lost, leading to unrecognized interruption of drug delivery. In selected cases, the choice of initial treatment may be guided by the results obtained from smears.

Topical broad-spectrum antibiotics are used initially in the empiric treatment of bacterial keratitis.<sup>7</sup> (See Table 3 for recommendations about antibiotic therapy.) For central or severe keratitis (e.g., deep stromal involvement or an infiltrate larger than 2 mm with extensive suppuration), a loading dose (e.g., every 5 to 15 minutes for the first 30 to 60 minutes), followed by frequent applications (e.g., every 30 minutes to 1 hour around the clock), is recommended. For less severe keratitis, a regimen with less frequent dosing is appropriate. Cycloplegic agents may be used to decrease synechia formation and to decrease pain in bacterial keratitis, and are indicated when substantial anterior chamber inflammation is present.

**TABLE 3 ANTIBIOTIC THERAPY FOR BACTERIAL KERATITIS**

Organism	Antibiotic	Topical Concentration	Subconjunctival Dose
No organism identified or multiple types of organisms	Cefazolin	50 mg/ml	100 mg in 0.5 ml
	with Tobramycin or gentamicin	9–14 mg/ml	20 mg in 0.5 ml
	or Fluoroquinolones*	Various†	
Gram-positive cocci	Cefazolin	50 mg/ml	100 mg in 0.5 ml
	Vancomycin‡	15–50 mg/ml	25 mg in 0.5 ml
	Bacitracin‡	10,000 IU	
	Fluoroquinolones*	Various†	
Gram-negative rods	Tobramycin or gentamicin	9–14 mg/ml	20 mg in 0.5 ml
	Ceftazidime	50 mg/ml	100 mg in 0.5 ml
	Fluoroquinolones	Various†	
Gram-negative cocci§	Ceftriaxone	50 mg/ml	100 mg in 0.5 ml
	Ceftazidime	50 mg/ml	100 mg in 0.5 ml
	Fluoroquinolones	Various†	
Nontuberculous mycobacteria	Amikacin	20–40 mg/ml	20 mg in 0.5 ml
	Clarithromycin	10 mg/ml	
	Azithromycin	10 mg/ml	
	Fluoroquinolones	Various†	
Nocardia	Sulfacetamide	100 mg/ml	
	Amikacin	20–40 mg/ml	20 mg in 0.5 ml
	Trimethoprim/sulfamethoxazole:		
	trimethoprim	16 mg/ml	
	sulfamethoxazole	80 mg/ml	

Adapted with permission from the American Academy of Ophthalmology Basic and Clinical Science Course Subcommittee. Basic Clinical and Science Course. External Disease and Cornea: Section 8, 2013-2014. Table 5-5. San Francisco: American Academy of Ophthalmology, 2013.

\* Fewer gram-positive cocci are resistant to gatifloxacin and moxifloxacin than other fluoroquinolones.

† Besifloxacin 6 mg/ml; ciprofloxacin 3 mg/ml; gatifloxacin 3 mg/ml; levofloxacin 15 mg/ml; moxifloxacin 5 mg/ml; ofloxacin 3 mg/ml, all commercially available at these concentrations.

‡ For resistant *Enterococcus* and *Staphylococcus* species and penicillin allergy. Vancomycin and bacitracin have no gram-negative activity and should not be used as a single agent in empirically treating bacterial keratitis.

§ Systemic therapy is necessary for suspected gonococcal infection.

|| Data from Chandra NS, Torres MF, Winthrop KL. Cluster of *Mycobacterium chelonae* keratitis cases following laser in-situ keratomileusis. Am J Ophthalmol 2001;132:819-30.

## **Bacterial Keratitis PPP: Treatment**

Single-drug therapy using a fluoroquinolone has been shown to be as effective as combination therapy utilizing antibiotics that are fortified by increasing their concentration over commercially available topical antibiotics.<sup>86-88</sup> Ciprofloxacin 0.3%, ofloxacin 0.3%, and levofloxacin 1.5% have been approved by the Food and Drug Administration (FDA) for the treatment of bacterial keratitis.<sup>89-91</sup> Compared with ofloxacin 0.3%, levofloxacin 1.5% demonstrated equal efficacy in the endpoints of complete re-epithelialization and no progression of infiltrate for two consecutive visits.<sup>71</sup> Some pathogens (e.g., *Streptococci*, anaerobes) reportedly have variable susceptibility to fluoroquinolones,<sup>87,92-96</sup> and the prevalence of resistance to the fluoroquinolones appears to be increasing.<sup>14,93,97,98</sup> Gatifloxacin and moxifloxacin have been reported to have better coverage of gram-positive pathogens than earlier generation fluoroquinolones in head-to-head in vitro studies.<sup>99</sup> Although widely used, the fourth-generation fluoroquinolones are not FDA-approved for the treatment of bacterial keratitis. However, in randomized controlled trials, both moxifloxacin and gatifloxacin performed at least as well as standard therapy, fortified cefazolin/tobramycin combination therapy, and potentially better than an earlier generation fluoroquinolone, ciprofloxacin.<sup>86,100-103</sup>

Besifloxacin 0.6% is a topical fluoroquinolone that was approved by the FDA in 2009 for bacterial conjunctivitis, and has a potency against ocular pathogenic bacteria that is similar to the fourth-generation agents.<sup>104</sup> Several industry-sponsored in vitro and in vivo rabbit studies have shown potential utility in the management of acute bacterial keratitis; however, there are no case reports or clinical trials in the peer-reviewed literature showing efficacy for this off-label indication to date.<sup>105-107</sup> Although there have been some concerns of increased risk of corneal perforation with fluoroquinolones in the treatment of severe bacterial keratitis compared with traditional fortified topical antibiotics (cefazolin and tobramycin),<sup>88,108</sup> these reports are retrospective, not from randomized controlled trials, and will need confirmation in future studies.

Combination fortified-antibiotic therapy is an alternative to consider for severe infection and for eyes unresponsive to initial treatment.<sup>88,109</sup> This should be performed by a compounding pharmacy that is a member of the Pharmacy Compounding Accreditation Board.<sup>110</sup> Treatment with more than one agent may be necessary for nontuberculous mycobacteria; infection with this pathogen has been reported in association with LASIK.<sup>111</sup> Methicillin-resistant *Staphylococcus aureus* has been isolated with increasing frequency from patients with bacterial keratitis<sup>112</sup> and has been reported following keratorefractive surgery.<sup>113</sup> Fluoroquinolones are generally poorly effective against MRSA ocular isolates.<sup>58,114</sup> Methicillin-resistant *Staphylococcus aureus* isolates generally are sensitive to vancomycin. (See Appendix 7 for instructions for preparing fortified topical antibiotics.) In cases of severe ulcer, more complete coverage with combination therapy can be considered.

