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Conjunctivitis Preferred Practice Pattern®

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Preferred Practice Pattern® guidelines are developed by the Academy's H. Dunbar Hoskins Jr., MD Center for Quality Eye Care without any external financial support. Authors and reviewers of the guidelines are volunteers and do not receive any financial compensation for their contributions to the documents. The guidelines are externally reviewed by experts and stakeholders before publication.

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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 Conjunctivitis 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.

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The **Preferred Practice Patterns Committee** members reviewed and discussed the document during a meeting in June 2018. The document was edited in response to the discussion and comments.

Preferred Practice Patterns Committee 2018
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The Conjunctivitis PPP was then sent for review to additional internal and external groups and individuals in July 2018. 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.

FINANCIAL DISCLOSURES

In compliance with the Council of Medical Specialty Societies' Code for Interactions with Companies (available at 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 www.aao.org/about-preferred-practice-patterns). A majority (70%) of the members of the Cornea/External Disease Preferred Practice Pattern Panel 2017–2018 had no financial relationships to disclose.

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The disclosures of relevant relationships to industry of other reviewers of the document from January to October 2018 are available online at www.aao.org/ppp.

TABLE OF CONTENTS

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 www.aao.org/about-preferred-practice-patterns) 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 Conjunctivitis 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[1] (SIGN) and the Grading of Recommendations Assessment, Development and Evaluation[2] (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 Quality, and the American College of Physicians. [3]

- 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[1] 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[2] 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[2] 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. Ratings are embedded throughout the PPP main text in italics.
- Literature searches to update the PPP were undertaken in February 2017 and June 2018 in PubMed and the Cochrane Library. Complete details of the literature search are available at www.aao.org/ppp.

HIGHLIGHTED FINDINGS AND RECOMMENDATIONS FOR CARE

Conjunctivitis rarely causes permanent visual loss or structural damage, but the economic impact of conjunctivitis is considerable and largely due to lost work or school time and the cost of medical visits, testing and treatment.[4,5]

Chronic and/or recalcitrant conjunctivitis may be indicative of an underlying malignancy, such as sebaceous or squamous cell carcinoma.

The ophthalmologist plays a critical role in breaking the chain of transmission of epidemic adenoviral conjunctivitis, primarily by educating the patient and family about proper hygiene. Infected individuals should be counseled to wash hands frequently and use separate towels, and to avoid close contact with others during the period of contagion.

Dilute bleach soak (sodium hypochlorite) at 1:10 concentration is an effective disinfectant for tonometers.[6,7] Notably, 70% isopropyl alcohol (e.g., alcohol wipes), 3% hydrogen peroxide, and ethyl alcohol are no longer recommended for tonometer disinfection.[7]

Surfaces should be disinfected with an EPA-registered hospital disinfectant in accordance with the directions and safety precautions on the label.

Indiscriminate use of topical antibiotics or corticosteroids should be avoided. Viral conjunctivitis will not respond to anti-bacterial agents, and mild bacterial conjunctivitis is likely to be self-limited. No evidence exists demonstrating the superiority of any topical antibiotic agent.[8] [I+, Good, Strong]

In adults, conjunctivitis caused by ocular mucous membrane pemphigoid (OMMP), graft-versus-host disease (GVHD), gonococcus, and chlamydia are important to detect early because it is necessary to treat the concomitant systemic disorder. Diagnosis of superior limbic keratoconjunctivitis (SLK) may lead to further investigations that reveal a thyroid disorder. Early detection of conjunctivitis associated with neoplasms may be lifesaving.

Herpes Zoster vaccination should be strongly recommended in patients 50 years or older.[9]

INTRODUCTION

DISEASE DEFINITION

Conjunctivitis is an inflammation that primarily affects the conjunctiva.

PATIENT POPULATION

The patient population includes individuals of all ages who present with symptoms and signs suggestive of conjunctivitis, such as red eye or discharge.

CLINICAL OBJECTIVES

- Establish the diagnosis of conjunctivitis, differentiating it from other causes of red eye
- Identify the cause(s) of conjunctivitis
- Establish appropriate therapy
- Relieve discomfort and pain
- Prevent complications
- Prevent the spread of communicable diseases
- Educate and engage both the patient and the referring healthcare providers in conjunctivitis management

BACKGROUND

Conjunctivitis, or inflammation of the conjunctiva, is a general term that refers to a diverse group of diseases/disorders that affect primarily the conjunctiva. Most varieties of conjunctivitis are self-limited, but some progress and may cause serious ocular and extraocular complications.

Conjunctivitis can be classified as noninfectious or infectious and as acute, chronic, or recurrent. Noninfectious types of conjunctivitis include allergic, mechanical/irritative/toxic, immune-mediated, and neoplastic, and these types may overlap. The causes of infectious conjunctivitis include viruses and bacteria.

It is important to differentiate among primary conjunctival disease and conditions in which conjunctival inflammation is secondary to systemic or ocular diseases. For example, dry eye and blepharitis are the most frequent causes of conjunctival inflammation, and the treatment for each of these entities should be directed at correcting the underlying problems.[10,11] Systemic diseases such as gonorrhea or atopy may also cause conjunctival inflammation, and treatment of conjunctivitis must include addressing the underlying systemic disease.

This PPP addresses the following types of conjunctivitis that are either most common or are particularly important to detect and treat:

- Allergic
  - Seasonal/perennial allergic conjunctivitis
  - Vernal conjunctivitis
  - Atopic conjunctivitis
- Mechanical/irritative/toxic
  - Superior limbic keratoconjunctivitis (SLK)
  - Blepharoconjunctivitis
  - Keratoconjunctivitis sicca (dry eye)
  - Rosacea conjunctivitis
  - Contact lens–related keratoconjunctivitis
  - Giant papillary conjunctivitis (GPC)
  - Floppy eyelid syndrome
  - Giant fornix syndrome
  - Pediculosis palpebrarum (*Phthirus pubis*)
  - Medication-induced/preservative-induced keratoconjunctivitis
  - Conjunctival chalasis
- Immune-mediated
  - Ocular mucous membrane pemphigoid (OMMP)
  - Graft-versus-host disease (GVHD)
  - Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN)
  - Graves disease ophthalmopathy
  - Vasculitis
- Neoplastic
  - Sebaceous carcinoma
  - Ocular surface squamous neoplasia
  - Melanoma
- Viral
  - Adenoviral conjunctivitis
  - Herpes simplex virus (HSV) conjunctivitis
  - Varicella (herpes) zoster virus (VZV) conjunctivitis
  - Molluscum contagiosum
- Bacterial

- Bacterial conjunctivitis (including nongonococcal and gonococcal)
- Chlamydial conjunctivitis

- Other
  - Ligneous conjunctivitis

PREVALENCE AND RISK FACTORS

Conjunctivitis is a diagnosis that encompasses a diverse group of diseases that occur worldwide and affect all ages, all social strata, and both genders. Although there are no reliable figures that document the incidence or prevalence of all forms of conjunctivitis, this condition has been cited as one of the most frequent causes of patient self-referral.[12] Conjunctivitis infrequently causes permanent visual loss or structural damage, but the economic impact of the disease in terms of lost work and school time, cost of medical visits, diagnostic testing, and medication is considerable.[4,5]

The risk factors for developing conjunctivitis depend on the etiology. The associated and predisposing factors for the types of conjunctivitis that are most common or most important to treat are listed in Table 1. Symptoms may be exacerbated by the coexistence of blepharitis, dry eye, or other causes of ocular surface inflammation.

NATURAL HISTORY

The natural history of each type of conjunctivitis depends on its etiology. Table 1 lists the natural history for the types of conjunctivitis that are most common or most important to treat.

TABLE 1 TYPICAL CLINICAL SIGNS OF, ASSOCIATED/PREDISPOSING FACTORS FOR, AND NATURAL HISTORY OF CONJUNCTIVITIS

Type of Conjunctivitis	Clinical Signs	Associated/Predisposing Factors	Natural History	Potential Sequelae
Allergic				
Seasonal/perennial	• Bilateral. Eyelid edema, periorbital hyperpigmentation (allergic shiners), conjunctival injection, chemosis, watery discharge, mild mucous discharge	• Environmental allergens (e.g., grasses, pollens) • Outdoor air pollution, secondary to fuel combustion, dust storms, truck traffic, mine dumps and industrial parks, pre- and postnatal exposure to environmental tobacco smoke[13-16] • Exposure to dogs, cats, farm animals[17]	• Recurrent, often associated with allergic rhinitis, dry eye, meibomian gland dysfunction (MGD) with mucin hyperproduction[18,19]	• Minimal, local
Vernal	• Bilateral. Giant papillary hypertrophy of superior tarsal conjunctiva, bulbar conjunctival injection, conjunctival scarring, watery and stringy mucoid discharge, limbal Horner-Trantas dots, limbal "papillae," corneal epithelial erosions, corneal neovascularization and scarring, corneal vernal plaque/shield ulcer	• Hot, dry environments such as West Africa; parts of India, Mexico, Central, North, and South America; and the Mediterranean region • May be associated with deficiencies of growth hormone, sex-hormone binding globulin, and dihydrotestosterone, or high levels of estrone[20,21] • Environmental allergens for acute exacerbations • Associated with a higher incidence of keratoconus	• Onset in childhood; chronic course with acute exacerbations during spring and summer. Gradual decrease in activity within 2 to 20 years. • Vernal keratoconjunctivitis (VKC)-like disease noted in young adults without history of childhood allergic disease[22]	• Eyelid thickening; ptosis; conjunctival scarring (predominantly superior tarsal); corneal neovascularization, thinning, ulceration, infection; visual loss; limbal stem cell deficiency, corticosteroid-induced cataract and glaucoma[23] • Adult VKC with diffuse subepithelial thickening of tarsal plate without giant papillae, lower rate of corneal shield ulcers (less common than in children)
Atopic	• Bilateral. Eczematoid blepharitis; eyelid thickening, scarring; lash loss; papillary hypertrophy of superior and inferior tarsal conjunctiva; conjunctival injection and scarring; watery and stringy mucoid discharge; boggy edema; corneal neovascularization, ulcers and scarring; punctate epithelial keratitis. Can be associated with keratoconus and/or subcapsular cataract	• Genetic predisposition to atopy • Environmental allergens and irritants for acute exacerbations • Associated with a higher incidence of keratoconus	• Later (than vernal) onset; chronic course with acute exacerbations	• Eyelid thickening or tightening, loss of lashes; MGD; [24] conjunctival scarring/cicatrization (include inferior); corneal scarring, neovascularization, thinning, infection, ulceration; cataract; visual loss; increased risk of retinal detachment, herpes simplex keratitis,[25] limbal stem cell deficiency

TABLE 1 ASSOCIATED/PREDISPOSING FACTORS FOR, NATURAL HISTORY OF, AND TYPICAL CLINICAL SIGNS OF CONJUNCTIVITIS (CONTINUED)

