

AMERICAN ACADEMY OF OPHTHALMOLOGY®

# SUMMARY BENCHMARKS FOR PREFERRED PRACTICE PATTERN® GUIDELINES

#### Introduction

These are summary benchmarks for the Academy's Preferred Practice Pattern® (PPP) guidelines. The Preferred Practice Pattern series of guidelines has been written on the basis of three principles.

- Each Preferred Practice Pattern should be clinically relevant and specific enough to provide useful information to practitioners.
- Each recommendation that is made should be given an explicit rating that shows its importance to the care process.
- Each recommendation should also be given an explicit rating that shows the strength of evidence that supports the recommendation and reflects the best evidence available.

**Preferred Practice Patterns 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 Preferred Practice Patterns 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.

The Preferred Practice Pattern<sup>®</sup> 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. For each major disease condition, recommendations for the process of care, including the history, physical exam and ancillary tests, are summarized, along with major recommendations for the care management, follow-up, and education of the patient. For each PPP, a detailed literature search of PubMed and the Cochrane Library for articles in the English language is conducted. The results are reviewed by an expert panel and used to prepare the recommendations, which are then given a rating that shows the strength of evidence when sufficient evidence exists.

To rate individual studies, a scale based on the Scottish Intercollegiate Guideline Network (SIGN) 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)



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#### Introduction (continued)

Recommendations for care are formed based on the body of the evidence. The body of evidence quality ratings are defined by Grading of Recommendations Assessment, Development and Evaluation (GRADE) as follows:

- Good quality (GQ): Further research is very unlikely to change our confidence in the estimate of effect
- Moderate quality (MQ): Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
- Insufficient quality (IQ): 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 as follows:

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

The PPPs are intended to serve as guides in patient care, with greatest emphasis on technical aspects. In applying this knowledge, it is essential to recognize that true medical excellence is achieved only when skills are applied in a such a manner that the patients' needs are the foremost consideration. The AAO is available to assist members in resolving ethical dilemmas that arise in the course of practice. (AAO Code of Ethics)

- Ocular symptoms (e.g., degree of pain, redness, discharge, blurred vision, photophobia, duration of symptoms, circumstances surrounding the onset of symptoms)
- Contact lens history (e.g., wearing schedule, overnight wear, type of contact lenses, contact lens solution, homemade saline, contact lens hygiene protocol, tap-water rinse of contact lenses, swimming, using a hot tub, or showering while wearing contact lenses, method of purchase, such as over the Internet, and decorative contact lens use)
- Review of other ocular history, including risk factors such as herpes simplex virus keratitis, varicella zoster virus keratitis, previous bacterial keratitis, trauma, dry eye, recurrent corneal erosion, and previous ocular surgery, including refractive and facial (including laser cosmetic and blepharoplasty) surgery
- Review of other medical problems, including immune status, rosacea, atopy, diabetes, systemic medications, and history of methicillin-resistant *Staphylococcus aureus* or other multidrug-resistant infection
- Current and recently used ocular and systemic medications
- Medication allergies

#### **Initial Physical Exam**

- Visual acuity
- General appearance of patient, including skin conditions, hands, and overall hygiene
- Facial examination (rosacea, herpes zoster)
- Globe position
- Eyelids and eyelid closure
- Conjunctiva (injection, chemosis)
- Nasolacrimal apparatus
- Corneal sensation if appropriate
- Slit-lamp biomicroscopy
  - Eyelid
  - Conjunctiva
  - Sclera
  - Cornea
  - Anterior chamber for depth and the presence of inflammation, including cell and flare, fibrin, hyphema, and hypopyon
  - Anterior vitreous for depth and the presence of inflammation
  - Contralateral eye for clues to etiology as well as possible similar underlying pathology

#### **Diagnostic Tests**

- Manage majority of community-acquired cases with empiric therapy and without smears or cultures
- Indications for smears and cultures:
  - Corneal infiltrate that is central, large, and/or associated with significant stromal involvement or melting
  - ≥1+ cells in anterior chamber
  - History of corneal surgery
  - Atypical clinical features suggestive of fungal, amœbic, or mycobacterial keratitis
  - Multiple corneal infiltrates
- 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
- Corneal scrapings for culture should be inoculated directly onto appropriate culture media to maximize culture yield. If this is not feasible, place specimens in transport media. In either case, immediately incubate cultures or take promptly to the laboratory.