Systemic antibiotics are rarely needed, but they may be considered in severe cases where the infectious process has extended to adjacent tissues (e.g., the sclera) or when there is impending or frank perforation of the cornea. Systemic therapy is necessary in cases of gonococcal keratitis.<sup>115</sup>

Frequency of re-evaluation of the patient with bacterial keratitis depends on the extent of disease, but severe cases (e.g., deep stromal involvement or larger than 2 mm with extensive suppuration) initially should be followed at least daily until stabilization or clinical improvement is documented.

### **Corticosteroid Therapy**

Topical corticosteroid therapy may have a beneficial role in treating some cases of infectious keratitis. The potential advantage is the probable suppression of inflammation, which may reduce subsequent corneal scarring and associated visual loss. Potential disadvantages include recrudescence of infection, local immunosuppression, inhibition of collagen synthesis predisposing to corneal melting, and increased intraocular pressure (IOP). There is no conclusive scientific evidence indicating that corticosteroids alter clinical outcome.<sup>116-118</sup> A large, multicenter, international prospective study determined no benefit of concurrent topical corticosteroid therapy with prednisolone phosphate 1% in

conjunction with broad-spectrum topical antibiotic. However, this study also did not find any increase in adverse events with corticosteroid use in bacterial keratitis therapy. In a subgroup analysis, the study did find potential benefit of corticosteroids when used in *Pseudomonas* keratitis and in more severe cases of bacterial keratitis.<sup>119</sup> The same trial found that treatment of *Nocardia* keratitis with corticosteroids resulted in poorer visual outcomes.<sup>120</sup>

Despite the risks involved, many experts believe that the judicious use of topical corticosteroids can reduce morbidity.<sup>119,121</sup> Patients being treated with ocular topical corticosteroids at the time of presentation of suspected bacterial keratitis should have their corticosteroid regimen reduced or eliminated until the infection has been controlled. Inflammation and symptoms (e.g., decreased vision, photophobia, lacrimation, injection, and hyperemia) may temporarily increase as corticosteroids are reduced due to the lack of inhibiting the local immune response. The increase in inflammation may not be due to worsening of the infection and, therefore, patients should be advised of possible increased symptoms. Chronic topical immunotherapy, such as use of corticosteroids, increases the risk of infectious crystalline keratopathy, which often requires discontinuation of the topical immunotherapy to achieve successful treatment. Typically, these patients complain of only mild symptoms, such as blurred vision, and have a relatively asymptomatic course prior to diagnosis, most likely due to the topical immunotherapy and sequestration of organisms in biofilm.

The objective of topical corticosteroid therapy is to use the minimum amount required to achieve control of inflammation. Successful treatment requires optimal timing, careful dose regulation, use of adequate concomitant antibacterial medication, and close follow-up. Optimal use of corticosteroid and antibiotic is largely determined by the clinician's experience and the individual patient's response to therapy. A conservative approach would avoid prescribing corticosteroid treatment for presumed bacterial ulcers until the organism has been identified. If the ulcer is associated with *Acanthamoeba*, *Nocardia*, fungus, or HSV, outcomes of corticosteroid therapy are likely to be poor; for most other bacteria, the risk is low and, in cases, may be beneficial. Although the use of corticosteroids in the initial treatment of corneal ulcers was found to be a risk factor for requiring a penetrating keratoplasty in a small, retrospective study that included fungal keratitis,<sup>122</sup> a more recent clinical trial has shown that corticosteroids may not have this direct correlation.<sup>119</sup> Therefore, judicious use with close follow-up would be prudent.<sup>119,122</sup>

In cases where the corneal infiltrate compromises the pupil, topical corticosteroid therapy may be added to the regimen following at least 2 to 3 days of progressive improvement with topical antibiotic treatment, typically after identification of the pathogen (and after fungal infection has been ruled out). Topical antibiotics, which are generally administered more frequently than corticosteroids during treatment of active infection, are continued at high levels and tapered gradually.

Patient compliance is essential, and IOP must be monitored. The patient should be examined within 1 to 2 days after initiation of topical corticosteroid therapy.

### **Modification of Therapy**

The efficacy of the therapeutic regimen is judged primarily by the clinical response. The results of cultures and sensitivity testing may have an impact on therapeutic decision making, especially if the patient is not responding to initial therapy. If the patient is improving, however, therapy need not be adjusted solely on the basis of laboratory studies. Dual antibiotic treatment designed to achieve broad-spectrum coverage may become unnecessary once the causative organism has been isolated.

In general, the initial therapeutic regimen should be modified when the eye shows a lack of improvement or stabilization within 48 hours. Keratitis due to *Pseudomonas* and other gram-negative organisms may exhibit increased inflammation during the first 24 to 48 hours despite appropriate therapy. Several clinical features suggest a positive response to antibiotic therapy.<sup>123</sup>

## **Bacterial Keratitis PPP: Provider and Setting**

- ◆ Reduced pain
- ◆ Reduced amount of discharge
- ◆ Lessened eyelid edema or conjunctival injection
- ◆ Consolidation and sharper demarcation of the perimeter of the stromal infiltrate
- ◆ Decreased density of the stromal infiltrate in the absence of progressive stromal loss
- ◆ Reduced stromal edema and endothelial inflammatory plaque
- ◆ Reduced anterior chamber cells, fibrin, or hypopyon
- ◆ Initial re-epithelialization
- ◆ Cessation of progressive corneal thinning

Modification of therapy may mean a change in the type, concentration, or frequency of antibiotic treatment.

Topical therapy is tapered according to clinical response, taking into account the severity of the initial clinical picture and the virulence of the pathogen. Specific tapering recommendations are difficult to make, due to wide variability in the severity of the infectious process in individual cases. Because prolonged use of topical antibiotics causes toxicity, they should be tapered as the infection improves. Medication toxicity can cause worsening inflammation or even corneal melting. If there is a persistent epithelial defect and the infection is under control, adjunctive therapies to rehabilitate the surface should be instituted, such as lubrication, antibiotic ointment, bandage contact lens, amniotic membrane coverage, or tarsorrhaphy. More prolonged therapy may be mandated by the presence of virulent or indolent organisms or for immunocompromised patients. Most antibiotic eye drops should not be tapered below three to four times a day because low doses are subtherapeutic and may increase the risk of developing antibiotic resistance.

### **Indications for Reculture**

Lack of a favorable clinical response, particularly in the setting of negative culture results, suggests the need for reculture and/or biopsy. Toxicity from medications or corticosteroid withdrawal may be confused with antibiotic failure, and medicamentosa may be a potential cause of an apparent lack of clinical improvement. Discontinuation of antibiotics for 12 to 24 hours prior to reculture may increase culture yield, as may avoidance of preserved solutions such as anesthetic or cycloplegic agents. Selected media capable of supporting the growth of atypical microorganisms may also increase culture yield and can be considered, such as Löwenstein-Jensen media for atypical mycobacteria. (See Appendix 5 for a list of culture media for bacterial keratitis.) Other atypical organisms to consider are fungal or parasitic, such as *Fusarium* and *Acanthamoeba*. *Fusarium* and *Acanthamoeba* are of particular concern because of a rise in the incidence of keratitis due to these pathogens. Although these infections can be diagnosed using appropriate staining of corneal smears, confocal microscopy can also be helpful in identifying the organisms in the tissue.