Type of Conjunctivitis	Clinical Signs	Associated/Predisposing Factors	Natural History	Potential Sequelae
Mechanical/Irritative/Toxic				
Superior limbic keratoconjunctivitis (SLK)	• Bilateral superior bulbar injection, laxity, edema, and keratinization. Superior corneal and conjunctival punctate epitheliopathy, corneal filaments	• Frequently associated with dysthyroid states, female gender	• Subacute onset of symptoms, usually bilateral. May wax and wane for years	• Superior conjunctival keratinization, pannus, filamentary keratitis, chemosis
Blepharoconjunctivitis Keratoconjunctivis sicca	• Chronic with exacerbations. Anterior blepharitis affects the eyelid skin, base of the eyelashes, and the eyelash follicles. Posterior blepharitis causes MGD, tear film instability, concomitant dry eye. Bilateral, can be asymmetric • (See Dry Eye PPP[11])	• Anterior: staphylococcal, *Demodex*, seborrheic • Posterior: MGD • Angular: *Staphylococcus aureus, Moraxella lacunata*	• Chronic blepharitis with acute exacerbation of conjunctival injection. May have a history of recurrent chalazia	• Chronic blepharitis, conjunctivitis, keratitis, corneal neovascularization, ulceration, thinning, scarring, perforation[26]
Rosacea conjunctivitis	• Bilateral chronic blepharitis, eyelid margin telangiectasias, meibomian gland inspissation with excessive sebum secretion, conjunctival injection, evaporative dry eye, chalazia, corneal neovascularization, stromal scarring	• Lid margin telangiectasias, MGD, blepharitis, conjunctival hyperemia, injection, pannus (see Blepharitis PPP[27])	• Eyelid margin telangiectasias, meibomian gland inspissation with excessive sebum secretion, conjunctival hyperemia	• Evaporative dry eye, corneal neovascularization, stromal scarring. Can be associated with acne rosacea with characteristic malar rash, facial erythema, telangiectasias, papules, pustules, prominent sebaceous glands, rhinophyma

TABLE 1 ASSOCIATED/PREDISPOSING FACTORS FOR, NATURAL HISTORY OF, AND TYPICAL CLINICAL SIGNS OF CONJUNCTIVITIS (CONTINUED)

Type of Conjunctivitis	Clinical Signs	Associated/Predisposing Factors	Natural History	Potential Sequelae
Contact-lens–related keratoconjunctivitis	• Ranges from mild to diffuse conjunctival injection, focal or diffuse corneal neovascularization, peripheral or circumferential corneal neovascularization, focal or diffuse superficial punctate keratopathy. Papillary hypertrophy of tarsal conjunctivitis is variable. May result in limbal stem cell deficiency	• Occurs in association with contact lens wear as reaction to mechanical irritation, chronic hypoxia, or preservatives	• Subacute to acute onset of symptoms. May take months or longer to resolve with treatment and withdrawal of contact lenses	• Corneal neovascularization; superior epitheliopathy and corneal scarring; limbal stem cell deficiency; may progress centrally into the pupillary area
Giant papillary conjunctivitis (GPC)[19]	• Laterality associated with contact lens wear pattern. Papillary hypertrophy of superior tarsal conjunctiva, mucoid discharge. Papillae with white fibrotic centers can be seen in patients with long-standing disease. In severe cases: lid swelling, ptosis	• Contact lens wear (risk factors include soft contact lenses, infrequent lens replacement, prolonged wearing time, poor lens hygiene, allergenic contact lens solutions, high water content, or poor contact lens fit) • Also occurs with irritation from exposed sutures and prostheses	• Chronic gradual increase in symptoms and signs with contact lens wear, exposed corneal or scleral sutures, ocular prosthesis	• Tarsal scarring, ptosis
Floppy eyelid syndrome	• Upper eyelid edema; upper eyelid easily everted, sometimes by simple elevation or lifting of lid; diffuse papillary reaction of superior tarsal conjunctiva; punctate epithelial keratopathy; pannus; mild discharge. Bilateral, often asymmetric	• Obesity, sleep apnea, upper-eyelid laxity, upper-eyelid excursion over lower eyelid (eyelid imbrication). Increased risk of keratoconus[28]	• Chronic ocular irritation due to nocturnal eyelid ectropion causing upper-tarsal conjunctiva to come in contact with bedding	• Punctate epithelial keratitis; corneal neovascularization, ulceration, and scarring
Giant fornix syndrome	• Enlarged superior fornix with coagulum of mucopurulent material, ptosis	• Elderly women (eighth to tenth decade), upper-eyelid ptosis with large superior fornix, which holds coagulum of mucopurulent material[29,30]	• Chronic mucopurulent conjunctivitis, which waxes and wanes with typical short courses of topical antibiotic therapy	• Ptosis, superior hyperemia, chronic conjunctivitis, large superior fornix with coagulum of mucopurulent material

TABLE 1 ASSOCIATED/PREDISPOSING FACTORS FOR, NATURAL HISTORY OF, AND TYPICAL CLINICAL SIGNS OF CONJUNCTIVITIS (CONTINUED)

Type of Conjunctivitis	Clinical Signs	Associated/Predisposing Factors	Natural History	Potential Sequelae
Pediculosis palpebrarum (*Phthirus pubis*)	• Unilateral or bilateral follicular conjunctivitis. Adult lice at the base of the eyelashes, nits (eggs) adherent to the eyelash shafts, blood-tinged debris on the eyelashes and eyelids	• Typically, sexually transmitted. May have associated pubic lice or other sexually transmitted diseases. In children, may be an indication of sexual abuse	• Blepharitis and conjunctivitis persist until treated	• Chronic blepharitis, conjunctivitis, and, rarely, marginal keratitis
Medication-induced/preservative - induced keratoconjunctivitis	• Laterality based on drug use. Conjunctival injection, punctal edema, inferior fornix and bulbar conjunctival follicles • Distinctive signs: contact dermatitis of eyelids with erythema, scaling in some cases	• Glaucoma medications, topical nonsteroidal anti-inflammatory drugs (NSAIDs), antibiotics, antivirals, others; may be associated with preservatives in all eye medications. Most common with multiple eye medications and/or frequent dosing	• Gradual worsening with continued use	• Corneal epithelial erosion, persistent epithelial defect, corneal ulceration, pannus, corneal and conjunctival scarring, punctal occlusion
Conjunctival chalasis	• Redundant conjunctiva	• Previous eye surgery • Dry eye • Redundant conjunctiva	• Redundant conjunctiva, chronic irritation, may follow previous chemosis	• Chronic irritation, dry eye keratitis

TABLE 1 ASSOCIATED/PREDISPOSING FACTORS FOR, NATURAL HISTORY OF, AND TYPICAL CLINICAL SIGNS OF CONJUNCTIVITIS (CONTINUED)

Type of Conjunctivitis	Clinical Signs	Associated/Predisposing Factors	Natural History	Potential Sequelae
Immune mediated				
Ocular mucous membrane pemphigoid (OMMP)	• Bilateral, often asymmetric. Bulbar conjunctival injection, papillary conjunctivitis, conjunctival subepithelial fibrosis and keratinization, conjunctival scarring beginning in the fornices, punctal stenosis and keratinization, progressive conjunctival shrinkage, symblepharon, entropion, trichiasis, corneal ulcers/perforation, neovascularization, and scarring	• Unknown (genetic predisposition may exist) • Topical drugs may produce OMMP-like disease, with spectrum of severity ranging from self-limited to progressive disease indistinguishable from OMMP. Associated drugs include pilocarpine and timolol. Cicatrizing conjunctivitis appearing similar to OMMP can be associated with other disorders including atopic disease and underlying neoplasms, such as paraneoplastic pemphigus and paraneoplastic lichen planus.[31]	• Onset generally over age 60 with goblet cell loss and mucin deficiency. Progressive chronic course, sometimes with remissions and exacerbations	• Conjunctival scarring and shrinkage with forniceal foreshortening; ankyloblepharon, symblepharon; trichiasis; corneal scarring, neovascularization, ulceration, perforation; ocular surface keratinization; bacterial conjunctivitis; cicatricial lid changes; severe tear deficiency; limbal stem cell deficiency; severe vision loss. May involve mucous membranes of the oral cavity, nasopharynx, larynx, esophagus, genitourinary tract, and anus
Graft-versus-host disease (GVHD)	• Bilateral. Conjunctival injection, chemosis, pseudomembranous conjunctivitis, keratoconjunctivitis sicca, superior limbic keratoconjunctivitis, cicatricial eyelid disease, episcleritis, corneal epithelial sloughing, limbal stem cell failure, calcareous corneal degeneration; rare intraocular involvement	• Patients who have undergone allogeneic stem cell transplantation	• Can involve multiple tissues including skin, liver, gastrointestinal system, lung, and eye. Graft-versus-host disease may follow acutely within the first 3 months following hematopoietic stem cell transplantation, but ocular disease is more common in the chronic phase	• Conjunctivitis; subconjunctival fibrosis; symblepharon; lacrimal gland involvement; keratoconjunctivitis sicca; cicatricial lid disease. Less commonly limbal stem cell deficiency, corneal scarring, or intraocular involvement

TABLE 1 ASSOCIATED/PREDISPOSING FACTORS FOR, NATURAL HISTORY OF, AND TYPICAL CLINICAL SIGNS OF CONJUNCTIVITIS (CONTINUED)

Type of Conjunctivitis	Clinical Signs	Associated/Predisposing Factors	Natural History	Potential Sequelae
Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN)	• Unilateral or bilateral. Bulbar conjunctival injection, conjunctival subepithelial fibrosis and keratinization, conjunctival scarring, punctal stenosis and keratinization, progressive conjunctival shrinkage, symblepharon, entropion, trichiasis, corneal ulcers/perforation, neovascularization, and scarring	• Genetic predisposition[32] • Prior infection (e.g., HSV, mumps, mycoplasma pneumoniae) • Systemic medications (e.g., sulfonamides, barbiturates, or phenytoin) produce inflammation and cicatricial changes of the various mucous membranes of the body including the bulbar and palpebral conjunctiva	• Severe mucocutaneous reaction with epidermal necrosis and may involve the various mucous membranes including the gastrointestinal system, lung and eye following the systemic use of sensitizing medication or infectious agents	• Conjunctival scarring and shrinkage with goblet cell loss and mucin deficiency; symblepharon; trichiasis; corneal scarring, neovascularization, ulceration; limbal stem cell deficiency; ocular surface keratinization; bacterial conjunctivitis; cicatricial lid changes; severe tear deficiency; severe vision loss
Thyroid eye disease	• Bilateral, but may be asymmetric. Edema and erythema of the periorbital tissues and conjunctivae, upper eyelid retraction, exposure keratopathy, extraocular-muscle enlargement, proptosis	• Majority of patients have Graves' disease (hyperthyroidism); also associated with normal-functioning or under-functioning thyroid (e.g., Hashimoto's thyroiditis) • Family history of thyroid eye disease or other thyroid disorders is a risk factor • Cigarette smoking or exposure to tobacco smoke, low blood levels of selenium, thyroid hormone levels may be affected by increased stress levels	• Associated with hyperthyroidism, most often occurs simultaneously or within 18 months of each other, although ophthalmopathy may precede or follow the onset of hyperthyroidism by many years	• Corneal ulceration, restrictive strabismus/diplopia, compressive optic neuropathy; globe subluxation

Vasculitis	• Unilateral or bilateral. Conjunctivitis,[33] conjunctival nodules,[34] or granuloma, symblepharon and/or cicatrization,[35] proptosis, restrictive myopathy, episcleritis, necrotizing scleritis,[36] peripheral ulcerative keratitis,[37] keratic precipitates, corneal ulcers,[38] iris nodules, trabecular meshwork nodules, peripheral anterior synechiae,[39] uveitis, choroidal granulomas, vitreous opacities, optic disc swelling[40]	• Sarcoidosis, granulomatosis with polyangiitis (granulomatosis with polyangiitis), Kawasaki disease, microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome), vasculitis secondary to infection, drug-induced vasculitis (methamphetamine, intravenous immunoglobulins, opioids, hydralazine, antifibrotics, antibiotics, leukotrienes),[41] or vasculitis associated with malignancies	• Sarcoidosis (bimodal age of presentation, with the highest incidence reported between ages 20 and 39[42]), Wagner syndrome, Kawasaki disease (primarily affects children, fever of 5 days or more, red, swollen tongue [strawberry tongue], cervical lymphadenopathy, swollen, red skin on the palms of the hands and the soles of the feet, polymorphous rash, irritability), linear IgA disease, mucous membrane pemphigoid	• Often involves multiple vessels, including the lungs, lymph nodes, kidneys, skin, nervous system • Coronary artery aneurysm is a lethal complication of Kawasaki disease