#### **Care Management**

- Topical antibiotic eye drops are capable of achieving high tissue levels, a preferred method of treatment in most cases
- Single-drug therapy using a fluoroquinolone is as effective as combination therapy utilizing fortified antibiotics. Fortified topical antibiotics to be considered for large and/or visually significant corneal infiltrates, especially if hypopyon is present. Combination fortified-antibiotic therapy is an alternative, especially for severe infection and eyes unresponsive to initial treatment. There is no difference found in corneal perforation rates across classes of topical antibiotics.
- Topical corticosteroid therapy may have a beneficial role, but much of the literature has not shown a difference in clinical outcome
- Subconjunctival antibiotics may be helpful where adherence is questionable or there is a delay in obtaining fortified antibiotics
- For central or severe keratitis (e.g., deep stromal involvement or an infiltrate larger than 2 mm with extensive suppuration), use a loading dose (e.g., every 5 to 15 minutes), followed by frequent applications (e.g., every hour is recommended.) Severe cases should be followed daily initially, at least until stable or improvement is confirmed.

## Bacterial Keratitis (Initial Evaluation) (continued)

- Systemic therapy is necessary for gonococcal keratitis. It may be considered in severe cases where the infectious process has extended or the cornea is perforated.
- For patients treated with ocular topical corticosteroids at time of presentation of suspected bacterial keratitis, reduce or eliminate corticosteroids until infection has been controlled
- When the corneal infiltrate compromises the visual axis, may add topical corticosteroid therapy following at least 2 to 3 days of progressive improvement with treatment with topical antibiotics typically after pathogen identification
- Examine patients within 1 to 2 days after initiation of topical corticosteroid therapy and monitor intraocular pressure
- In general, modify the initial regimen if there is lack of improvement or stabilization within 48 hours

#### **Patient Education**

- Inform patients with risk factors predisposing them to bacterial keratitis of their relative risk, the signs and symptoms of infection, and to consult an ophthalmologist promptly if they experience such warning signs or symptoms
- Educate about the severe visual impairment from bacterial keratitis and need for strict adherence to the therapeutic regimen
- Discuss possibility of permanent visual loss and need for future visual rehabilitation
- Educate patients with contact lenses about increased risk of infection associated with contact lens, overnight wear, and importance of adherence to techniques to promote contact lens hygiene
- Refer patients with significant visual impairment or blindness for vision rehabilitation if they are not surgical candidates (see <u>https://www.aao.org/</u> education/low-vision-and-vision-rehab)

| Organism                         | Topical<br>Antibiotic  | Topical<br>Concentration | Subconjunctival<br>Dose              |
|----------------------------------|--|--------------------------|--------------------------------------|
| None or<br>multiple types        | Fortified Cefazolin<br>with  | 50 mg/mL                 | 100 mg in 0.5 mL                     |
| of organisms                     | Fortified Tobramycin<br>or   | 9-14 mg/mL               | 20 mg in 0.5 mL                      |
|                                  | Fluoroquinolones   | 3-6 mg/mL                | Not available                        |
| Gram-positive<br>cocci           | Cefazolin<br>Vancomycin<br>Moxifloxacin, gatifloxacin,                                 | 50 mg/mL<br>25-50 mg/mL  | 100 mg in 0.5 mL<br>25 mg in 0.5 mL  |
|                                  | levofloxacin, besifloxacin   | 5-6 mg/mL                | Not available                        |
| Gram-negative<br>rods            | Tobramycin<br>Ceftazidime<br>Ciprofloxacin, ofloxacin,<br>moxifloxacin, gatifloxacin,  | 9-14 mg/mL<br>50 mg/mL   | 20 mg in 0.5 mL<br>100 mg in 0.5 mL  |
|                                  | levofloxacin, besifloxacin   | 3-6 mg/mL                | Not available                        |
| Gram-negative<br>cocci           | Ceftriaxone<br>Ceftazidime<br>Ciprofloxacin, ofloxacin,<br>moxifloxacin, gatifloxacin, | 50 mg/mL<br>50 mg/mL     | 100 mg in 0.5 mL<br>100 mg in 0.5 mL |
|                                  | levofloxacin, besifloxacin   | 3-6 mg/mL                | Not available                        |
| Mycobacteria                     | Clarithromycin<br>Moxifloxacin, gatifloxacin,  | 10 mg/mL 0.03%           |                                      |
|                                  | besifloxacin<br>Amikacin   | 5-6 mg/mL<br>20-40 mg/mL | Not available<br>20 mg in 0.5 mL     |
| Gram-positive rods<br>(Nocardia) | Sulfacetamide<br>Amikacin<br>Trimethoprim/<br>Sulfamethoxazole:                        | 100 mg/mL<br>20-40 mg/mL | 20 mg in 0.5 mL                      |
|                                  | Trimethoprim<br>Sulfamethoxazole   | 16 mg/mL<br>80mg/mL      |                                      |