### **Therapy for Complicated Cases**

Coexisting risk factors, such as eyelid abnormalities, should be corrected for optimal results. Additional treatment is necessary in cases where the integrity of the eye is compromised, such as when there is an extremely thin cornea, impending or frank perforation, or progressive or unresponsive disease or endophthalmitis. Application of tissue adhesive, penetrating keratoplasty, and lamellar keratoplasty are among the treatment options. When corneal tissue is removed, it should be sent for pathologic and microbiologic analysis.

## **PROVIDER AND SETTING**

The diagnosis and management of patients with bacterial keratitis require the clinical training and experience of an ophthalmologist, because the disease has the potential to cause visual loss or blindness. If the diagnosis or treatment is in question, or if the condition is severe or refractory to treatment, consultation with or referral to an ophthalmologist who has expertise and experience in the management of bacterial keratitis is desirable.

The majority of patients with bacterial keratitis are treated on an outpatient basis. Hospitalization may be necessary if the keratitis is severe or vision-threatening, if compliance is impractical, or if pain is severe. Compliance may be doubtful since frequent instillation of eye drops is required—the patient may be unable to instill the eye drops because of age, mental, or physical disability, or an adequate support system may be lacking at home.

## **COUNSELING AND REFERRAL**

Patients and care providers should be educated about the destructive nature of bacterial keratitis and the need for strict adherence to the therapeutic regimen. The possibility of permanent visual loss and need for future visual rehabilitation should be discussed. Patients who wear contact lenses should be educated about the increased risk of infection associated with contact lens wear, overnight wear, and the importance of adherence to techniques that promote contact lens hygiene.<sup>27,124-126</sup> (See Appendix 6.) Following bacterial keratitis, the risks and timing of resuming contact lens wear should be discussed with the patient, and the lens choice and fitting should be reassessed by the eye care professional.

Visual rehabilitation restores functional ability,<sup>127</sup> and patients with substantial visual impairment should be referred for vision rehabilitation and social services if they are not candidates for surgery.<sup>128</sup> More information on vision rehabilitation, including materials for patients, is available at [www.aao.org/smartsight](http://www.aao.org/smartsight).

## **SOCIOECONOMIC CONSIDERATIONS**

Bacterial keratitis is a major cause of visual disability because it can lead to corneal opacification. The World Health Organization (WHO) recognizes it as a silent epidemic.<sup>129</sup> Developing countries have a much higher incidence of bacterial keratitis compared with developed countries. For example, Olmsted County, Minnesota, had an incidence of microbial keratitis of 11 per 100,000<sup>130</sup> compared with an incidence of 113 per 100,000 in India<sup>131</sup> and 799 per 100,000 in Nepal.<sup>82</sup> The largest risk factor for bacterial keratitis in the United States is contact lens use,<sup>130,132</sup> whereas corneal abrasions are the largest risk factor in Southeast Asia.<sup>82,133</sup>

There have been successful attempts at prevention of bacterial keratitis in developing countries.<sup>7</sup> In the Bhaktapur Eye Study, patients with corneal abrasions confirmed by clinical examination who presented within 48 hours of the injury without signs of corneal infection were enrolled and given chloramphenicol ointment 1% three times a day for 3 days. Only 18 of 442 patients went on to develop corneal ulcers.<sup>82</sup> The WHO applied the Bhaktapur Eye Study model in Bhutan.<sup>134</sup> Volunteer health workers were trained to follow the inhabitants of 55 villages and to use the same chloramphenicol ointment regimen for corneal abrasions. There were 115 corneal abrasions during the study period, and no cases of keratitis developed. Districts outside of the study zone held the same rate of corneal ulcers of 339 per 100,000. This effort is being expanded to other countries, and it is a cost-effective method of preventing the morbidity and further health care costs of bacterial keratitis.<sup>135</sup>

The incidence of infectious keratitis has been shown in multiple studies to be higher in patients of lower socioeconomic status, compared to those of higher socioeconomic status.<sup>31,136</sup> There is a significant financial burden of bacterial keratitis that results from direct costs due to medications, visits to ophthalmologists, and diagnostic testing, and from indirect costs due to loss of income, assistance from caregivers, and eyeglass purchases.<sup>137</sup> A study on contact-lens-associated microbial keratitis performed in Australia found that associated costs (including costs of hospital-bed days, outpatient and emergency department visits, drugs, pathology testing, and indirect costs such as lost productivity for patients and caregivers) were AU\$5515 for severe cases with vision loss, AU\$1596 for severe cases without vision loss, and AU\$795 for mild keratitis.<sup>137</sup> Another study performed in a tertiary eye center in south India found that the average total cost was \$85 USD. While the costs in India are much lower than in Australia, they are higher than the average monthly wage for this population.<sup>138</sup> The estimated cost of contact-related microbial keratitis in the United States in 2010 was approximately \$58 million.<sup>139</sup>

When topical antibiotics are considered specifically, the cost of fortified antibiotics is much higher than commercially available antibiotics because of the use of compounding pharmacies. As mentioned earlier in this report, use of a topical fluoroquinolone has been shown to be comparable to fortified antibiotics.<sup>140</sup> However, no randomized controlled study comparing the outcomes of fluoroquinolones with the outcomes of fortified antibiotics in severe cases of bacterial keratitis has been performed.



# APPENDIX 1. QUALITY OF OPHTHALMIC CARE CORE CRITERIA

*Providing quality care  
is the physician's foremost ethical obligation, and is  
the basis of public trust in physicians.  
AMA Board of Trustees, 1986*

Quality ophthalmic care is provided in a manner and with the skill that is consistent with the best interests of the patient. The discussion that follows characterizes the core elements of such care.

The ophthalmologist is first and foremost a physician. As such, the ophthalmologist demonstrates compassion and concern for the individual, and utilizes the science and art of medicine to help alleviate patient fear and suffering. The ophthalmologist strives to develop and maintain clinical skills at the highest feasible level, consistent with the needs of patients, through training and continuing education. The ophthalmologist evaluates those skills and medical knowledge in relation to the needs of the patient and responds accordingly. The ophthalmologist also ensures that needy patients receive necessary care directly or through referral to appropriate persons and facilities that will provide such care, and he or she supports activities that promote health and prevent disease and disability.

The ophthalmologist recognizes that disease places patients in a disadvantaged, dependent state. The ophthalmologist respects the dignity and integrity of his or her patients, and does not exploit their vulnerability.

Quality ophthalmic care has the following optimal attributes, among others.