TABLE 1 ASSOCIATED/PREDISPOSING FACTORS FOR, NATURAL HISTORY OF, AND TYPICAL CLINICAL SIGNS OF CONJUNCTIVITIS (CONTINUED)

Type of Conjunctivitis	Clinical Signs	Associated/Predisposing Factors	Natural History	Potential Sequelae
Neoplastic				
Sebaceous carcinoma	• Unilateral. Intense bulbar conjunctival infection, conjunctival scarring. May have a mucopurulent discharge. Corneal epithelial invasion may occur • Eyelids may exhibit a hard nodular, nonmobile mass of the tarsal plate with yellowish discoloration; may appear as a subconjunctival, multilobulated yellow mass, may resemble a chalazion	• Unknown (rarely follows radiation therapy)	• Occurs in fifth to ninth decades of life with fairly rapid progression[43]	• Orbital invasion, regional or distant metastases, melanoma
Ocular surface squamous neoplasia	• Conjunctival hyperemia, papillomatous or sessile nodules	• Associated with human papillomavirus (HPV); associated with significant exposure to ultraviolet (UV) light; long-standing chronic inflammation may be associated[44]	• May be history of HPV, significant UV exposure, chronic inflammation; may be mistreated as an unresponsive blepharoconjunctivitis	• Conjunctival hyperemia, carcinoma in situ, or ocular surface squamous neoplasia, which can be locally invasive with regional metastases
Melanoma	• Painless, flat or nodular, brown or white-pink lesion on the bulbar or palpebral conjunctiva or caruncle. Enlargement of the lesion, blood vessels or thickening, often trigger an office visit	• Significant UV exposure, previous history of melanoma, previous primary acquired melanosis or Nevus of Ota	• Tends to spread to other adnexal structures and metastasize	• Pigmented or nonpigmented lesion, invasive regional metastases, history of previous melanoma, primary may not be conjunctiva

TABLE 1 ASSOCIATED/PREDISPOSING FACTORS FOR, NATURAL HISTORY OF, AND TYPICAL CLINICAL SIGNS OF CONJUNCTIVITIS (CONTINUED)

Type of Conjunctivitis	Clinical Signs	Associated/Predisposing Factors	Natural History	Potential Sequelae
Viral				
Adenoviral	• Abrupt onset. Unilateral or bilateral (often sequentially bilateral). Varies in severity. Bulbar conjunctival injection, watery discharge, follicular reaction of inferior tarsal conjunctiva, chemosis, eyelid swelling, and erythema • Distinctive signs: preauricular lymphadenopathy, petechial and subconjunctival hemorrhage, corneal epithelial defect, multifocal epithelial punctate keratitis evolving to anterior stromal keratitis, membrane/pseudomembrane formation, eyelid ecchymosis	• Exposure to infected individual (especially in school setting), recent ocular testing, concurrent upper respiratory infection	• Self-limited, with improvement of symptoms and signs within 5–14 days	• Mild cases: none. Severe cases: conjunctival scarring, symblepharon, keratitis, and subepithelial corneal infiltrates from epidemic keratoconjunctivitis (EKC), corneal scarring
Herpes simplex virus (HSV)	• Usually unilateral. Bulbar conjunctival injection, watery discharge, mild follicular reaction of conjunctiva. May have palpable preauricular node. Can be bilateral in atopic or immunocompromised patients[45,46] • Distinctive signs: vesicular rash or ulceration of eyelids, pleomorphic or excavated dendritic epithelial keratitis of cornea or conjunctiva	• Prior infection with HSV: trigger for reactivation may include stress, other acute viral or febrile illnesses, ultraviolet exposure, surgery, or trauma • Primary HSV infection: exposure to infected individual	• Usually subsides without treatment within 4–7 days unless complications occur	• Epithelial conjunctivitis and/or blepharitis, endotheliitis, keratitis, stromal keratitis, neovascularization, scarring, thinning, perforation, uveitis, trabeculitis, retinitis, corneal edema

Varicella (herpes) zoster virus (VZV)	• Usually unilateral or bilateral. Bulbar conjunctival injection, watery discharge, mild follicular reaction of conjunctiva. May have palpable preauricular node. Typically, punctate keratitis in primary disease; punctate or dendritic keratitis in recurrent disease • Distinctive signs: vesicular dermatomal rash or ulceration of eyelids, pleomorphic or nonexcavated pseudodendritic epithelial keratitis of cornea or conjunctiva	• Acute chicken pox, exposure to an individual with active chicken pox or recurrent VZV (shingles)	• Primary infection (chicken pox), as well as conjunctivitis from recurrent infection, usually subsides in a few days. Vesicles can form at the limbus, especially in primary infection	• Necrosis and scarring from vesicles on the eyelid margins, conjunctiva, and in the corneal stroma in primary disease in children. Conjunctival scarring from secondary infection can lead to cicatricial ectropion. In recurrent disease, keratitis of the epithelium or stroma with subsequent scarring and late corneal anesthesia or dry eye, retinitis
Molluscum contagiosum	• Typically unilateral, but can be bilateral. Mild to severe follicular reaction, punctate epithelial keratitis. May have corneal pannus, especially if long-standing • Distinctive signs: single or multiple shiny, dome-shaped umbilicated lesion(s) of the eyelid skin or margin	• Predominantly older children and young adults. Immunocompromised state (e.g., HIV) may predispose to multiple and/or large molluscum lesions on the lids or paraoculare • Associated with follicular conjunctivitis	• Conjunctivitis is associated with eyelid lesions, which can spontaneously resolve or persist for months to years	• Conjunctival scarring, epithelial keratitis, pannus; less commonly, subepithelial infiltrates/haze/scar, occlusion of the puncta, follicular conjunctivitis

TABLE 1 ASSOCIATED/PREDISPOSING FACTORS FOR, NATURAL HISTORY OF, AND TYPICAL CLINICAL SIGNS OF CONJUNCTIVITIS (CONTINUED)

Type of Conjunctivitis	Clinical Signs	Associated/Predisposing Factors	Natural History	Potential Sequelae
Bacterial				
Nongonococcal	• Unilateral or bilateral. Bulbar conjunctival injection, purulent or mucopurulent discharge • See age stratification of associated/predisposing factors below		• Mild: self-limited in adults. May progress to complications in children • Severe: may persist without treatment, rarely hyperacute	• Rare, but possibly corneal infection, preseptal cellulitis • Corneal infection; may be associated with pharyngitis, otitis media, meningitis
Gonococcal	• Unilateral or bilateral. Marked eyelid edema, marked bulbar conjunctival injection, marked purulent discharge, preauricular lymphadenopathy • Important sign to detect: corneal infiltrate or ulcer, which often begins superiorly, may lead to corneal perforation • See age stratification of associated/predisposing factors below		• Neonate: manifests within 1–7 days after birth, later if a topical antibiotic was used. Rapid evolution to severe, purulent conjunctivitis • Adult: rapid development of severe hyperpurulent conjunctivitis	• Neonate: corneal infection, corneal scarring, corneal perforation, septicemia with arthritis, meningitis • Adult: corneal infection, corneal scarring, corneal perforation, urethritis, pelvic inflammatory disease, septicemia, arthritis
Neonate		• Vaginal delivery by infected mother; inadequate prenatal care		
Infant		• Nasolacrimal duct obstruction, concomitant bacterial otitis media or pharyngitis, exposure to infected individual		

TABLE 1 ASSOCIATED/PREDISPOSING FACTORS FOR, NATURAL HISTORY OF, AND TYPICAL CLINICAL SIGNS OF CONJUNCTIVITIS (CONTINUED)

Type of Conjunctivitis	Clinical Signs	Associated/Predisposing Factors	Natural History	Potential Sequelae
Child		• Contact with infected individual; concomitant bacterial otitis media, sinusitis, or pharyngitis; nasopharyngeal bacterial colonization; oculogenital spread with sexual abuse		
Adult		• Contact with infected individual, oculogenital spread, unhygienic living conditions, infection or abnormality of adnexal structure, lid malposition, severe tear deficiency, immunosuppression, trauma		
Chlamydial (inclusion)	• Neonate/infant: unilateral or bilateral. Eyelid edema, bulbar conjunctival injection, discharge may be purulent or mucopurulent, no follicles • Adult: unilateral or bilateral. Follicular conjunctivitis, chemosis, papillary hypertrophy, corneal pannus, Herbert pits, conjunctival scarring, cicatricial entropion, trichiasis, limbal stem cell deficiency, corneal scarring/opacification	• Sexually transmitted • Caused by *Chlamydia trachomatis* serotypes D-K	• Neonate: manifests 5–19 days following birth, earlier if placental membranes have ruptured prior to delivery. Untreated cases may persist for 3–12 months • Adult: follicular conjunctivitis, papillary hypertrophy, corneal pannus	• Neonate: corneal scarring, conjunctival scarring; up to 50% have associated nasopharyngeal, genital, or pulmonary infection • Adult: Herbert pits, conjunctival scarring, cicatricial entropion, trichiasis, limbal stem cell deficiency, corneal scarring/opacification
Chlamydial (trachoma)	• Unilateral or bilateral. Bulbar conjunctival injection, follicular reaction of tarsal conjunctiva, mucoid discharge, corneal pannus, punctate epithelial keratitis, corneal opacity, entropion, trichiasis, preauricular lymphadenopathy • Distinctive sign: bulbar conjunctival follicles	• Caused by *C. trachomatis* serotypes A, B, and C • In developing world without adequate access to clean water and sanitation • Can be spread by direct or indirect contact with secretions from an affected person's eyes, nose, or throat	• Conjunctivitis with mucopurulent discharge, preauricular lymphadenopathy • May persist/recur if untreated	• Corneal infiltrates, pannus, cervicitis, urethritis, salpingitis, endometritis, perihepatitis

TABLE 1 ASSOCIATED/PREDISPOSING FACTORS FOR, NATURAL HISTORY OF, AND TYPICAL CLINICAL SIGNS OF CONJUNCTIVITIS (CONTINUED)

Type of Conjunctivitis	Clinical Signs	Associated/Predisposing Factors	Natural History	Potential Sequelae
Deficiency Disease (other)				
Ligneous conjunctivitis	• 50% of cases are bilateral, chronic, recurrent conjunctivitis with bilateral, mucoid discharge, tearing, conjunctival injection, followed by pseudomembrane formation of palpebral conjunctiva involving upper lid, lower lid, or bulbar conjunctiva	• Genetic predisposition (may be inherited in autosomal recessive pattern) • Single report of ligneous and immunoglobulin G4-related disease.[47]	• Systemic plasminogen deficiency characterized by recurrent mucoid conjunctivitis followed by palpebral fibrinous pseudomembrane formation and mucosal thickening. • Can involve systemic pseudomembranous lesions and can be associated with fever, upper respiratory tract infection, ear infections, and/or urogenital tract infection. • Associated with congenital hydrocephalus and juvenile colloid milium	• Thick, firm/woody pseudomembranous structures on the palpebral conjunctiva. • Can cause chronic inflammation; corneal scarring, neovascularization, perforation, amblyopia, and vision loss. • Can be life threatening if involving the respiratory tract

NOTE: Typical clinical signs may not be present in all cases. Distinctive signs are most useful in making a clinical diagnosis but may occur uncommonly. In all entities, laterality may vary and may be asymmetrical.

CARE PROCESS

PATIENT OUTCOME CRITERIA

Outcome criteria for treating conjunctivitis include the following:

- Eliminate or reduce signs and symptoms of conjunctivitis
- Restore or maintain normal visual function
- Detect and treat the underlying systemic disease process when applicable
- Prevent or reduce the likelihood of damage to the ocular surface

DIAGNOSIS

The initial evaluation of a patient should include the relevant aspects of the comprehensive medical eye evaluation,[48,49] but some elements of the evaluation may be deferred in patients with symptoms and signs suggestive of infectious conjunctivitis.