#### Antibiotic Therapy of Bacterial Keratitis

Modified 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, 2022-2023. Table 10-6. San Francisco: American Academy of Ophthalmology, 2022.

# **Blepharitis (Initial and Follow-up Evaluation)**

#### **Initial Exam History**

- Ocular symptoms and signs (e.g., redness, irritation, burning, tearing, itching, crusting of eyelashes, loss of eyelashes, eyelid sticking, blurring or fluctuating vision, contact lens intolerance, photophobia, increased frequency of blinking and recurrent hordeolum)
- Time of day when symptoms are worse
- Duration of symptoms
- Unilateral or bilateral presentation
- Exacerbating conditions (e.g., smoke, allergens, wind, contact lenses, low humidity, retinoids, diet and alcohol consumption, eye makeup, aqueous tear deficiency)
- Symptoms related to systemic diseases (e.g., rosacea, atopy, herpes zoster Ophthalmicus, psoriasis, and graft-versus-host disease)
- Current and previous systemic and topical medications (e.g., antihistamines or drugs with anticholinergic effects, or drugs used in the past such as isotretinoin that might have an effect on the ocular surface)
- Recent exposure to an infected individual (e.g., pediculosis palpebrarum [*P. pubis*])
- Ocular history
- Medical history

#### **Initial Physical Exam**

- Visual acuity
- External examination
  - Skin
  - Eyelids
- Slit-lamp biomicroscopy
  - Tear film
  - Anterior eyelid margin
  - Eyelashes
  - Posterior eyelid margin
  - Tarsal conjunctiva (everting eyelids)
  - Bulbar conjunctiva
  - Cornea

#### **Diagnostic Tests**

- Cultures may be indicated for patients with recurrent anterior blepharitis with severe inflammation as well as for patients who are not responding to therapy
- Biopsy of the eyelid to exclude the possibility of carcinoma may be indicated in cases of marked asymmetry, resistance to therapy or unifocal recurrent chalazia that do not respond well to therapy

• Consult with the pathologist prior to obtaining the biopsy if sebaceous cell carcinoma is suspected

#### **Care Management**

- Treat patients with blepharitis initially with a regimen of warm compresses and eyelid cleansing
- A topical antibiotic such as bacitracin or erythromycin can be prescribed to be applied one or more times daily or at bedtime on the eyelid margins for a few weeks
- For patients with meibomian gland dysfunction, whose chronic symptoms and signs are not adequately controlled with eyelid cleansing or meibomian gland expression, oral tetracyclines and topical antibiotics may be helpful
- Topical azelaic acid, topical ivermectin, brimonidine, doxycycline, and isotretinoin are effective treatments for patients with systemic rosacea (*I+*, *GQ*, *SR*)
- A brief course of topical corticosteroids may be helpful for eyelid or ocular surface inflammation including marginal keratitis, or phlyclenules. The minimal effective dose of corticosteroid should be utilized and long-term corticosteroid therapy should be avoided if possible.
- An eyelid tumor should be suspected in patients with atypical eyelid-margin inflammation or disease not responsive to medical therapy, and these patients should be carefully re-evaluated

#### **Follow-Up Evaluation**

- Follow-up visits should include:
  - Interval history
  - Measurement of visual acuity
  - External examination
  - Slit-lamp biomicroscopy
- If corticosteroid therapy is prescribed, re-evaluate patient within a few weeks to determine the response to therapy, measure intraocular pressure, and assess treatment compliance

- Counsel patients about the chronicity and recurrence of the disease process
- Inform patients that symptoms can frequently be improved but are rarely eliminated
- Patients with an inflammatory eyelid lesion that appears suspicious for malignancy should be referred to an appropriate specialist