- ◆ The essence of quality care is a meaningful partnership relationship between patient and physician. The ophthalmologist strives to communicate effectively with his or her patients, listening carefully to their needs and concerns. In turn, the ophthalmologist educates his or her patients about the nature and prognosis of their condition and about proper and appropriate therapeutic modalities. This is to ensure their meaningful participation (appropriate to their unique physical, intellectual, and emotional state) in decisions affecting their management and care, to improve their motivation and compliance with the agreed plan of treatment, and to help alleviate their fears and concerns.
- ◆ The ophthalmologist uses his or her best judgment in choosing and timing appropriate diagnostic and therapeutic modalities as well as the frequency of evaluation and follow-up, with due regard to the urgency and nature of the patient's condition and unique needs and desires.
- ◆ The ophthalmologist carries out only those procedures for which he or she is adequately trained, experienced, and competent, or, when necessary, is assisted by someone who is, depending on the urgency of the problem and availability and accessibility of alternative providers.
- ◆ Patients are assured access to, and continuity of, needed and appropriate ophthalmic care, which can be described as follows.
  - ◆ The ophthalmologist treats patients with due regard to timeliness, appropriateness, and his or her own ability to provide such care.
  - ◆ The operating ophthalmologist makes adequate provision for appropriate pre- and postoperative patient care.
  - ◆ When the ophthalmologist is unavailable for his or her patient, he or she provides appropriate alternate ophthalmic care, with adequate mechanisms for informing patients of the existence of such care and procedures for obtaining it.
  - ◆ The ophthalmologist refers patients to other ophthalmologists and eye care providers based on the timeliness and appropriateness of such referral, the patient's needs, the competence and qualifications of the person to whom the referral is made, and access and availability.
  - ◆ The ophthalmologist seeks appropriate consultation with due regard to the nature of the ocular or other medical or surgical problem. Consultants are suggested for their skill, competence, and accessibility. They receive as complete and accurate an accounting of the problem as necessary to provide efficient and effective advice or intervention, and in turn they respond in an adequate and timely manner.

**Appendix 1. Quality of Ophthalmic Care Core Criteria**

- ◆ The ophthalmologist maintains complete and accurate medical records.
- ◆ On appropriate request, the ophthalmologist provides a full and accurate rendering of the patient's records in his or her possession.
- ◆ The ophthalmologist reviews the results of consultations and laboratory tests in a timely and effective manner and takes appropriate actions.
- ◆ The ophthalmologist and those who assist in providing care identify themselves and their profession.
- ◆ For patients whose conditions fail to respond to treatment and for whom further treatment is unavailable, the ophthalmologist provides proper professional support, counseling, rehabilitative and social services, and referral as appropriate and accessible.
- ◆ Prior to therapeutic or invasive diagnostic procedures, the ophthalmologist becomes appropriately conversant with the patient's condition by collecting pertinent historical information and performing relevant preoperative examinations. Additionally, he or she enables the patient to reach a fully informed decision by providing an accurate and truthful explanation of the diagnosis; the nature, purpose, risks, benefits, and probability of success of the proposed treatment and of alternative treatment; and the risks and benefits of no treatment.
- ◆ The ophthalmologist adopts new technology (e.g., drugs, devices, surgical techniques) in judicious fashion, appropriate to the cost and potential benefit relative to existing alternatives and to its demonstrated safety and efficacy.
- ◆ The ophthalmologist enhances the quality of care he or she provides by periodically reviewing and assessing his or her personal performance in relation to established standards, and by revising or altering his or her practices and techniques appropriately.
- ◆ The ophthalmologist improves ophthalmic care by communicating to colleagues, through appropriate professional channels, knowledge gained through clinical research and practice. This includes alerting colleagues of instances of unusual or unexpected rates of complications and problems related to new drugs, devices, or procedures.
- ◆ The ophthalmologist provides care in suitably staffed and equipped facilities adequate to deal with potential ocular and systemic complications requiring immediate attention.
- ◆ The ophthalmologist also provides ophthalmic care in a manner that is cost effective without unacceptably compromising accepted standards of quality.

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## APPENDIX 2. INTERNATIONAL STATISTICAL CLASSIFICATION OF DISEASES AND RELATED HEALTH PROBLEMS (ICD) CODES

Bacterial keratitis includes entities with the following ICD-9 and ICD-10 classifications:

	ICD-9 CM	ICD-10 CM
Corneal ulcer, unspecified	370.00	H16.00-
Marginal corneal ulcer	370.01	H16.04-
Ring corneal ulcer	370.02	H16.02-
Central corneal ulcer	370.03	H16.01-
Hypopyon ulcer	370.04	H16.03-
Perforated corneal ulcer	370.06	H16.07-

CM = Clinical Modification used in the United States; (-) = 1, right eye; 2, left eye; 3, bilateral

Additional information for ICD-10 codes:

- Certain ICD-10 CM categories have applicable 7<sup>th</sup> characters. The applicable 7<sup>th</sup> character is required for all codes within the category, or as the notes in the Tabular List instruct. The 7<sup>th</sup> character must always be the 7<sup>th</sup> character in the data field. If a code that requires a 7<sup>th</sup> character is not 6 characters, a placeholder X must be used to fill in the empty characters.
- For bilateral sites, the final character of the codes in the ICD-10 CM indicates laterality. If no bilateral code is provided and the condition is bilateral, separate codes for both the left and right side should be assigned. Unspecified codes should only be used when there is no other code option available.
- When the diagnosis code specifies laterality, regardless of which digit it is found in (i.e., 4<sup>th</sup> digit, 5<sup>th</sup> digit, or 6<sup>th</sup> digit):
  - Right is always 1
  - Left is always 2
  - Bilateral is always 3





## APPENDIX 3. PREFERRED PRACTICE PATTERN RECOMMENDATION GRADING

The grades herein report the SIGN grade associated with the included studies supporting each recommendation (I++; I+; I-; II++; II+; II-; III), the GRADE evaluation of the body of evidence (Good, Moderate, Insufficient), and the GRADE assessment of the strength of the recommendation (Strong, Discretionary). Details of these grading systems are reported in the Methods and Key to Ratings section.