History

Questions about the following elements of the patient history may elicit helpful information:

- Symptoms and signs (e.g., 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

The ocular history includes details about previous episodes of conjunctivitis, concomitant ocular surface diseases and previous ophthalmic surgery.

The medical history considers the following:

- Compromised immune status (e.g., human immunodeficiency virus [HIV], chemotherapy, immunosuppressants)
- Current or prior systemic diseases (e.g., atopy, SJS /TEN, carcinoma, leukemia, chicken pox, GVHD)

The social history should include smoking habits, exposure to second-hand smoke, occupation and hobbies, exposure to air pollutants, travel, exercise habits, diet, sexual activity, and use of illicit drugs.[14,15]

Physical Examination

The initial eye examination includes measurement of visual acuity, an external examination, and slit-lamp biomicroscopy. The typical clinical signs for the types of conjunctivitis that are most common or most important to treat are listed in Table 1.

The external examination should include careful evaluation of the following:

- Regional lymphadenopathy, particularly preauricular
- Skin: signs of rosacea, eczema, seborrhea
- Abnormalities of the eyelids and adnexae: swelling, discoloration, malposition, laxity, ulceration, nodules, ecchymosis, neoplasia, lateral flare, lash loss
- Orbits: fullness, asymmetry
- Conjunctiva: laterality, type of conjunctival reaction (follicular vs papillary), distribution (diffuse vs sectoral or quadrantic), subconjunctival hemorrhage, chemosis, cicatricial change, symblepharon, masses, discharge

The slit-lamp biomicroscopy should include careful evaluation of the following:

- Eyelid margins: inflammation, edema, hyperpigmentation, meibomian gland dysfunction (MDG), ulceration, discharge, nodules or vesicles, blood-tinged debris, keratinization
- Eyelashes: loss of lashes, crusting, scurf, mites (*Demodex*), nits, lice, trichiasis
- Lacrimal puncta and canaliculi: pouting, discharge, edema
- Tarsal and forniceal conjunctiva:
  - Presence and size of papillae and/or follicles
  - Cicatricial changes, subepithelial fibrosis, fornix foreshortening, and symblepharon

- Forniceal enlargement
- Pseudomembranes and true membranes
- Ulceration
- Hemorrhages
- Foreign material
- Mucus discharge
- Masses
- Eyelid laxity

- Bulbar conjunctiva/limbus: follicles, edema, nodules, chemosis, laxity, papillae, ulceration, scarring, phlyctenules, hemorrhages, foreign material, keratinization
- Cornea:
  - Epithelial defects
  - Punctate keratopathy
  - Dendritic keratitis
  - Subepithelial infiltrates
  - Filaments
  - Ulceration
  - Infiltration, including subepithelial infiltrates and phlyctenules
  - Vascularization
  - Keratic precipitates with or without corneal edema
- Dye-staining pattern: conjunctiva and cornea (see Appendix 3)
- Anterior chamber/iris: inflammatory reaction, synechiae, transillumination defects

Diagnostic Tests

Some cases of conjunctivitis can be diagnosed on the basis of history and examination (e.g., viral conjunctivitis in the presence of an upper respiratory infection). In other cases, however, additional diagnostic tests may be helpful.

Cultures

Cultures for routine conjunctivitis (in the absence of listed risk factors) are rarely helpful in deciding on the treatment course or cost-effective. Cultures of the conjunctiva are indicated in all cases of suspected infectious neonatal conjunctivitis.[50] Bacterial cultures also may be helpful for recurrent, severe, or chronic purulent conjunctivitis in any age group and in cases where the conjunctivitis has not responded to medication.

Viral Diagnostic Tests

Viral cultures are not routinely used in practice to establish the diagnosis of adenovirus, but they may prevent misdiagnosis, disease spread, unnecessary antibiotic use, increased health care costs and lost productivity. A rapid, in-office immunodiagnostic test using antigen detection is available for adenovirus conjunctivitis. In a study of 186 patients with acute conjunctivitis, this test had a sensitivity of 88% to 89% and a specificity of 91% to 94%.[51] Immunoassay and immunochromatography testing has demonstrated high specificity for adenovirus but variable sensitivity, ranging between 40% and 93%.[52,53] Other highly sensitive and specific tests that may assist in the early diagnosis of adenovirus include Raman spectroscopy of tears and the quantification of hyaluronic acid in tear fluid.[54,55] Polymerase chain reaction (PCR) may be used to detect viral deoxyribonucleic acid. Availability will vary depending on the laboratory.

Chlamydial Diagnostic Tests

Suspected cases of adult and neonatal chlamydial conjunctivitis can be confirmed by laboratory testing.[56] Immunologically based diagnostic tests are available, including a direct immunofluorescent antibody test and enzyme-linked immunosorbent assay.[56,57] These tests have been largely supplanted by PCR for genital specimens, and, therefore, their availability for conjunctival specimens is more limited. The availability of PCR for testing ocular samples varies. Although specimens from the eye have been used with satisfactory performance,[58-60] these applications have not been approved by the US Food and Drug Administration (FDA). Further testing can be performed through culture.

Smears/Cytology

Smears for cytology and special stains (e.g., Gram, Giemsa) are recommended in cases of suspected infectious neonatal conjunctivitis, chronic or recurrent conjunctivitis, and in cases of suspected gonococcal conjunctivitis in any age group.[43,50] Conjunctival scrapings of patients with vernal conjunctivitis often contain eosinophils.[61]

Biopsy

Conjunctival biopsy may be helpful in cases of conjunctivitis that are unresponsive to therapy. Because such eyes may harbor a neoplasm, directed biopsy may be both vision saving and lifesaving.[44] Conjunctival biopsy and immunofluorescent staining diagnostic tests may be helpful to establish the diagnosis of diseases such

as OMMP and paraneoplastic syndromes.[62,63] A biopsy of bulbar conjunctiva should be performed and a sample should be taken from an eye with active inflammation when OMMP is suspected.[62] Biopsy itself may cause further conjunctival scarring in OMMP, so arrangements should be made in advance for appropriate immune staining. Unfixed, fresh biopsies should be sent in Michel's media or normal saline. Although a positive immunofluorescent staining is diagnostic, false negatives are common.[64,65] If the biopsy is negative and the disease is progressive, OMMP should be assumed, and multiple biopsies should be avoided. In cases of suspected sebaceous carcinoma, a full-thickness lid biopsy is indicated.[66] When considering a biopsy, a preoperative consultation with the pathologist is advised to ensure proper handling and staining of specimens. Tissue biopsy from the skin, conjunctiva, lacrimal glands, orbital tissue, lungs, or lymph nodes remains the gold standard for the diagnosis of sarcoidosis and autoimmune vasculitis.[67]

Allergy Skin Testing

Allergy skin testing is highly sensitive and specific for aeroallergens. Skin prick testing and pollen immunoglobin E (IgE) detection may be helpful in identifying allergens to target with immunosuppression.

One Italian study showed that of patients with ocular allergy, 82% had positive tests for specific allergic sensitizations.[68] In vernal keratoconjunctivitis (VKC), a positive skin prick test identified at least one allergen in 43% to 55% of patients.[22]

Tear Immunoglobin E

Tear IgE quantitatively measures IgE in tears and may be useful in diagnosing allergic conjunctivitis and assessing its severity.[69] In patients with vernal conjunctivitis, IgE mediated hypersensitivity by component-resolved diagnostics (CRD) in tears and serum may be helpful.[70] CRD maps the allergen sensitization at a molecular level, using purified natural or recombinant allergenic molecules instead of allergen extracts.

The association of vernal conjunctivitis with allergy/atopy is widely accepted, but it is associated with specific IgE sensitization in less than 50% of cases.

Conjunctival Allergen Challenge

An allergen challenge of the conjunctiva exposes the eyes to increasing concentrations of a specific allergen (that previously elicited a positive skin test

reaction) until a reaction is induced on the ocular surface. The subjects evaluate ocular itching and trained clinicians evaluate redness.

Because the challenge reproduces the signs and symptoms of seasonal allergic conjunctivitis, it can be used to test the duration and activity of pharmacologic therapies. Although it is used primarily for study purposes, the challenge may be useful in predicting the impact of preseasonal immunotherapy on symptoms.[71]

Blood Tests

Thyroid antibody tests are indicated for patients with SLK who do not have known thyroid disease.[72]

Vitamin D level may be lower and serum IgE levels may be higher in patients with allergic conjunctivitis.[73,74] The benefits of supplementation with vitamin D are being studied.[75-77]

Patients with sarcoidosis often have elevated serum angiotensin-converting enzyme levels, elevated serum lysozyme, and/or abnormal liver enzyme tests. Testing for antineutrophil cytoplasmic antibodies (ANCA) may be used to diagnose autoimmune vasculitis, including granulomatosis with polyangiitis (granulomatosis with polyangiitis), microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome).

Imaging Studies

A chest x-ray, chest computed tomography scan, and/or gallium scintigraphy may aid the diagnosis of sarcoidosis. In cases of Kawasaki disease, a transthoracic echocardiogram may detect cardiac artery abnormalities.

MANAGEMENT

Prevention

The most important reason for early detection of conjunctivitis is that prompt, appropriate treatment, available for most types of conjunctivitis, speeds resolution of the disease, minimizing both the sequelae of untreated conjunctivitis and time away from work or school. Early detection of conjunctivitis is also important so that public health measures can be instituted at home and work or school to reduce the disease's spread. Awareness that conjunctivitis may herald the existence of serious systemic disease should be kept in mind when patients have nonocular symptoms. For example, some types of neonatal conjunctivitis are associated with pneumonia, otitis media, or Kawasaki disease. In adults, conjunctivitis caused by OMMP, GVHD, gonococcus, and

chlamydia is important to detect early because it is necessary to treat the concomitant systemic disorder. Diagnosis of SLK may lead to further investigations that reveal a thyroid disorder.[78,79] Diagnosis of floppy eyelid may aid in the diagnosis of sleep apnea.[80] Progression of HSV vesicular blepharitis to keratoconjunctivitis may not be adequately halted by oral antiviral treatment alone.[81] Therefore, adding topical antivirals can be considered. Early detection of conjunctivitis associated with neoplasms may be lifesaving.

Individuals can protect against some chemical and toxin exposures by using adequate eye protection. Contact lens wearers can be instructed in appropriate lens care and frequent lens replacement to reduce the risk or severity of GPC.

Allergen-specific immunotherapy is beneficial in reducing allergic conjunctivitis, more so in children than adults.[82] [I+, Good, Strong] Furthermore, consumption of probiotic milk during pregnancy and by an infant after 6 months of age may decrease the risk of developing allergic conjunctivitis between 18 and 36 months.[83] Surveys have shown that patients under the care of an allergist/immunologist or otolaryngologist are more likely to undergo allergy testing and allergen immunotherapy than patients under the care of family medicine and pediatric practitioners.[84] A point-of-care ocular allergy diagnostic system is now commercially available, which may allow ophthalmologists to assume a greater role in identifying the trigger allergens and customizing a treatment protocol. In refractory cases, comanagement of allergic conjunctivitis may be beneficial.

Infectious conjunctivitis in neonates can often be prevented by means of prenatal screening and treatment of the expectant mother and by prophylactic treatment of the infant at birth. Single-use tubes of ophthalmic ointment containing 0.5% erythromycin are used as the standard prophylactic agent to prevent ophthalmia neonatorum.[85] Povidone-iodine solution 2.5% has been suggested as an alternative to antibiotic ointments to prevent neonatal conjunctivitis,[86,87] but it may be less effective and more toxic to the ocular surface.[88]

Studies show bacteria are cleared in 7 days in self-limiting adult mucopurulent acute bacterial conjunctivitis. The use of a 7-day course of antibiotics has been shown to eradicate bacteria within 5 days. When neonatal infectious conjunctivitis does occur, antibiotic treatment is very important to reduce the time course of the conjunctivitis as well as to prevent the development of secondary bacterial corneal ulceration.