- Ocular symptoms and signs (e.g., conjunctival infection, mattering and adherence of eyelids, itching, tearing, discharge, irritation, pain, photophobia, blurred vision)
- Duration of symptoms and time course
- Exacerbating factors
- Unilateral or bilateral presentation
- Character of discharge
- Recent exposure to an infected individual
- Trauma: mechanical, chemical, ultraviolet
- Recent surgery
- Mucus fishing behavior (i.e., repetitive manipulation and wiping of the conjunctiva leading to mechanical irritation)
- Contact lens wear (lens type, hygiene and use regimen)
- Symptoms and signs potentially related to systemic diseases (e.g., genitourinary discharge, dysuria, dysphagia, upper respiratory infection, skin and mucosal lesions)
- Allergy, asthma, eczema
- Use of topical and systemic medications
- Ocular history (e.g., previous episodes of conjunctivitis, concomitant ocular surface diseases, and previous ophthalmic surgery)
- Compromised immune status (e.g., Human Immunodeficiency Virus, chemotherapy, immunosuppressents)
- Current and prior systemic diseases (e.g., atopy, Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis, carcinoma, leukemia, chickenpox, graftversus-host disease), vaccination history
- Social history: smoking habits, exposure to secondhand smoke, occupation and hobbies, exposure to air pollutants, travel, exercise habits, diet, sexual activity, and use of illicit drugs

## **Initial Physical Exam**

- Visual acuity
- External examination
  - Regional lymphadenopathy, particularly preauricular
  - Skin
  - Eyelids and adnexae
  - Orbits
  - Conjunctiva

- Slit-lamp biomicroscopy
  - Eyelid margins
  - Eyelashes
  - Lacrimal puncta and canaliculi
  - Tarsal and forniceal conjunctiva
  - Bulbar conjunctiva/limbus
  - Cornea
  - Dye-staining pattern
  - Anterior chamber/iris

#### **Diagnostic Tests**

- Cultures are indicated in all cases of suspected infectious neonatal conjunctivitis
- Cultures and antibiotic susceptibility testing may be helpful for recurrent, severe, or chronic purulent conjunctivitis in any age group and where conjunctivitis has not responded to medication
- Smears for cytology and special stains are recommended in cases of suspected infectious neonatal conjunctivitis, chronic or recurrent conjunctivitis, and gonococcal conjunctivitis in any age group
- Confirm diagnosis of adult and neonate chlamydial conjunctivitis with laboratory testing
- Conjunctival biopsy and immunofluorescent staining diagnostic tests may be helpful when ocular mucous membrane pemphigoid or paraneoplastic syndrome is suspected
- A full-thickness lid biopsy is indicated in cases of suspected sebaceous carcinoma
- Thyroid antibody tests are indicated for patients with superior limbic keratoconjunctivitis who do not have known thyroid disease

# **Conjunctivitis (Management Recommendations)**

#### **Care Management**

- The majority of cases in the adult population are viral and self-limited, and do not require antimicrobial treatment. There is no proven effective treatment for eradication of adenoviral infection; artificial tears, topical antihistamines, topical corticosteroids, oral analgesics or cold compresses may mitigate symptoms. The use of antibiotics should be avoided because of potential adverse treatment effects.
- Allergen-specific immunotherapy is beneficial in reducing allergic conjunctivitis, more so in children than in adults
- Treat mild allergic conjunctivitis with an over-thecounter antihistamine/vasoconstrictor agent or second-generation topical histamine H1-receptor antagonists. If the condition is frequently recurrent or persistent, mast-cell stabilizers can be used. New medications combine antihistamine activity with mast-cell stabilizing properties.
- Treatment for vernal conjunctivitis include modifying the environment and use of cold compresses and ocular lubricants. For acute exacerbations, topical corticosteroids are usually needed to control severe symptoms. (*I-*, MQ, SR)
- For contact lens-related keratoconjunctivitis, discontinue contact lens wear until the cornea returns to normal. In mild cases, a brief course of topical corticosteroids, in addition to longer-term use of topical cyclosporine can be considered.
- Use systemic antibiotic treatment for conjunctivitis due to *Neisseria gonorrhoeae* or *Chlamydia trachomatis*
- Treat sexual partners to minimize recurrence and spread of disease when conjunctivitis is associated with sexually transmitted diseases and refer patients and their sexual partners to an appropriate medical specialist
- Refer patients with manifestation of a systemic disease to an appropriate medical specialist