### Highlighted Findings and Recommendations for Care

Page 4: The majority of community-acquired cases of bacterial keratitis resolve with empiric therapy and are managed without smears or cultures: III; Insufficient; Discretionary

Page 4: Smears and cultures are indicated, however, in cases that involve a corneal infiltrate that is central, large and extends to the middle to deep stroma; that are chronic in nature or unresponsive to broad spectrum antibiotic therapy; or that have atypical clinical features suggestive of fungal, amoebic, or mycobacterial keratitis: III; Insufficient; Discretionary

Page 4: Patching the eye of a contact-lens-wearing patient with a corneal abrasion is not advised because of the increased risk of bacterial keratitis: III; Insufficient; Discretionary

Page 4: Cycloplegic agents may be used to decrease synechia formation and to decrease pain in bacterial keratitis and are indicated when substantial anterior chamber inflammation is present: III; Insufficient; Discretionary

Page 4: Corticosteroids may be considered after 48 hours when the causative organism is known: I+; Good; Discretionary

Page 4: Corticosteroids should be avoided in cases of infection involving *Acanthamoeba*, *Nocardia*, and fungus: III; Insufficient; Discretionary

Page 4: Due to the increasing resistance of methicillin-resistant *Staphylococcus aureas* (MRSA) to topical fluoroquinolones, combination therapy including vancomycin should be considered in this setting: III; Insufficient; Discretionary

Page 4: Topical antibiotics should be prescribed to prevent ulceration in patients presenting to the emergency room within 24 hours of a corneal abrasion: II+; Good; Strong

### Care Process – Diagnosis

Page 8: Evaluation of the patient with presumed bacterial keratitis includes those features of the comprehensive medical eye evaluation specifically relevant to bacterial keratitis: II++; Good; Strong

Page 8: Obtaining a detailed history is important in evaluating patients with bacterial keratitis: III; Good; Strong

Page 8: Pertinent information includes ocular symptoms: III; Good; Strong

Page 8: Pertinent information includes contact lens history: II+; Good; Strong

Page 8: Pertinent information includes review of other ocular history: III; Good; Strong

Page 8: Pertinent information includes review of other medical problems, systemic medications, and history of MRSA or other multidrug resistant infections: III; Good; Strong

Page 8: Pertinent information includes current and recently used ocular medications: III; Good; Strong

## **Bacterial Keratitis PPP:**

### **Appendix 3. PPP Recommendation Grading**

Page 8: Pertinent information includes medication allergies: III; Good; Strong

Page 8: The physical examination includes measurement of visual acuity, an external examination, and slit-lamp biomicroscopy: III; Good; Strong

Page 8: It is useful to document baseline visual acuity and to ascertain that it is consistent with the anterior segment examination: III; Good; Strong

Page 8: An external examination should be performed with particular attention to the general appearance of the patient, a facial examination, globe position, eyelids and eyelid closure, conjunctiva, nasolacrimal apparatus, and corneal sensation: III; Good; Strong

Page 9: Slit-lamp biomicroscopy should include evaluation of the eyelid margins, conjunctiva, sclera, cornea, anterior chamber, anterior vitreous, and contralateral eye: III; Good; Strong

Page 9: Fluorescein staining of the cornea is usually performed and may provide additional information about other factors: III; Insufficient; Discretionary

Page 10: The majority of community-acquired cases of bacterial keratitis resolve with empiric therapy and are managed without smears or cultures: III; Insufficient; Discretionary

Page 10: Smears and cultures are indicated, however, in cases that involve a corneal infiltrate that is central, large, and extends to the middle to deep stroma; that are chronic in nature or unresponsive to broad-spectrum antibiotic therapy; or that have atypical clinical features suggestive of fungal, amoebic, or mycobacterial keratitis: III; Insufficient; Discretionary

Page 10: Smears and cultures are often helpful for eyes that have an unusual history: III; Insufficient; Discretionary

Page 10: The hypopyon that occurs in eyes with bacterial keratitis is usually sterile, and aqueous or vitreous taps should not be performed unless there is a high suspicion of microbial endophthalmitis, such as following an intraocular surgery, perforating trauma, or sepsis: III; Insufficient; Discretionary

Page 10: Before initiating antimicrobial therapy, cultures are indicated in sight-threatening or severe keratitis of suspected microbial origin: III; Insufficient; Discretionary

Page 10: Cultures are helpful to guide modification of therapy in patients with a poor clinical response to treatment and to decrease toxicity by eliminating unnecessary medications: III; Insufficient; Discretionary

Page 10: Polymerase chain reaction and immunodiagnostic techniques may be useful: II+; Moderate; Strong

Page 10: Corneal material is obtained by instilling a topical anesthetic agent (tetracaine should be avoided due to antimicrobial effect) and using a heat-sterilized platinum (Kimura) spatula, blade, jeweler's forceps, or other similar sterile instrument to obtain scrapings of material from the advancing borders of the infected area of the cornea: III; Insufficient; Discretionary

Page 10: Culture yield may be improved by avoiding anesthetics with preservatives: III; Insufficient; Discretionary

Page 10: A thiol or thioglycollate broth-moistened dacron/calcium alginate or sterile cotton swab may also be used to obtain material: III; Insufficient; Discretionary

Page 10: If using transport media, similar methods of obtaining corneal material are used. The material is then transferred to the cotton swab, which is then placed in the tube: III; Insufficient; Discretionary

Page 10: Corneal scrapings for culture should be inoculated directly onto appropriate culture media to maximize culture yield: III; Insufficient; Discretionary

Page 10: If this is not feasible, specimens should be placed in transport media: II+; Moderate; Discretionary

Page 10: Cultures of contact lenses, the lens case, and contact lens solution may provide additional information to guide therapy: III; Insufficient; Discretionary

Page 10: It may be helpful to obtain cultures from eyes treated empirically that were not first cultured and in which the clinical response is poor, although a delay in pathogen recovery may occur, so keeping cultures for longer may be helpful: III; Insufficient; Discretionary

Page 10: If the cultures are negative, the ophthalmologist may consider stopping antibiotic treatment for 12 to 24 hours and then reculturing: III; Insufficient; Discretionary

Page 11: Corneal biopsy may be indicated if the response to treatment is poor, or if repeated cultures have been negative and the clinical picture continues to strongly suggest an infectious process: III; Good; Strong

Page 11: It may also be indicated if the infiltrate is located in the mid or deep stroma with overlying uninvolved tissue: III; Insufficient; Discretionary

Page 11: With a cooperative patient, corneal biopsy may be performed while at the slit-lamp biomicroscope or operating microscope: III; Good; Strong

Page 11: The biopsy specimen should be delivered to the laboratory in a timely fashion: III; Good; Strong

Page 11: An option for a deep corneal abscess may be to use a suture that can be passed through the abscess without disturbing the overlying intact corneal epithelium and stroma: III; Insufficient; Discretionary

Page 11: Another option in cases of a deep corneal abscess with overlying clear cornea is to take the biopsy from below a lamellar flap: III; Insufficient; Discretionary

Page 11: Confocal technology has been shown to be of some use in the diagnosis of infectious keratitis including bacterial, fungal, and most notably, parasitic: II++; Moderate; Discretionary

Page 11: When in doubt, it is often best initially to manage eyes with viral keratitis as infected: III; Insufficient; Discretionary

### **Care Process – Management**

Page 12: Avoiding or correcting predisposing factors may reduce the risk of bacterial keratitis: II++; Moderate; Strong

Page 12: For those patients who require a bandage contact lens for therapy of an ocular pathology, topical antibiotic prophylaxis is recommended: III; Insufficient; Discretionary

Page 12: Most ocular trauma can be avoided by using protective eyewear for sports and other high-risk activities: III; Good; Strong

Page 12: Patients should be informed of the risk of infectious keratitis when wearing a bandage contact lens and the need to contact their treating ophthalmologist if redness, pain, or increased photophobia develops: III; Good; Strong