The incidence of varicella (herpes) zoster virus is reduced by the chickenpox and the shingles vaccines. Zoster vaccine live (ZVL), the only vaccine available until 2017, is a live, attenuated virus (making it dangerous for use in immunocompromised individuals) and has a lower efficacy compared with RZV (70% vs. 96%). Presently, there are two herpes zoster vaccines available for adults: ZVL and recombinant zoster vaccine (RZV). Ophthalmologists should recommend strongly that patients 50 years of age and older without contraindications obtain vaccination with the RZV and should work with primary care physicians, internists, dermatologists, other medical doctors, and health care professionals to recommend vaccination strongly against herpes zoster starting at 50 years of age.[9] The Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices made the following three recommendations in its report of October 2017.[89]

1. Recombinant zoster vaccine is recommended for the prevention of herpes zoster and related complications for immunocompetent adults aged 50 years or older.
2. Recombinant zoster vaccine is recommended for the prevention of herpes zoster and related complications for immunocompetent adults who previously received ZVL.
3. Recombinant zoster vaccine is preferred over ZVL for the prevention of herpes zoster and related complications.

The spread of measles can be effectively limited by vaccination. The CDC and the World Health Organization strongly recommend measles vaccination for children age 1 year and older and adults born in 1957 or later who do not display measles immunity.[90]

The ophthalmologist plays a critical role in breaking the chain of transmission of epidemic adenoviral conjunctivitis, primarily by educating the patient and family about proper hygiene. Infected individuals should be counseled to wash hands frequently with soap and water (as opposed to sanitizer only), use separate towels, and avoid close contact with others during the period of contagion. Avoiding contact with others is especially important for individuals in professions with high potential for transmission, such as health care workers and child care providers. While the exact length of the period of infectivity is variable, many consider 7 days from the onset of symptoms (in the second eye, when involved) as the contagious period, because the recovery of virus from infected cases is difficult after 7 to 10 days of infection.[91] Other studies have suggested that patients should be considered potentially contagious for at least 10 to 14 days.[92,93]

Health care facilities have occasionally been associated with epidemic outbreaks of adenoviral keratoconjunctivitis.[6,92-95] To avoid cross-contamination, multiple-dose eyedrop containers should be discarded after inadvertent contact with the ocular surface.[96] Hand-washing procedures with antimicrobial soap and water[97] and disinfecting ophthalmic equipment may reduce the risk of transmission of viral infection, as the virus can remain infectious in a desiccated state on surfaces for up to 28 days.[98,99]

The CDC and tonometer manufacturers recommend dilute bleach soaks (sodium hypochlorite) at 1:10 concentration for effective disinfection against adenovirus and HSV, the viruses most commonly associated with transmission in offices and subsequent outbreaks. Tonometer tips should be wiped clean and then disinfected by immersing them for 5 to 10 minutes. Any disinfecting agent can result in iatrogenic corneal de-epithelialization and haze if not properly removed from the tonometer tip before use by thorough rinsing in tap water and air drying.[6]

Notably, 70% isopropyl alcohol (e.g., alcohol wipes), 3% hydrogen peroxide, and ethyl alcohol are no longer recommended for tonometer disinfection.[6,7] The common practice of wiping the tonometer tip with a 70% isopropyl alcohol wipe may not provide adequate disinfection after exposure to a patient who has adenoviral keratoconjunctivitis.

Tonometer manufacturers recommend replacing tonometer prisms every 2 years, after a maximum of 100 disinfection cycles with 1:10 sodium hypochlorite, or if damaged.[7,100,101]

Disinfecting agents can also cause damage to the tonometer tip. Though not in wide use, disposable tonometer tips can also be considered to eliminate cross infections.[102] Alternatively, intraocular pressure (IOP) can be checked using a tonometer with a disposable coverlet.

Exposed surfaces on equipment can be decontaminated by wiping with sodium hypochlorite (a 1:10 dilution of household chlorine bleach) or other appropriate disinfectants.[96,97,103] Surfaces should be disinfected with an EPA-registered hospital disinfectant in accordance with the label's use directions and safety precautions.

In one hospital setting, the use of an experimental rapid PCR testing for adenovirus in health care workers presenting with red eye was implemented. This testing algorithm was effective in preventing the spread of infection and minimizing the loss of productivity by employees who were not infectious. Currently, there is no commercially

available PCR test. Serotyping can assist in identifying patients at risk of developing epidemic keratoconjunctivitis (EKC).[104]

Despite the use of reasonable measures, it may not be possible to prevent all transmission of viral infection. Unless absolutely necessary, deferring IOP measurement for a patient with acute conjunctivitis should be considered. Attention should be paid to disinfecting items in addition to tonometer tips that may have come in contact with the patient's secretions. During an active epidemic, consideration should be given to triaging patients upon arrival to the office and directing those who appear infected to a dedicated "red-eye room."

Treatment

Treatment of conjunctivitis is ideally directed at the root cause. Early detection and treatment can be both sight saving and, in select cases, life saving. Indiscriminate use of topical antibiotics or corticosteroids should be avoided, because antibiotics can induce toxicity and corticosteroids can potentially prolong adenoviral infections and worsen HSV infections. Treatment methods are described below for the most common types of conjunctivitis and for those types that are particularly important to treat.

Seasonal/Perennial Allergic Conjunctivitis

Simple measures that are applicable to almost all situations include wearing sunglasses as a barrier to airborne allergens, cold compresses, refrigerated artificial tears, avoiding eye rubbing, and avoiding allergen. Hypoallergenic bedding, eyelid cleansers to remove allergens, frequent clothes washing, and bathing/showering before bedtime may also be helpful.

Mild allergic conjunctivitis can be treated with an over-the-counter topical antihistamine/vasoconstrictor agent or with the more effective second-generation topical histamine H_1-receptor antagonists.[105-108] [I+, Good, Strong] Many topical medications can be stored in the refrigerator, as the cooling sensation upon instillation of the eye drop can provide symptomatic relief. Chronic use of vasoconstrictor agents can be associated with rebound vasodilation once the agent is stopped. If the condition is frequently recurrent or persistent, mast-cell stabilizers can be used.[105] Many new medications combine antihistamine activity with mast-cell stabilizing properties and can be used for either acute or chronic disease.[107,109-115]

The use of topical mast-cell inhibitors can also be helpful in alleviating the symptoms of allergic rhinitis. Mast-cell inhibitors formulated as a nasal spray and

aerosols are also helpful in alleviating the symptoms of allergic rhinitis and asthma in some patients.[116]

If the symptoms are not adequately controlled, a brief course (1 to 2 weeks) of topical corticosteroids with a low side effect profile can be added to the regimen. Table 2 lists topical medications that can be used for seasonal allergic conjunctivitis. Oral antihistamines are commonly used but may induce or worsen dry eye syndrome, impair the tear film's protective barrier, and actually worsen allergic conjunctivitis. Concomitant use of cooled artificial tears may alleviate coexisting tear deficiency and dilute allergens and inflammatory mediators on the ocular surface.[117,118] In severe cases, topical cyclosporine or tacrolimus can be considered.[119-121] [I+, Good, Discretionary]

TABLE 2 TOPICAL MEDICATIONS FOR SEASONAL ALLERGIC CONJUNCTIVITIS

Generic Name	Trade Name	Class	Typical Daily Dose
Alcaftadine	Lastacaft	H_1-antagonist	1
Azelastine HCl	Optivar Available generically	H_1-antagonist/mast-cell inhibitor	2
Bepotastine besilate	Bepreve	H_1-antagonist/mast-cell inhibitor	2
Cromolyn sodium	Crolom Available generically	Mast-cell inhibitor	4–6
Emedastine difumarate	Emadine	H_1-antagonist	4
Epinastine HCl	Elestat	H_1- and H_2-antagonist/mast-cell inhibitor	2
Ketoralac tromethamine	Acular, Acular LS, Acular PF	NSAID†	4
Ketotifen fumarate	Alaway, Zaditor (OTC)	H_1-antagonist/mast-cell inhibitor	2
Lodoxamide tromethamine	Alomide	Mast-cell inhibitor	4
Loteprednol etabonate (0.2% or 0.5%)	Alrex, Lotemax	Corticosteroid‡	4
Naphazoline/antazoline	Vasocon-A (OTC)	Antihistamine/decongestant	4
Naphazoline/pheniramine	Naphcon-A (OTC) Opcon-A (OTC) Visine-A (OTC)	Antihistamine/decongestant/ Vasoconstrictor*	4
Nedocromil sodium	Alocril	Mast-cell inhibitor	2
Olopatadine HCl (0.1%, 0.2%, or 0.7%)	Patanol, Pataday, or Pazeo	H_1-antagonist/mast-cell inhibitor	2, 1, or 1

Adapted with permission from PDR Network LLC. Table 11. Agents for Relief of Seasonal Allergic Conjunctivitis. In: *PDR® for Ophthalmic Medicines 2012*, 40th ed. Montvale, NJ: PDR Network LLC; 2011:9.

HCL = hydrochloride; NSAID = nonsteroidal anti-inflammatory drug; OTC = over the counter

* Caution: should not be used long term owing to rebound vasodilation

† Use with caution in patients who have ocular surface disease

‡ Increased Intraocular pressure, cataractogenesis

Punctal plugs should be avoided because they prevent flushing of the allergens and inflammatory mediators from the ocular surface. Associated eye rubbing from uncontrolled allergic conjunctivitis may lead to an increased risk of punctal plug complications, including extrusion, canalicular migration with secondary nasolacrimal obstruction, canaliculitis or dacryocystitis.

Consultation with an allergist or dermatologist may be helpful for patients who have disease that cannot be adequately controlled with topical medications and oral antihistamines. Allergen-specific immunotherapy, in which increasing subcutaneous or sublingual doses of the trigger allergens are administered to achieve hyposensitization, are useful,[82,122-124] [I+, Good, Strong] but usage may be limited by expense, long-term patient commitment, and the risk of anaphylaxis.[125-127]

Frequency of follow-up visits is based on the severity of disease presentation, etiology, and treatment. Timing visits during symptomatic periods should be considered. A follow-up visit should include an interval history, measurement of visual acuity, and slit-lamp biomicroscopy. If corticosteroids are used in chronic or recurrent conjunctivitis, baseline and periodic measurement of IOP and pupillary dilation should be performed to evaluate for glaucoma[128] and cataract. Allergic conjunctivitis and atopic disease are associated with keratoconus—in these cases, adequate control of allergy and eye rubbing are important to decrease progression of ectasia.[129-132] This is discussed in more detail in the Corneal Ectasia PPP. [133]

Vernal/Atopic Conjunctivitis

General treatment measures for vernal/atopic conjunctivitis include modifying the environment to minimize exposure to allergens or irritants and using cool compresses and ocular lubricants. Topical and oral antihistamines and topical mast-cell stabilizers can be useful to maintain comfort.

For acute exacerbations of vernal/atopic conjunctivitis, topical corticosteroids are usually necessary to control severe symptoms and signs.[134] Topical cyclosporine 2% has demonstrated a reduction in signs and symptoms compared with placebo after two weeks of use in patients with VKC.[135,136] Commercially available 0.05% topical cyclosporine has also been shown to be effective in more frequent dosing for the treatment of severe vernal/atopic conjunctivitis [I+, Good, Strong] and it has been shown to be effective in preventing seasonal recurrences.[137-141] Use of cyclosporine may allow for reduced use of topical steroids.[142]

For entities such as VKC, which may require repeat short-term therapy with topical corticosteroids, patients should be informed about potential complications of corticosteroid therapy, and general strategies to minimize corticosteroid use should be employed.