#### **Follow-Up Evaluation**

- Follow-up visits should include
  - Interval history
  - Visual acuity
  - Slit-lamp biomicroscopy
- If corticosteroids are used, perform baseline and periodic measurement of IOP and pupillary dilation to evaluate for glaucoma and cataract

- Counsel patients with contagious varieties to minimize or prevent spread of disease and encourage minimization of contact with other people for 10 to 14 days after onset of symptoms in the community
- Inform patients who may require repeat short-term therapy with topical corticosteroid of potential complications of corticosteroid use
- Advise patients with allergic conjunctivitis that hypoallergenic bedding, eyelid cleansers to remove allergens, frequent clothes washing and bathing/ showering before bedtime may be helpful

- Disease onset and course: varies with type and degree of thinning disorder
- Vision (degree of impairment): varies with degree of findings on topography and tomography
- Ocular history: changes in glasses prescription, especially one eye more than the fellow eye, type and duration of contact lens wear, noting stability and comfort of lens, history of keratorefractive surgery
- Medical history: history of atopy associated with eye rubbing, asthma and hay fever
- Family history: first-degree relatives with keratoconus, genetic syndromes such as Down syndrome, Leber congenital amaurosis, Ehlers-Danlos syndrome, and Noonan syndrome

#### **Initial Physical Exam**

- Visual function assessment
- External examination
  - Eyelid skin
- Slit-lamp biomicroscopy
  - Presence, extent, and location of corneal thinning or protrusion
  - Evidence of previous ocular surgery
  - Vogt striae
  - Prominent corneal nerves
  - Fleischer ring
  - Evidence of corneal scarring or previous hydrops
- IOP measurement
- Fundus examination: assessment of red reflex for dark area, and retina for tapetoretinal degenerations

## **Diagnostic Tests**

- Keratometry
- Corneal topography and tomography
  - Topographic power map
- Tomographic elevation map
- Optical coherence tomography

#### **Care Management**

- Therapy is tailored to the individual patient, depending on the visual impairment and a risk/ benefit analysis of each treatment option
- Vision can be corrected with eyeglasses, but contact lenses may be required as keratoconus progresses to correct vision and reduce distortion

- Rigid corneal gas permeable (RGP) contact lenses can mask corneal irregularities. Hybrid contact lenses provide higher oxygen permeability and greater RGP/hydrogel junction strength. Piggyback contact lenses may be employed for greater comfort and less epithelial disruption. Scleral lenses may be useful when other contact lenses fail to achieve a good fit due to lens decentration.
- Corneal cross-linking (CXL) has long term data supporting its safety and stability and should be considered for patients in early stages of progressive keratoconus
- Intrastromal corneal ring segment implantation can improve uncorrected and corrected visual acuity, reduce high-order corneal aberrations, and facilitate fitting of contact lenses. They are not indicated in subclinical disease and don't alter disease progression.
- Lamellar keratoplasty using deep anterior lamellar keratoplasty can be considered for contact-lensintolerant patients or patients with inadequate visual function. The benefit is that it preserves the host endothelial layer and has less stringent tissue requirements than penetrating keratoplasty.
- Persistent corneal edema following hydrops is an indication for full-thickness keratoplasty. Penetrating keratoplasty (PK) may be preferred over DALK in cases of deep stromal scarring in which perforation is more likely to occur during deep lamellar resection.
- A lamellar graft can be performed for tectonic support as a primary procedure when ectasia occurs in the far periphery of the cornea and additional PK can be performed for visual rehabilitation

#### **Follow-Up Evaluation**

- Follow-up visits should include:
  - Interval history
  - Visual acuitv
  - External examination
  - Slit-lamp biomicroscopy
  - Assessment of corneal contour and thickness by topography and tomography
- With the advent of CXL, more frequent follow-up (i.e., 3-6 months) for progression is now indicated. Younger patients may need to be followed even more frequently.