Page 12: They should also be informed that they are still at risk for infection, despite the use of antibiotics: III; Good; Strong

Page 12: Ideally, bandage contact lenses should be used for a finite treatment period; however, in many cases, their use may be protracted. In this situation, periodic exchange of the lens is advised: III; Good; Strong

Page 12: Regular follow-up is necessary under these circumstances to reassess the lens, to look for evidence of a change in the patient's ocular status, and to re-emphasize the need for vigilance on the part of the patient: III; Good; Strong

## **Bacterial Keratitis PPP:**

### **Appendix 3. PPP Recommendation Grading**

Page 12: Patients with risk factors predisposing them to bacterial keratitis should be educated about their relative risk, be acquainted with the signs and symptoms of infection, and be informed that they should consult an ophthalmologist promptly if they experience such warning signs or symptoms: III; Good; Strong

Page 12: Ocular surface disease such as corneal epithelial defects, severe tear deficiency, or lagophthalmos should be treated: III; Good; Strong

Page 12: Prophylactic antibiotics can be considered for patients with chronic epithelial defects; however, the routine use of prophylactic topical antibiotics in this setting is controversial, because their efficacy has not been established and chronic use may promote growth of resistant organisms: III; Insufficient; Discretionary

Page 12: Prophylactic topical antibiotics following corneal abrasion may prevent ulceration when treatment is started within 24 hours of the abrasion: III; Good; Strong

Page 12: For those contact-lens-wearing patients who develop a traumatic abrasion, it is advisable to avoid pressure patching, even if the patch might increase the patient's comfort: III; Insufficient; Discretionary

Page 12: Topical antibiotic eye drops are capable of achieving high tissue levels and are the preferred method of treatment in most cases: III; Good; Strong

Page 12: Subconjunctival antibiotics may be helpful where there is imminent scleral spread or perforation or in cases where adherence to the treatment regimen is questionable: III; Insufficient; Discretionary

Page 12: Systemic therapy may be useful in cases of scleral or intraocular extension of infection or systemic infection such as gonorrhea: III; Insufficient; Discretionary

Page 12: Collagen shields or soft contact lenses soaked in antibiotics are sometimes used and may enhance drug delivery: III; Insufficient; Discretionary

Page 12: They may also be useful in cases where there is an anticipated delay in initiating appropriate therapy, but these modalities have not been fully evaluated in terms of efficacy and the potential risk for inducing drug toxicity: III; Insufficient; Discretionary

Page 12: Topical broad-spectrum antibiotics are used initially in the empiric treatment of bacterial keratitis: III; Insufficient; Discretionary

Page 12: For central or severe keratitis, a loading dose, followed by frequent applications, is recommended: III; Insufficient; Discretionary

Page 13: For less severe keratitis, a regimen with less frequent dosing is appropriate: III; Insufficient; Discretionary

Page 13: Cycloplegic agents may be used to decrease synechia formation and to decrease pain in bacterial keratitis, and are indicated when substantial anterior chamber inflammation is present: III; Insufficient; Discretionary

Page 13: Single-drug therapy using a fluoroquinolone has been shown to be as effective as combination therapy utilizing antibiotics that are fortified by increasing their concentration over commercially available topical antibiotics: I+; Good; Discretionary

Page 14: Combination fortified-antibiotic therapy is an alternative to consider for severe infection and for eyes unresponsive to initial treatment: III; Insufficient; Discretionary

Page 14: Treatment with more than one agent may be necessary for nontuberculous mycobacteria: III; Insufficient; Discretionary

Page 14: In cases of severe ulcer, more complete coverage with combination therapy can be considered: III; Insufficient; Discretionary

Page 14: Systemic antibiotics are rarely needed, but they may be considered in severe cases where the infectious process has extended to adjacent tissues (e.g., the sclera) or when there is impending or frank perforation of the cornea: III; Insufficient; Discretionary

Page 14: Systemic therapy is necessary in cases of gonococcal keratitis: II++; Good; Strong

Page 14: Frequency of re-evaluation of the patient with bacterial keratitis depends on the extent of disease, but severe cases initially should be followed at least daily until stabilization or clinical improvement is documented: III; Insufficient; Discretionary

Page 14: There is no conclusive scientific evidence indicating that corticosteroids alter clinical outcome: I+; Strong; Discretionary

Page 14: Patients being treated with ocular topical corticosteroids at the time of presentation of suspected bacterial keratitis should have their corticosteroid regimen reduced or eliminated until the infection has been controlled: III; Good; Strong

Page 15: Chronic topical immunotherapy, such as use of corticosteroids, increases the risk of infectious crystalline keratopathy, which often requires discontinuation of the topical immunotherapy to achieve successful treatment: III; Good; Strong

Page 15: The objective of topical corticosteroid therapy is to use the minimum amount required to achieve control of inflammation: III; Good; Strong

Page 15: Successful treatment requires optimal timing, careful dose regulation, use of adequate concomitant antibacterial medication, and close follow-up: III; Good; Strong

Page 15: A conservative approach would avoid prescribing corticosteroid treatment for presumed bacterial ulcers until the organism has been cultured: III; Insufficient; Discretionary

Page 15: In cases where the corneal infiltrate compromises the pupil, topical corticosteroid therapy may be added to the regimen following at least 2 to 3 days of progressive improvement with topical antibiotic treatment, typically after identification of the pathogen: III; Insufficient; Discretionary

Page 15: Topical antibiotics, which are generally administered more frequently than corticosteroids during treatment of active infection, are continued at high levels and tapered gradually: III; Insufficient; Discretionary

Page 15: Patient compliance is essential, and IOP must be monitored: III; Good; Strong

Page 15: The patient should be examined within 1 to 2 days after initiation of topical corticosteroid therapy: III; Insufficient; Discretionary

Page 15: The results of cultures and sensitivity testing may have an impact on therapeutic decision making, especially if the patient is not responding to initial therapy: III; Good; Strong

Page 15: Dual antibiotic treatment designed to achieve broad-spectrum coverage may become unnecessary once the causative organism has been isolated: III; Insufficient; Discretionary

Page 15: In general, the initial therapeutic regimen should be modified when the eye shows a lack of improvement or stabilization within 48 hours: III; Insufficient; Discretionary

Page 16: Topical therapy is tapered according to clinical response, taking into account the severity of the initial clinical picture and the virulence of the pathogen: III; Good; Strong

Page 16: If there is a persistent epithelial defect and the infection is under control, adjunctive therapies to rehabilitate the surface should be instituted, such as lubrication, antibiotic ointment, bandage contact lens, or tarsorrhaphy: III; Insufficient; Discretionary

## **Bacterial Keratitis PPP:**

### **Appendix 3. PPP Recommendation Grading**

Page 16: More prolonged therapy may be mandated by the presence of virulent or indolent organisms or for immunocompromised patients: III; Insufficient; Discretionary

Page 16: Most antibiotic eye drops should not be tapered below three to four times a day, because low doses are subtherapeutic and may increase the risk of antibiotic resistance developing: III; Insufficient; Discretionary