For severe sight-threatening atopic keratoconjunctivitis that is not responsive to topical therapy, supratarsal injection of corticosteroid can be considered.[143]

Systemic immunosuppression is rarely warranted, but options include montelukast,[144] aspirin, interferons,[145] and oral T-cell inhibitors, such as cyclosporine and tacrolimus.[25,61,146-149] [I+, Good, Discretionary] In patients 2 years old or older, eyelid involvement can be treated with pimecrolimus cream 1% or topical tacrolimus ointment.[150-152] Tacrolimus drops/ointment 0.03% is used for children 2 years to 15 years old; either 0.03% or 0.1% is used for patients 16 years and older.[153] Randomized clinical trials have demonstrated the efficacy of topical tacrolimus 0.1% applied conjunctivally in patients who had failed conjunctivitis therapy with topical corticosteroids, cyclosporine, and/or antiallergy medications.[154] These agents may make patients more susceptible to herpes simplex keratitis.[155] Tacrolimus or pimecrolimus are rarely associated with development of skin cancer or lymphoma.[156,157]

Frequency of follow-up visits is based on the severity of disease presentation, etiology, and treatment. Consultation with a dermatologist is often helpful. A follow-up visit should include an interval history, measurement of visual acuity, and slit-lamp biomicroscopy. If corticosteroids are prescribed, baseline and periodic measurement of IOP and pupillary dilation should be performed to evaluate for glaucoma and cataract. Discussion of treatment of complications such as corneal plaques and ulceration is beyond the scope of this document.[158] Keratoconus, which is also associated with allergic and vernal conjunctivitis, is discussed in more detail in the Corneal Ectasia PPP. [133] Notably, vernal and atopic keratoconjunctivitis should be controlled prior to corneal cross-linking to decrease the risk of developing sterile keratitis.[159]

Superior Limbic Keratoconjunctivitis

Mild cases of SLK may respond to treatment of concomitant dry eye syndrome with lubricants, mast-cell stabilizers, cyclosporine,[160] soft contact lenses, and/or punctal occlusion; however, the response may be temporary. Associated filamentary keratitis may occasionally respond to topical 10% acetylcysteine[161] or

hypertonic (5%) saline.[162] Unlike contact-lens–related keratoconjunctivitis, which is caused by hypoxia, SLK seems to be caused by a tight upper eyelid with loose superior bulbar conjunctiva. This tight eyelid drags the loose conjunctiva down chronically with every blink over the superior cornea, creating chronic irritation and inflammation. Persistent symptoms may necessitate surgical intervention such as cautery (chemical or thermal) to tighten redundant conjunctiva or conjunctival resection.[163] Up to 65% of patients with SLK may have underlying thyroid dysfunction, and many of these have associated ophthalmopathy.[164] An underlying thyroid disorder should be investigated by means of thyroid antibody tests.[72,164] Because SLK may persist with exacerbations over a period of years, treatment and frequency of follow-up are driven by the patient's symptoms. Systemic treatment of underlying thyroid disease does not have an impact on the SLK, however. Patients should be informed that this is a chronic and recurrent condition that rarely can decrease vision.

Blepharoconjunctivitis

See the Blepharitis PPP. [27]

Rosacea Conjunctivitis

Treatments include eyelid hygiene, warm compresses, systemic tetracyclines, omega-3 fatty acid supplements, topical corticosteroids and cyclosporine, topical metronidazole creams and ointment, mechanical thermal pulsations, and intense pulse light therapy (see the Blepharitis PPP for more details.) [27]

Contact-Lens–Related Keratoconjunctivitis

This phenomenon is essentially hypoxia of the limbal stem cells creating punctate epithelial keratitis, pannus, neovascularization, inflammation, edema, and ultimately epitheliopathy, which can impact visual function and, if ignored, can be permanent. If moderate or severe pain is present, amoebic keratitis should be considered. In cases of contact lens–related keratoconjunctivitis, contact-lens wear should be discontinued until the cornea returns to normal. A brief (1–2 weeks) course of topical corticosteroids may be prescribed, in addition to longer-term use of topical cyclosporine 0.05%. If related to limbal stem cell failure, symptoms may be prolonged, but they will usually ultimately clear with contact lens abstinence.[165-167] At the follow-up evaluation, the contact lens fit, type, and care regimen should be reviewed (e.g., nonpreserved lens care systems, daily disposable contact lenses, high DK/T ratio material, lens materials, reduction in contact lens wear time) and

consideration should be given to alternatives to contact lenses (e.g., eyeglasses or refractive surgery) once the keratoconjunctivitis has resolved.

Giant Papillary Conjunctivitis

The treatment of GPC generally involves modifying the causative entity. Protruding suture knots can be treated by removing or replacing the sutures, rotating the knots, or using a therapeutic contact lens. However, long-term use of therapeutic contact lenses may be associated with an increased risk of microbial keratitis and GPC. Ocular prostheses that cause GPC can be cleaned, polished, or replaced. Mild contact lens–related GPC may respond to replacing lenses more frequently, decreasing contact lens wearing time, using preservative-free lens care systems, administering mast-cell stabilizing agents,[168] refitting contact lenses, switching to disposable lenses (daily-wear disposables are recommended), and/or changing the contact lens polymer. Associated abnormalities such as aqueous tear deficiency and MGD should be treated. In GPC, discontinuation of contact lens use in conjunction with topical anti-inflammatory agents may be effective.[169] If corticosteroids are used for conjunctivitis, baseline and periodic measurement of IOP and pupillary dilation should be performed to evaluate for glaucoma and cataract.

Frequency of follow-up visits is based on the severity of disease and treatment used. At the follow-up visit, an interval history, measurement of visual acuity, and slit-lamp biomicroscopy should be performed.

Floppy Eyelid Syndrome

Temporary relief of floppy eyelid syndrome is afforded by taping the patient's eyelids shut or by having the patient wear a protective shield while sleeping.[170,171] Lubricants may help in managing mild cases. Definitive therapy involves surgical procedures such as lateral canthus repair,[172] horizontal shortening of the upper eyelid, or excision of the medial upper lid.[173-176] Follow-up depends on the patient's clinical course. Floppy eyelid syndrome has been associated with keratoconus and obesity, [177-179] and providers may consider consultations with specialists.[180]

Giant Fornix Syndrome

Cultures are nearly always positive for *Staphylococcus aureus*, although other organisms are possible.[29,181] Many patients have concomitant nasolacrimal duct obstruction and chronic dacryocystitis, which may need to be addressed surgically.

Treatment with antibiotic regimens used for routine cases of bacterial conjunctivitis generally result in only temporary improvement. Recommended treatment strategies include the prolonged use of systemic anti-staphylococcal antibiotics and intensive topical antibiotics and corticosteroids. More recently, supratarsal injections of antibiotics and corticosteroids, along with irrigation and sweeping of the fornix with povidone-iodine solution, have been advocated. Given the increasing frequency of methicillin-resistant *S. aureus* (MRSA) in the general population, conjunctival cultures before starting treatment can help guide the appropriate choice of antibiotic. In addition, surgical correction of ptosis may be helpful.

Pediculosis Palpebrarum (*Phthirus pubis*)

Jeweler's forceps can be used to mechanically remove the adult lice and nits (eggs) from the eyelids and eyelashes. Adherent nits may require epilation of the involved lashes. Cutting the lashes at their base with Westcott or other microsurgical scissors is an alternative for heavy infestation of adherent nits. A bland ophthalmic ointment (e.g., petrolatum, erythromycin, bacitracin) applied two to three times a day for 10 days will smother the adult lice and nits. Compliance is important for eradication. Patients and close contacts should be advised to use anti-lice lotion and shampoo for nonocular areas and to wash and dry clothing and bedding thoroughly (using the highest temperature of the dryer for 30 minutes). Patients and sexual contacts should be informed about the possibility of concomitant disease and should be referred appropriately. Sexual abuse should be considered in children with this condition. Pediculosis palpebrarum can also be transferred from one child to another in a situation of close contact (e.g., during school).

Medication-induced/Preservative-Induced Keratoconjunctivitis

Discontinuation of the agent responsible for medication-induced keratoconjunctivitis results in resolution over a period of weeks to months. If severe inflammation of the conjunctiva or eyelid is present, a brief course of topical corticosteroids is indicated, often with preservative-free steroid ointment or cream. Nonpreserved artificial tears or low dose topical corticosteroids may be beneficial. The clinician should look for subepithelial fibrosis (See the subsection Ocular Mucous Membrane Pemphigoid Conjunctivitis below for more details).

A recent study showed conjunctival cicatricial changes after chronic use of glaucoma medications. Importantly, the process may continue despite stopping the offending medications.

TABLE 3 SYSTEMIC ANTIBIOTIC THERAPY FOR GONOCOCCAL AND CHLAMYDIAL CONJUNCTIVITIS

Cause	Drug of Choice	Dosage
Adults		
Gonococcus*	Ceftriaxone†	250 mg IM, single dose
	and	
	Azithromycin	1 g orally, single dose
	or	
	Doxycycline	100 mg orally, twice a day for 7 days
	For cephalosporin-allergic patients:	
	Azithromycin‡	2 g orally, single dose
Chlamydia‖	Azithromycin	1 g orally, single dose
	or	
	Doxycycline	100 mg orally twice a day for 7 days
Children§ (<18 years)		
Gonococcus		
Children who weigh <45 kg	Ceftriaxone	125 mg IM, single dose
	or	
	Spectinomycin¶	40 mg/kg (maximum dose 2 g) IM, single dose
Children who weigh ≥45 kg	Same treatment as adults	
Chlamydia		
Children who weigh <45 kg	Erythromycin base or ethylsuccinate	50 mg/kg/day orally divided into four doses daily for 14 days
Children who weigh ≥45 kg but are aged <8 years	Azithromycin	1 g orally, single dose
Children ≥8 years	Azithromycin	1 g orally, single dose
	or	
	Doxycycline	100 mg orally, twice daily for 7 days

TABLE 3 SYSTEMIC ANTIBIOTIC THERAPY FOR GONOCOCCAL AND CHLAMYDIAL CONJUNCTIVITIS (CONTINUED)

Cause	Drug of Choice	Dosage
Neonates		
Ophthalmia neonatorum caused by *N. gonorrhoeae*	Ceftriaxone	25–50 mg/kg intravenous or IM, single dose, not to exceed 125 mg
Chlamydia	Erythromycin base or ethylsuccinate	50 mg/kg/day orally divided into four doses daily for 14 days**

NOTE: Pregnant women should not be treated with doxycycline, quinolones, or tetracyclines. Either erythromycin or amoxicillin is recommended for treatment of chlamydia during pregnancy.

Data from:

Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2010. *MMWR Morb Mortal Wkly Rep.* 2010;59 (No. RR-12):44–55.

Update in: Centers for Disease Control and Prevention. Update to CDC's Sexually transmitted diseases treatment guidelines, 2010. Oral cephalosporins no longer a recommended treatment for gonococcal infections. *MMWR Morb Mortal Wkly Rep*. 2012;61 (No. 31):590–594.

* The Centers for Disease Control and Prevention (CDC) currently recommends that patients treated for gonococcal infection also be treated routinely with a regimen effective against uncomplicated genital *Chlamydia trachomatis* infection, because patients infected with *Neisseria gonorrhoeae* often are coinfected with *C. trachomatis*.

† If ceftriaxone is not available, cefixime 400 mg in a single dose or doxycycline 100 mg orally, twice a day for 7 days may be used. Consider lavage of infected eyes with saline solution once.

‡ A single oral dose of azithromycin 2 g is effective against uncomplicated gonococcal infections, but the CDC does not recommend widespread use of azithromycin because of concerns over emerging antimicrobial resistance to macrolides. Because data are limited regarding alternative regimens for treating gonorrhea among persons who have severe cephalosporin allergy, providers treating such patients should consult infectious disease specialists.

§ The CDC recommends advising all women and men with chlamydial or gonococcal infection to be retested approximately 3 months after treatment.