# Corneal Ectasia (Initial and Follow-up Evaluation) (continued)

- Counsel all patients to avoid eye rubbing
- Discuss the benefits and potential risks of early crosslinking in patients at high risk for progression or who historically have noted progressive loss of vision
- Patients undergoing corneal transplantation should be made aware of the warning signs of rejection and should seek medical attention promptly if symptoms occur. The practitioner should be aware of the slit-lamp biomicroscopic findings of epithelial, stromal, and endothelial rejection.

# **Corneal Edema and Opacification (Initial Evaluation)**

#### **Initial Exam History**

- Symptoms and signs: blurred or variable vision often with a diurnal character; photophobia; redness; tearing; intermittent foreign body sensation; intense, disabling, or task-disrupting pain
- Recent history of other ocular surgery
- Age of onset
- Rapidity of onset: acute symptoms vs. gradual or fluctuating
- Persistence: transient or permanent
- Unilateral or bilateral presentation
- Moderating factors or situations
- Past ocular and medical history
- Topical and systemic medications
- Trauma: blunt or penetrating injury to eye or periocular region, forceps delivery, chemical injury
- Contact lens wear: type of lens, wear time, and cleaning routine
- Family and social history

#### **Initial Physical Exam**

- Visual acuity
  - Comparison of visual acuity measurement and functional status
  - Glare testing
- External examination
  - Evidence of proptosis, ptosis, lagophthalmos, or floppy eyelid syndrome
  - Eyelid or facial asymmetry, scarring, and malfunction
  - Miscellaneous (e.g., pupil responses, corneal diameter, dry eye evaluation)

- Slit-lamp biomicroscopy
  - Unilateral or bilateral abnormalities
  - Diffuse or localized edema
  - Primarily epithelial or stromal edema
  - Evidence of epithelial breakdown, stromal infiltration, epithelial ingrowth, striae, focal thickening, thinning, scarring, interface haze, inflammation, or stromal vascularization or deposits
  - Evidence of guttae, Descemet's membrane tear or detachment, endothelial vesicles, keratic precipitates (KP), pigment, peripheral anterior synechiae
  - Selective involvement of host or donor tissue, if there is a corneal transplant
  - Evidence of sectoral corneal edema and a cluster line of KP, or an anterior chamber reaction
  - Status, shape, and position of the pupil and iris
  - Status and position of the crystalline lens or IOL and any other intraocular device
  - Evidence of past keratorefractive procedures
  - Healed or recent corneoscleral wounds, areas of scleral thinning associated with previous surgery, surgical devices, and signs of intraocular inflammation
- IOP measurement
- Fundus examination
- Gonioscopy

#### **Diagnostic Tests**

- Genetic testing
- Potential acuity testing
- Contact lens over-refraction
- Pachymetry
- Topography/tomography
- Specular microscopy
- Confocal microscopy
- Anterior segment optical coherence tomography
- Ultrasound biomicroscopy

# Corneal Edema and Opacification (Management Recommendations)

#### **Care Management**

- Therapeutic goal is to control the cause of corneal edema or opacity and enhance a patient's quality of life by improving visual acuity and comfort
- In most cases treatment starts with medical management, when this is insufficient, surgery may be considered
- Corneal edema: medical management
  - Lowering an elevated IOP is helpful
  - Topical carbonic anhydrase inhibitors should not be the first line of therapy when endothelial dysfunction is suspected
  - Topical corticosteroid can control inflammation once infection has been ruled out or controlled
  - Microcystic or bullous epithelial disease may produce discomfort or pain necessitating the placement of a bandage contact lens. Thin lenses with high water content and high oxygen diffusion coefficients may be safest.
  - Supportive management should be initiated to reduce inflammation and/or pain in cases of acute hydrops
- Corneal edema: surgical management
  - Patients with corneal edema and persistent discomfort, but limited or no visual potential, are generally better candidates for the following procedures:
    - Conjunctival flap
    - Amniotic membrane tissue transplantation
    - A number of scarification procedures
  - For patients with corneal edema and reduced vision or significant pain due to bullous keratopathy, a number of keratectomy and keratoplasty procedures can be considered
- Corneal opacification: medical management
  - Corneal opacity treatment can be divided into two phases: a) management of the principal, initiating process (i.e., infection, trauma), and b) management of the resulting problems (i.e., surface erosions and irregularity, scarring, thinning, and vascularization)
  - Conventional treatment involves an antibiotic drop or ointment to protect against secondary bacterial infection
  - Temporary tarsorrhaphy with botulinum toxin, or suture can be helpful when blinking or eyelid closure is inadequate
  - A bandage contact lens or amniotic membrane may be helpful in cases of delayed healing
  - Pressure patching used to be standard treatment, but a study found that this does not positively impact comfort or speed of healing