Page 16: Lack of a favorable clinical response, particularly in the setting of negative culture results, suggests the need for reculture and/or biopsy: III; Insufficient; Discretionary

Page 16: Discontinuation of antibiotics for 12 to 24 hours prior to reculture may increase culture yield, as may avoidance of preserved solutions such as anesthetic or cycloplegic agents: III; Insufficient; Discretionary

Page 16: Selected media capable of supporting the growth of atypical microorganisms may also increase culture yield and can be considered, such as Löwenstein-Jensen media for atypical mycobacteria: III; Insufficient; Discretionary

Page 16: Although these infections can be diagnosed using appropriate staining of corneal smears, confocal microscopy can also be helpful in identifying the organisms in the tissue: III; Insufficient; Discretionary

Page 16: Coexisting risk factors, such as eyelid abnormalities, should be corrected for optimal results: III; Good; Strong

Page 16: Additional treatment is necessary in cases where the integrity of the eye is compromised, such as when there is an extremely thin cornea, impending or frank perforation, or progressive or unresponsive disease or endophthalmitis: III; Good; Strong

Page 16: Application of tissue adhesive, penetrating keratoplasty, and lamellar keratoplasty are among the treatment options: III; Insufficient; Discretionary

Page 16: When corneal tissue is removed, it should be sent for pathologic and microbiologic analysis: III; Good; Strong

### **Provider and Setting**

Page 16: The diagnosis and management of patients with bacterial keratitis require the clinical training and experience of an ophthalmologist: III; Good; Strong

Page 16: If the diagnosis or treatment is in question, or if the condition is severe or refractory to treatment, consultation with or referral to an ophthalmologist who has expertise and experience in the management of bacterial keratitis is desirable: III; Good; Strong

Page 16: Hospitalization may be necessary if the keratitis is severe or vision-threatening, if compliance is impractical, or if pain is severe: III; Good; Strong

### **Counseling and Referral**

Page 16: Patients and care providers should be educated about the destructive nature of bacterial keratitis and the need for strict adherence to the therapeutic regimen: III; Good; Strong

Page 16: The possibility of permanent visual loss and need for future visual rehabilitation should be discussed: III; Good; Strong

Page 16: Patients who wear contact lenses should be educated about the increased risk of infection associated with contact lens wear, overnight wear, and the importance of adherence to techniques that promote contact lens hygiene: II+; Good; Strong



## APPENDIX 4. DIAGNOSTIC STAINS

Table A4 lists diagnostic stains that are used in cultures to identify causes of bacterial keratitis.

**TABLE A4 STAINS USED TO IDENTIFY COMMON CAUSES OF BACTERIAL KERATITIS IN THE UNITED STATES**

Type of Stain	Organisms Visualized	Comments
Gram stain*	Best for bacteria; can also visualize fungi, <sup>†</sup> amoeba	Distinguishes gram-positive from gram-negative organisms; widely available; rapid (5 minutes)
Giemsa stain*	Bacteria, fungi, <sup>†</sup> <i>Chlamydia</i> , <i>Acanthamoeba</i>	Basis for Aema-color and Diff-Quik tests; widely available; rapid (2 minutes)
Acid fast	<i>Mycobacterium</i> , <i>Nocardia</i>	Widely available; takes 1 hour; reliable stain for <i>Mycobacteria</i>
Acridine orange*	Bacteria, fungi, <sup>†</sup> <i>Acanthamoeba</i> <sup>‡</sup>	Requires use of epifluorescent microscope; rapid (2 minutes)
Calcofluor white	Fungi, <sup>†</sup> <i>Acanthamoeba</i> <sup>‡</sup>	Requires use of epifluorescent microscope; rapid (2 minutes)

\* Most useful stains for screening purposes.

<sup>†</sup> PAS (periodic acid-Schiff) and GMS (Gomori methenamine silver) also can be used to identify fungi.

<sup>‡</sup> H&E (hematoxylin and eosin) and PAS also can be used to identify *Acanthamoeba*.

Data from:

Infections of the eyes, ears, and sinuses. In: Forbes BA, Sahm DF, Weissfeld AS, eds. Bailey and Scott's Diagnostic Microbiology. St. Louis, MO: Mosby; 2007:832-41.

Laboratory methods for diagnosis of parasitic infections. In: Forbes BA, Sahm DF, Weissfeld AS, eds. Bailey and Scott's Diagnostic Microbiology. St. Louis, MO: Mosby; 2007:543-627.

Laboratory methods in basic mycology. In: Forbes BA, Sahm DF, Weissfeld AS, eds. Bailey and Scott's Diagnostic Microbiology. St. Louis, MO: Mosby; 2007:629-716.

Role of microscopy. In: Forbes BA, Sahm DF, Weissfeld AS, eds. Bailey and Scott's Diagnostic Microbiology. St. Louis, MO: Mosby; 2007:78-92.

Murray PR, Shea VR. In: Pocket Guide to Clinical Microbiology. Washington, DC: ASM; 2004:131-81.



## APPENDIX 5. CULTURE AND TRANSPORT MEDIA

Table A5 lists culture and transport media that are used in the management of bacterial keratitis.

TABLE A5 CULTURE AND TRANSPORT MEDIA FOR BACTERIAL KERATITIS

Media	Common Isolates
<b>Standard</b>	
Blood agar	Aerobic and facultatively anaerobic bacteria, including <i>P. aeruginosa</i> , <i>S. aureus</i> , <i>S. epidermidis</i> , and <i>S. pneumoniae</i>
Chocolate agar	Aerobic and facultatively anaerobic bacteria, including <i>H. influenzae</i> , <i>N. gonorrhea</i> , and <i>Bartonella</i> species
Thioglycollate broth	Aerobic and facultatively anaerobic bacteria
Sabouraud dextrose agar	Fungi
<b>Supplemental</b>	
Anaerobic blood agar (CDC, Schaedler, Brucella)	<i>P. acnes</i> , <i>Peptostreptococcus</i>
Löwenstein-Jensen medium	<i>Mycobacterium</i> species, <i>Nocardia</i> species
Middlebrook agar	<i>Mycobacterium</i> species
Thayer-Martin agar	Pathogenic <i>Neisseria</i> species
<b>Transport</b>	
BHI (brain heart infusion [Oxid]) medium	Aerobic and facultatively anaerobic bacteria
Amies medium without charcoal	Aerobic and facultatively anaerobic bacteria; Fungi

NOTE: Fungi and *Acanthamoeba* can be recovered on blood agar. However, more specific media are available (fungi: Sabouraud dextrose agar, brain-heart infusion agar; *Acanthamoeba*: buffered charcoal yeast extract, non-nutrient agar with *E. coli* overlay).

### References:

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- Murray PR, Shea VR. In: Pocket Guide to Clinical Microbiology. Washington, DC: ASM; 2004:131-81, 269-70.