‖ Sexual abuse must be considered a cause of infection in preadolescent children. A diagnosis of *C. trachomatis* or *N. gonorrhoeae* infection in preadolescent children should be documented by standard culture.

¶ Spectinomycin is not available in the United States; updated information from the CDC on the availability of spectinomycin will be available at www.cdc.gov/std/treatment.

** An association between oral erythromycin and infantile hypertrophic pyloric stenosis has been reported in infants aged less than 6 weeks who were treated with this drug. Infants treated with erythromycin should be followed for signs and symptoms of infantile hypertrophic pyloric stenosis.

Ocular Mucous Membrane Pemphigoid Conjunctivitis

This condition is a progressive, immune-mediated process targeting the conjunctival basement membrane. The diagnosis is typically one of exclusion, and a conjunctival biopsy for immunopathology confirms the diagnosis, although false negatives are frequent.[182] Early symptoms may include very nonspecific ocular surface complaints such as redness, foreign body sensation, dryness, tearing, discharge. Early signs are mild conjunctival injection, staining of the cornea and conjunctiva, and subepithelial fibrosis or cicatricial changes of the palpebral conjunctiva, especially the superior. As the condition progresses, the inflammation may increase and the complaints may persist and worsen. Symblephara, conjunctival cul de sac foreshortening, and progressive conjunctival scarring may result in ankyloblepharon in the later stages. As a result of the conjunctival scarring, entropion occurs, and trichiasis and acquired distichiasis cause corneal trauma with eventual scarring.

Ocular mucous membrane pemphigoid is found more commonly in elderly women. Indirect immunofluorescence of the serum is rarely used but may detect autoantibodies.[183] If the patient is using any of the drugs associated with medication-induced mucous membrane pemphigoid, trial discontinuation of the medication should be attempted. These include epinephrine and glaucoma medications, especially the miotics.

Because OMMP is a chronic, progressive disease characterized by subepithelial fibrosis with frequent remissions and exacerbations of disease activity, it may be difficult to gauge the response to therapy accurately. Grading systems and photographic documentation of the conjunctiva may be helpful to assess disease progression.[63,184] Although topical corticosteroid therapy may aid in controlling acute conjunctival inflammation, systemic immunosuppressive therapy is required to inhibit inflammation, prevent keratopathy, and prevent progression of conjunctival scarring.[185,186] The rate of disease progression and the physical and medical condition of the patient, and the potential complications of immunosuppressive therapy should be considered and discussed with the patient before initiating therapy. Systemic corticosteroids may be indicated to control inflammation initially, but they should be weaned as other immunosuppressive therapy becomes effective to avoid complications of chronic corticosteroid use.

Mild and slowly progressive disease may be treated using mycophenolate mofetil, dapsone, azathioprine, or methotrexate.[185,187,188]

If dapsone is considered, caution should be taken in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.[189] For severe inflammation or for inflammation unresponsive to treatment with other agents, cyclophosphamide should be considered.[185,190] Other therapies that may be effective for treatment or adjunctive therapy include oral tetracycline and niacinamide,[191] sulfasalazine,[192] mycophenolate mofetil,[64,187,188,193] intravenous immunoglobulin,[194] and biologics.[64] These therapies can be used alone or in combination. Refractory cases may benefit from combination intravenous immunoglobulin and rituximab.[195] In general, a physician with expertise in immunosuppressive therapy should administer and monitor the treatment to minimize and manage side effects.[196,197] The role of subconjunctival antimetabolites is unclear.

Associated dry eye state should be treated aggressively, and trichiasis, distichiasis, and entropion should be treated nonsurgically if possible. Mucous membrane or amniotic membrane grafting for fornix reconstruction is possible if eyes are not severely dry and inflammation is under control. In advanced disease with corneal blindness, keratoprosthesis surgery may improve vision, however, all ocular reconstructive surgery is considered high risk.[11,198,199]

The timing and frequency of follow-up visits is based on the severity of disease presentation, etiology, and treatment. A follow-up visit should include an interval history, visual acuity measurement, slit-lamp biomicroscopy, and documentation of corneal and conjunctival changes to monitor progression. Ocular procedures such as cataract surgery may worsen the disease. Perioperative immunosuppression and close postoperative follow-up are warranted in such cases.[190]

Graft-versus-Host Disease

Patients with multiorgan systemic GVHD are treated with systemic immunosuppression. Systemic corticosteroids are the mainstay of initial treatment and are commonly used in conjunction with a T-cell inhibitor (cyclosporine or tacrolimus). In corticosteroid-refractory GVHD, numerous therapies have been studied, including cyclophosphamide, biologics, and photopheresis,[200] with varied success depending on the tissues involved and the severity of the disease.

For ocular GVHD, aggressive lubrication and punctal occlusion are particularly useful in treating patients with secondary keratoconjunctivitis sicca, which is very

common. There is a role for topical corticosteroids in treating conjunctival hyperemia and scarring.[201] Topical T-cell modulator (cyclosporine) autologous serum tears can be used to treat dry eye syndrome associated with GVHD.[202-205] Treating the underlying inflammatory process may help to reduce conjunctival damage leading to dry eye disease. Other secondary complications of ocular GVHD, such as cicatricial eyelid malposition or limbal stem cell failure, should be managed on a case-by-case basis. For vision correction and relief from dry eye symptoms in these patients, scleral lenses are helpful.[206,207]

Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are a disease continuum characterized by severe mucocutaneous reactions, triggered by medications or by infectious agents. Stevens-Johnson syndrome/toxic epidermal necrolysis is a clinical diagnosis but can be confirmed by skin biopsy of an effected area. Identification of an inciting medication and prompt discontinuation is imperative. Acute systemic management by a multidisciplinary medical team often involves immunosuppressive and immunomodulatory therapies.

Early intervention is critical to prevent late ocular complications.[208-210] Acutely, SJS/TEN ranges from hyperemia of the conjunctiva to complete sloughing of the ocular surface epithelium. Concomitant inflammation may be associated with pseudomembranes, symblephara, shortening of the fornices, and corneal ulceration and/or perforation. In chronic cases, the tear film is often compromised in addition to atrophy of the meibomian glands, scarring of the puncta, and limbal stem cell deficiency. Scarring and fusion of the conjunctival surfaces can lead to permanent symblephara ankyloblepharon, eyelid malpositioning, trichiasis, and keratinization of the conjunctiva and eyelids.[210] Patients are at risk for persistent corneal epithelial defects, inflammation, neovascularization, ulcers, scarring, and loss of vision.

Medical management with topical lubricants, antibiotics, and anti-inflammatories is recommended.[211] Lid hygiene and periodic sweeping of the conjunctival fornices interrupts synechiae formation.[208] Early amniotic membrane transplantation is a useful adjunct to stabilize the ocular surface and prevent and treat cicatrization and conjunctival and corneal defects.[212,213]

Sebaceous Carcinoma

When a diagnosis of sebaceous carcinoma is confirmed by an eyelid biopsy, local excision is indicated. The excision should be performed by a surgeon experienced in the treatment of eyelid tumors, and adjunctive therapy should be used as needed for any residual pagetoid component.[214] If uncertainty in labelling, handling, or processing of the specimen exists, discussion with the pathologist who is to prepare and read the specimen (prior to the biopsy) is beneficial..

Ocular Surface Squamous Neoplasia

When a diagnosis of ocular surface squamous neoplasia is confirmed by biopsy, treatment may consist of local excision with cryotherapy to the edges,[215] and/or topical chemotherapeutic agents (interferon, mitomycin-C, or fluorouracil [5-FU]). In addition, some studies have indicated that topical chemotherapeutics alone may completely resolve the malignancy. The optimal treatment is still under debate, and, therefore, management should be done by an experienced specialist.[216] Anterior segment optical coherence tomography may facilitate follow-up for patients with ocular surface squamous neoplasia.

Adenoviral Conjunctivitis

The majority of cases of acute, infectious conjunctivitis in the adult population are viral and self-limited; these cases do not require antimicrobial treatment. Patients with adenoviral conjunctivitis need to understand that the condition is highly contagious and that this is a hearty virus that can survive for many weeks on a countertop or similar surface if careful disinfection doesn't occur. Because of its ability to infect multiple members of a family, classmates at school, or fellow staff or clients at work, this infection is often termed EKC.[217] The patient should be educated about measures that will help reduce the spread of this infection[6] and encouraged to make every attempt to minimize contact with other people for 10 to 14 days from the onset of symptoms in the last eye affected.[218][I+, Good, Strong]

The clinician is often asked for advice on how to balance public health concerns and work/school requirements. This can be a particularly difficult issue for patients working in health care, food service, or sales. Some occupations allow for work at home or from the privacy of an individual office or similar setting.

There is no proven effective treatment for eradication of adenovirus infection; however, artificial tears, topical antihistamines, topical steroids, oral analgesics, or cold compresses may be used to mitigate symptoms. The use of antibiotics in the

management of this viral infection should be avoided because of potential adverse treatment effects.

Topical corticosteroids are helpful to reduce symptoms and may reduce scarring in severe cases of adenoviral keratoconjunctivitis with marked chemosis or lid swelling, epithelial sloughing, or membranous conjunctivitis. Close follow-up is warranted for patients with adenoviral conjunctivitis who are being treated with corticosteroids. In an animal model of adenoviral conjunctivitis, administration of topical corticosteroids led to prolonged viral shedding.[219] It is not known whether this is the case in humans. Because of its broad antimicrobial spectrum, povidone-iodine has been investigated as a treatment consideration. Povidone-iodine 0.4% alone or in combination with dexamethasone 0.1% has demonstrated reductions in viral titers, virus spread, shortening of the clinical course, and preservation of visual function.[220-223] There is currently an ongoing clinical trial examining the use of a higher concentration povidone-iodine 0.6% alone and in combination with dexamethasone 0.1% versus placebo (NCT02998541).[224] Off-label use of topical ganciclovir 0.15% ophthalmic gel has been investigated for the treatment of EKC and has shown potential benefit against specific adenovirus serotypes, but further efficacy on a larger scale needs to be demonstrated before definitive recommendations can be made.[225] For patients with membranous conjunctivitis, debridement of the membrane can be considered to prevent corneal epithelial abrasions or permanent cicatricial changes (e.g., foreshortening of the conjunctival fornix).

Patients with severe disease who have corneal epithelial ulceration or membranous conjunctivitis should be re-evaluated within 1 week. Patients who are prescribed prolonged topical corticosteroids should be monitored by periodically measuring IOP and pupillary dilation to evaluate for glaucoma and cataract. Topical corticosteroids should be tapered once inflammation is controlled.

Patients who are not treated with topical corticosteroids should be instructed to return for follow-up if they continue to experience symptoms of red eye, pain, or decreased vision after 2 to 3 weeks. This follow-up visit should include an interval history, measurement of visual acuity, and slit-lamp biomicroscopy.

During follow-up, patients should be evaluated for the presence of corneal subepithelial infiltrates, which typically occur 1 or more weeks after the onset of conjunctivitis. Treatment of subepithelial infiltrates varies with the severity of the disease. In mild cases, observation is sufficient. In cases with blurring,

photophobia, and decreased vision, topical corticosteroids at the minimum effective dose may be considered.

Patients who are being treated with topical corticosteroids should have the dosage slowly tapered to the minimum effective dose. Corticosteroids with poor ocular penetration, including fluorometholone or site-specific corticosteroids such as rimexolone or loteprednol, may be less likely to result in elevated IOP or cataract formation. A follow-up examination should be conducted regularly. Visits should include an interval history, measurement of visual acuity and IOP, and slit-lamp biomicroscopy. Recurrence of subepithelial infiltrates has been reported in patients with a history of adenoviral infection who have undergone photorefractive keratectomy or LASIK.[226] Secondary HSV stromal keratitis may benefit from topical steroid treatment but in conjunction with oral antiviral therapy.