- Progressive thinning of cornea or a small perforation usually requires structural support with application of a tissue adhesive
- Topical corticosteroids are often used to reduce intraocular and corneal inflammation. IOP and cataract formation should be monitored with long-term topical corticosteroid use.
- A rigid gas permeable lens or hybrid or scleral lens when greater stability is needed — will often improve vision when surface irregularity is a factor; such lenses may obviate the need for more invasive procedures
- Corneal opacification: surgical management
  - Surgical strategy for managing corneal opacities depends on the tissue layer(s) involved:
    - ° Lamellar keratoplasty may be indicated for removal of deeper deposits
    - Penetrating keratoplasty may be indicated for removal of even deeper multilevel opacities
    - Ethylenediaminetetraacetic acid (EDTA) may be used to remove calcific band keratopathy

## Follow-Up Evaluation

- In the management of corneal edema, new or worse pain, redness, photophobia, and/or vision can herald disruption of the ocular surface, infection, inflammation, recurrence, or worsening that prompts immediate medical attention
- In the management of corneal opacification, follow up to monitor corneal clarity and degree of surface irregularity is necessary
- Coexisting problems, particularly intraocular inflammation and IOP, need regular reassessment

- Provide an understanding of balanced expectations of the amount of visual function that can realistically be preserved or recovered and risk of complications
- Detailed discussion of the causes of edema or opacity, and various treatment options, is important
- When the disease process or management is complex, every effort should be made to counsel the patient regarding such challenges to allow for appropriate expectations and informed decisionmaking

- Ocular symptoms and signs (e.g., irritation, tearing, burning, stinging, dry or foreign body sensation, mild itching, photophobia, blurry vision, contact lens intolerance, redness, mucous discharge, increased frequency of blinking, eye fatigue, diurnal fluctuation, symptoms that worsen later in the day)
- Exacerbating conditions (e.g., air travel, decreased humidity, fans, prolonged visual efforts associated with decreased blink rate such as reading and digital devices, poorly fitted sleep apnea devices)
- Duration of symptoms
- Ocular history, including
  - Topical medications and their associated preservatives (e.g., artificial tears, eyewash, antihistamines, glaucoma medications, vasoconstrictors, corticosteroids, antiviral medications, homeopathic or herbal preparations)
  - Contact lens history
  - Allergic conjunctivitis
  - Ocular surgical history (e.g., prior keratoplasty, cataract surgery, keratorefractive surgery)
  - Ocular surface disease (e.g., herpes simplex virus, varicella zoster virus, ocular mucous membrane pemphigoid, aniridia)
  - Eyelid surgery (e.g. punctal cautery, prior ptosis repair, blepharoplasty, entropion/ectropion repair)
  - Bell's palsy, cranial nerve injury
  - Eye cosmetic use (e.g., eyeliner, eyelash growth products)

- Medical history, including
  - Digital screen use
  - Smoking or exposure to second-hand smoke
  - Dermatological diseases
  - Technique and frequency of facial washing including eyelid and eyelash hygiene
  - Seasonal allergies/atopy
  - Systemic inflammatory diseases
  - Other systemic conditions
  - Systemic medications
  - Trauma
  - Chronic viral infections
  - Nonocular surgery
  - Orbital radiation
  - Neurological conditions
  - Diet/nutrition
  - Gastrointestinal surgical history
- Nonocular symptoms

#### Initial Physical Exam

- Visual acuity
- External examination
  - Skin
  - Eyelids
  - Adnexa
  - Proptosis
  - Cranial nerve function
  - Hands
- Slit-lamp biomicroscopy
  - Tear film
  - Eyelashes
  - Anterior and posterior eyelid margins
  - Puncta
  - Conjunctiva
  - Cornea

# Dry Eye Syndrome (Management Recommendations)

#### **Diagnostic Tests**

- Aqueous tear production (Schirmer test)
- Fluorescein dye disappearance test/tear function index
- Fluorescein tear break-up time
- Ocular surface dye staining (e.g., fluorescein, lissamine, rose bengal)
- Lacrimal gland function
- Tear Osmolarity
- Matrix metalloproteinase-9