## APPENDIX 6. CONTACT LENS CARE

The following recommendations have been excerpted from the Refractive Errors and Refractive Surgery PPP.<sup>141</sup>

### PATIENT EDUCATION AND CONTACT LENS CARE

The United States Food and Drug Administration (FDA) has made the following recommendations for contact lens wearers regarding proper lens care practices:<sup>77</sup>

- ◆ Wash hands with soap and water, and dry (lint-free method) before handling contact lenses.
- ◆ Wear and replace contact lenses according to the schedule prescribed by the doctor.
- ◆ Follow the specific contact lens cleaning and storage guidelines from the doctor and the solution manufacturer.
- ◆ Keep the contact lens case clean and replace it every 3 to 6 months.
- ◆ Remove the contact lenses and consult your doctor immediately if you experience symptoms such as redness, pain, tearing, increased light sensitivity, blurry vision, discharge, or swelling.

When contact lenses are initially prescribed and dispensed, patients should be trained and supervised in contact lens insertion and removal. Contact lens cleaning and disinfection should be carefully explained, because improper care may be associated with complications of contact lens wear.<sup>71,142-144</sup> Patients should be instructed that rubbing is an important part of the cleaning step before disinfection for any lens that is to be reworn. Hydrogen peroxide systems may be superior to preserved disinfecting solutions in reducing pathogen binding and cysticidal disinfection, but they require more complex care regimens.<sup>145-147</sup> Patients should be instructed to use only sterile products that are commercially prepared specifically for contact lens care and to replace these at the intervals recommended by the manufacturers.<sup>148</sup>

Specifically, patients should be instructed not to rinse contact lenses or lens cases with nonsterile water (e.g., tap water, bottled water).<sup>144</sup> (*strong recommendation, moderate evidence*) Patients should also be instructed to clean and replace contact lens cases frequently, because they can be a source of lens contamination.<sup>144,149,150</sup> (*strong recommendation, good evidence*) Patients should be instructed to replace the solution in contact lens cases each time the lenses are disinfected (i.e., the old solution should not be topped off).<sup>151</sup>

Patients should be made aware that using contact lenses can be associated with the development of ocular problems, including corneal infections that may threaten vision, and that overnight wear of contact lenses is associated with an increased risk of these corneal infections.<sup>27,33,34,125,126</sup> This increased risk of corneal infections with overnight contact lens wear should be discussed with patients who are considering this modality of vision correction. If patients choose overnight wear, they should be instructed to use only lenses specifically approved for extended wear.

Swimming with contact lenses has been associated with the development of *Acanthamoeba* keratitis,<sup>126</sup> and showering with lenses seems to be part of a pattern of risk.<sup>71</sup> Patients should be instructed to minimize water contact when wearing contact lenses and informed of the risks of wearing contact lenses while swimming, in a hot tub, or showering.

### CONTACT LENS CARE

Proper contact lens care involves a combination of cleaning, disinfecting, rinsing, and wetting solutions.<sup>151</sup> Surfactant cleaning solutions act like detergents to solubilize debris that is not chemically bonded to the contact lens. Rubbing the contact lens enhances the cleaning performance of the solution, likely by removing loosely bound deposits.<sup>104,152,153</sup> Enzymatic cleaners remove deposits that are chemically bonded to the surface. Disinfecting solutions reduce the number of microorganisms carried on the contact lens. Wetting solutions make a water-repellant lens surface hydrophilic. Many manufacturers combine these agents into multipurpose solutions.

Patients should also be instructed to clean and replace contact lens cases frequently, because they can be a source of lens contamination,<sup>144,149,150</sup> and damaged or cracked cases should be discarded.

Patients should be advised to have annual exams to monitor fit of the contact lens, ocular health including pannus, scarring, inflammation and ectasia, and reinforce proper lens care and hygiene.

The American Academy of Ophthalmology ([www.aao.org/store](http://www.aao.org/store)) and the Contact Lens Association of Ophthalmologists ([www.claa.org/Publications/Products/tabid/87/Default.aspx](http://www.claa.org/Publications/Products/tabid/87/Default.aspx)) have patient information brochures for contact lens care.



## APPENDIX 7. PREPARATION OF FORTIFIED TOPICAL ANTIBIOTICS

Preparation of fortified topical antibiotics should be performed using sterile techniques. The use of antibiotics in the treatment of post-LASIK bacterial keratitis is discussed in the Refractive Errors and Refractive Surgery PPP.<sup>141</sup> Instructions for preparing fortified topical antibiotics used in treating bacterial keratitis are as follows:

### **Cefazolin 50 mg/ml or Ceftazidime 50 mg/ml**

1. Add 9.2 ml of artificial tears to a vial of cefazolin, 1 g (powder for injection).
2. Dissolve. Take 5 ml of this solution and add it to 5 ml of artificial tears.
3. Refrigerate and shake well before instillation.

### **Tobramycin 14 mg/ml or Gentamicin 14 mg/ml**

1. Withdraw 2 ml from an injectable vial of intravenous tobramycin or gentamicin (40 mg/ml).
2. Add the withdrawn 2 ml to a 5 ml bottle of tobramycin or gentamicin ophthalmic solution to give a 14 mg/ml solution.
3. Refrigerate and shake well before instillation.

### **Vancomycin 15 mg/ml, Vancomycin 25 mg/ml, or Vancomycin 50 mg/ml**

1. To a 500 mg vial of vancomycin:
  - a. Add 33 ml of 0.9% sodium chloride for injection USP (no preservatives) or artificial tears to produce a solution of 15 mg/ml.
  - b. Add 20 ml of 0.9% sodium chloride for injection USP (no preservatives) or artificial tears to produce a solution of 25 mg/ml.
  - c. Add 10 ml of 0.9% sodium chloride for injection USP (no preservatives) or artificial tears to produce a solution of 50 mg/ml.
2. Refrigerate and shake well before instillation.

### **Amikacin 40 mg/ml**

Intravenous formulation can be used (80 mg/2 cc ampules).

### **Trimethoprim/sulfamethoxazole**

16 mg/ml / 80 mg/ml commercial preparation can be used.

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## RELATED ACADEMY MATERIALS

### Basic and Clinical Science Course

External Disease and Cornea (Section 8, 2013–2014)

### Information Statement –

Free download available at <http://one.aao.org/guidelines-browse?filter=clinicalstatement>.

Extended Wear of Contact Lenses (2013)

### Focal Points

Antibiotic Use in Corneal and External Eye Infections (2011)

### Patient Education Brochure

Contact Lenses (2011)

**Preferred Practice Pattern® Guidelines – Free download available at [www.aao.org/ppp](http://www.aao.org/ppp).**

Comprehensive Adult Medical Eye Evaluation (2010)

Pediatric Eye Evaluations (2012)

To order any of these products, except for the free materials, please contact the Academy's Customer Service at 866.561.8558 (U.S. only) or 415.561.8540 or [www.aao.org/store](http://www.aao.org/store).



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