#### **Care Management**

- Treat any causative factors that are amenable to treatment as patients with dry eye symptoms often have many contributory factors
- Specific therapies may be chosen from any category (see Table) regardless of the level of disease severity, depending on physician experience and patient preference

#### **Follow-Up Evaluation**

- Purpose is to assess response to therapy as a basis for altering or adjusting treatment as necessary, to monitor for ocular surface damage, and to provide reassurance
- Frequency and extent will depend on the severity of disease, therapeutic approach and response to therapy

- Educate patients about the chronic nature of the disease and provide specific instructions for therapeutic regimens
- Periodically assess patient's compliance, understanding of the disease, benefits of treatment and potential complications, and re-inform patient as necessary
- Establish realistic expectations for effective management with patients
- Provide specific instructions for therapeutic regimens
- Reassess periodically the patient's compliance and understanding of the disease, benefits of treatment and potential complications and re-inform as necessary
- Refer patients with manifestation of a systemic disease to an appropriate medical specialist
- Effective treatment for dry eye should be achieved before keratorefractive surgery. Uncontrolled dry eye syndrome is a contraindication for keratorefractive surgery.

#### STAGED MANAGEMENT AND TREATMENT RECOMMENDATIONS FOR DRY EYE SYNDROME\*\*\*

#### Step 1

- Education on the condition, its management, treatment, and prognosis
- Modification of local environment
- Education regarding potential dietary modifications (including oral essential fatty acid supplementation)
- Identification and potential modification/elimination of offending systemic and topical medications
- Ocular lubricants of various types (if MGD is present, then consider lipid-containing supplements)
- Eyelid hygiene of various types and warm compresses

#### Step 2

If the above options are inadequate consider:

- Nonpreserved ocular lubricants to minimize preservative-induced toxicity
- Tea tree oil or lotilaner drop treatment for *Demodex* (if present), also off-label use of ivermectin 1% cream for *Demodex*
- Tear conservation
  - Punctal occlusion
  - Moisture chamber spectacles/goggles
- Overnight treatments (such as ointment or moisture chamber devices)
- In-office, physical heating and expression of the meibomian glands (including thermal pulsation devices)
- Prescription drugs to manage DED<sup>§</sup>
  - Topical antibiotic or corticosteroid applied to the lid margins short-term for anterior blepharitis (if present)
  - Topical corticosteroid (limited duration)
  - Topical secretagogues
  - Topical nonglucocorticoid immunomodulatory drugs (such as cyclosporine)
  - Topical LFA-1 antagonist drugs (such as lifitegrast)
  - Topical water-free lipophilic liquid (perfluorohexyloctane)
  - Nasal spray (such as varenicline), cholinergic neuroactivation via the trigeminal parasympathetic pathway
  - Oral macrolide or tetracycline antibiotics

#### Step 3

If the above options are inadequate consider:

- Oral secretagogues
- Autologous/allogeneic serum eye drops
- Platelet-rich plasma eye drops
- Blood based products
- Therapeutic contact lens options
  - Soft bandage lenses with caution
  - Rigid scleral lenses

#### Step 4

If the above options are inadequate consider:

- Topical corticosteroid for longer duration
- Amniotic membrane grafts
- Surgical punctal occlusion (punctal cautery)
- Other surgical approaches (e.g., tarsorrhaphy, minor salivary gland transplantation)

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DED = dry eye disease; LFA-a = lymphocyte function-associated antigen 1; MGD = meibomian gland dysfunction.

\* Potential variations within the disease spectrum are acknowledged to exist between patients and the management options listed above are not intended to be exclusive. The severity and etiology of the DED state will dictate the range and number of management options selected from one or more steps.

<sup>&</sup>lt;sup>+</sup> One or more options concurrently within each category can be considered within that step of the dry eye disease state. Options within a category are not ranked according to importance and may be equally valid.

<sup>‡</sup> It should be noted that the evidence available to support the various management options differs and will inevitably be lower for newer management options. Thus, each treatment option should be considered in accordance with the level of evidence available at the time management is instigated.

S The use of prescription drugs needs to be considered in the context of the individual patient presentation, and the relative level of evidence supporting their use for those specific indications, as this group of agents differs widely in mechanism of action.