Herpes Simplex Virus Conjunctivitis

Herpes simplex virus conjunctivitis is a self-limited acute condition. Treatment is usually instigated upon high suspicion or concomitant corneal involvement. Possible topical options include ganciclovir 0.15% gel used three to five times per day[227] or trifluridine 1% solution five to eight times per day.[228] Oral treatments for HSV keratitis include acyclovir (200 to 400 mg five times per day),[229] valacyclovir (500 mg two or three times per day),[230] or famciclovir (250 mg twice a day).[231] Anecdotal experience suggests that higher doses of oral antivirals may also be effective in cases that appear to demonstrate resistance to therapy. Topical trifluridine inevitably causes epithelial toxicity if used for more than 2 weeks. Topical ganciclovir is less toxic to the ocular surface.[232] Oral antivirals alone may not be adequate in preventing the progression of HSV blepharoconjunctivitis, but the addition of topical antiviral treatment has been effective.[81] Lower doses of oral antivirals are considered for long-term prophylaxis against recurrent HSV keratitis. Topical corticosteroids potentiate HSV infection and should be avoided. Within 1 week of treatment, patients should have a follow-up visit consisting of an interval history, visual acuity measurement, and slit-lamp biomicroscopy. Neonates require prompt consultation with the pediatrician or primary care physician, because systemic HSV infection is a life-threatening condition.[233]

Varicella (Herpes) Zoster Virus Conjunctivitis

Children with chicken pox may present with conjunctivitis that is sometimes associated with eyelid ulceration and/or limbal or conjunctival vesicles. Many

clinicians treat such patients with topical antibiotics to prevent secondary infection because the vesicles will undergo necrosis before healing. Severe conjunctival scarring from secondary bacterial infection can even lead to cicatricial ectropion.[234] Topical antivirals alone have not been shown to be helpful in treating VZV conjunctivitis but may be used as additive treatment in unresponsive patients.[235] In rare cases, dendritic or stromal keratitis can occur. Varicella zoster virus conjunctivitis can be associated with other forms of ocular disease including pseudodendrites, keratitis, corneal scarring, corneal vascularization, iritis/uveitis, sectoral iris atrophy, and secondary glaucoma.[236] With persistent or recalcitrant acute/subacute disease in immunocompetent patients, oral antivirals may be beneficial at a dose of 800 mg five times daily for 7 days for acyclovir, 1000 mg every 8 hours for 7 days for valacyclovir, or 500 mg three times daily for 7 days for famciclovir.[230,231,237] Patients who have chronic disease may require prolonged treatment with adjustment of the dose according to the clinical response. Patients with chronic sequelae may require prolonged treatment and/or long-term prophylaxis. Immunocompromised patients may need to be treated more aggressively. Caution is advised in patients with impaired renal clearance. Late sequelae include dry eye and corneal anesthesia with neurotrophic keratitis.[238]

Molluscum Contagiosum

Conjunctivitis and keratitis from molluscum contagiosum are due to viral shedding from the eyelid lesion(s) onto the surface of the eye. Molluscum lesions may spontaneously resolve, but they can also persist for months to years. Treatment to remove the lesions is indicated in symptomatic patients. Treatment options include incision and curettage (aggressive enough to cause bleeding), simple excision, excision and cautery, and cryotherapy. In patients with multiple lesions, care should be taken to identify and treat nascent lesions in order to reduce the risk of recurrence, but reduction of the viral load often allows the host immunologic response to eliminate residual virus. The conjunctivitis may require weeks to resolve after elimination of the lesion. In adults, large and multiple molluscum lesions with relatively little conjunctival inflammation may indicate an immunocompromised state.[239] Follow-up is not usually necessary unless the conjunctivitis persists. Referral to a dermatologist may be necessary for examination of other suspicious lesions.

Bacterial Conjunctivitis

Mild Bacterial Conjunctivitis

Mild bacterial conjunctivitis is usually self-limited, and it typically resolves spontaneously without specific treatment in immune-competent adults.[240] [8] [I+, Good, Strong] Use of topical antibacterial therapy is associated with earlier clinical and microbiological remission compared with placebo in days 2 to 5 of treatment.[240] [I+, Good, Strong] These advantages persist over days 6 to 10, but the extent of benefit over placebo lessens over time.[240] Treatment may reduce transmissibility and allow for an earlier return to school for children.[241] The choice of antibiotic is usually empiric. Because a 5- to 7-day course of a broad-spectrum topical antibiotic is usually effective, the most convenient or least expensive option can be selected; there is no clinical evidence suggesting the superiority of any particular antibiotic. Povidone-iodine 1.25% ophthalmic solution may be as effective as topical antibiotic therapy for treating bacterial conjunctivitis and could be considered when access to antibiotics is limited, such as in the developing world.[242] While there are no data supporting the cost-effectiveness of using antibiotics in mild bacterial conjunctivitis, the shortened morbidity associated with their use makes choice of therapy an individual decision.[240,243]

Moderate to Severe Bacterial Conjunctivitis

Moderate to severe bacterial conjunctivitis is characterized by copious purulent discharge, pain, and marked inflammation of the eye. Conjunctival cultures and slides for Gram staining should be obtained if gonococcal infection is a possibility. In these cases, the choice of antibiotic is guided by the results of laboratory tests. Methicillin-resistant *Staphylococcus aureus* has been isolated with increasing frequency from patients with bacterial conjunctivitis.[244,245] Increasing colonization of MRSA has been found in nursing home residents,[246] and the incidence of community-acquired MRSA infections also has risen.[247] Methicillin-resistant *S. aureus* organisms are resistant to many commercially available topical antibiotics.[244,245,248] Microbiology laboratory testing may guide therapy, which may include compounded topical antibiotics such as vancomycin (see Bacterial Keratitis PPP).

Systemic antibiotic therapy is necessary to treat conjunctivitis due to *Neisseria gonorrhoeae* and *Chlamydia trachomatis* (see Table 3).[43] Initiation of systemic therapy should be considered prior to obtaining culture results when there is high clinical suspicion. Topical therapy, while not necessary, is usually also used.

Saline lavage may promote comfort and more rapid resolution of inflammation in gonococcal conjunctivitis. If corneal involvement is present, the patient should also be treated topically as for bacterial keratitis (see Bacterial Keratitis PPP[249]). Patients and sexual contacts should be informed about the possibility of concomitant disease and referred appropriately. Sexual abuse should be considered in children with this condition.

Patients with gonococcal conjunctivitis should be seen daily until resolution of the conjunctivitis. At each follow-up visit, an interval history, visual acuity measurement, and slit-lamp biomicroscopy should be performed. For other types of bacterial conjunctivitis, patients should be advised to return for a visit in 3 to 4 days if they note no improvement. *N. meningitis* should be eliminated as the causative organism before concluding that *N. gonorrhoeae* is responsible.

An epidemiologic study found that infants within the neonatal intensive care setting due to low birth weight and/or low gestational age have an increased incidence of gram-negative conjunctivitis that is often resistant to gentamicin.[250]

Chlamydial Conjunctivitis

Table 3 provides recommendations for the treatment of chlamydial conjunctivitis. Because more than 50% of infants with chlamydial conjunctivitis may also be infected at other sites such as the nasopharynx, genital tract, or lungs, systemic therapy is indicated.[43,251] Empiric antibiotic therapy can be considered in patients with symptoms and signs highly suggestive of chlamydia (e.g., follicular conjunctivitis that persists for several weeks). There are no data to support the use of topical therapy in addition to systemic therapy. Because the incidence of treatment failure can be as high as 19%,[50] patients should be re-evaluated following treatment. The follow-up visit should consist of an interval history, visual acuity measurement, and slit-lamp biomicroscopy. Adult conjunctivitis usually responds to systemic therapy, and sexual contacts should be treated at the same time. Patients and sexual contacts should be informed about the possibility of concomitant disease and should be referred appropriately. Sexual abuse should be considered in children with this condition. In developing countries where antibiotic access is limited, povidone-iodine 1.25% ophthalmic solution can be used to treat chlamydial conjunctivitis.[242]

Vasculitis

When a diagnosis of vasculitis is confirmed, topical/periocular steroids may be considered in cases of unilateral ocular involvement. Bilateral ocular involvement, advanced vision loss, and/or systemic comorbidities often necessitate systemic immunosuppression with corticosteroids, antimetabolites, calcineurin inhibitors,[252] biologics,[253] or intravenous immunoglobulins.[254] Notably, infectious causes must be ruled out before considering immunosuppression.

Ligneous Conjunctivitis

Ligneous conjunctivitis is caused by plasminogen deficiency resulting in pseudomembranous disease of mucous membranes in the mouth, nasopharynx, trachea, and female genital tract. This chronic childhood membranous conjunctivitis has been treated successfully using intravenous lysplasminogen[255] or topical plasminogen drops,[256] or surgical excision with immediate anticoagulation and immunosuppression.[257]

PROVIDER AND SETTING

Because there is a spectrum of etiologies and treatment, optimal diagnosis and management of conjunctivitis require broad medical skills and experience. Some types of conjunctivitis are associated with systemic diseases and may require systemic drug treatment.

Patients with conjunctivitis who are evaluated by nonophthalmologist health care providers should be referred promptly to the ophthalmologist in any of the following circumstances:

- Visual loss
- Moderate or severe pain
- Severe, purulent discharge
- Corneal involvement
- Conjunctival scarring
- Lack of response to therapy
- Recurrent episodes
- History of HSV eye disease
- History of immunocompromise

Most patients with conjunctivitis can be treated effectively in an outpatient setting. Hospitalization may be necessary to administer parenteral therapy for severe gonococcal conjunctivitis and is mandatory for neonatal conjunctivitis.[8] [I+, Good, Strong]

COUNSELING AND REFERRAL

Counseling is imperative for all contagious varieties of conjunctivitis to minimize or prevent spread of the disease in the community. Modes of transmission include eye-hand contact, sexual contact, exposure to contaminated droplets, and exposure to airborne pathogens. Hand-washing is important to reduce the risk of transmission of viral infection. Return to school or work depends on the age of the patient, occupation, and type and severity of conjunctivitis.

When conjunctivitis is associated with sexually transmitted disease, treatment of sexual partners is essential to minimize recurrence and spread of the disease. Patients as well as their sexual partners should be referred to an appropriate medical specialist. The physician must remain alert to the possibility of child abuse in cases of potentially sexually transmitted ocular disease in children. In many states, sexually transmitted diseases and suspected child abuse must be reported to local health authorities or other state agencies.

In cases of ophthalmia neonatorum due to gonococcus, chlamydia, and HSV, the infant should be referred to an appropriate specialist. Infants who require systemic treatment are best managed in conjunction with a pediatrician.

When conjunctivitis appears to be a manifestation of systemic disease, patients should be referred to an appropriate medical specialist for evaluation.

SOCIOECONOMIC CONSIDERATIONS

Conjunctivitis is very common worldwide, and it has a broad spectrum of disease severity and underlying etiologies.

Allergic Conjunctivitis

Allergic conjunctivitis alone has been estimated to occur in 6% to 40% of the general population and symptoms are noted in 30% to 71% of patients with allergic rhinitis.[258,259] There have been multiple studies that have examined how allergic conjunctivitis causes a reduction in quality of life[260-263] and increases economic costs.[261,263-265] The costs include not only direct costs such as doctors' visits and medications but also indirect costs such as missed days from work and school, and decreased productivity while at work.[266]

Higher socioeconomic position or type 1 diabetes may be related to increased risk of developing allergies.[267,268] In countries with high rates of allergic diseases, it has been noted that children who had recently immigrated may have a protective premigration environment that results in a lower prevalence of asthma, conjunctivitis, and eczema.

An observational cross-sectional study on allergic rhinitis in four European countries showed that the presence of ocular symptoms reduces quality of life, reduces work productivity, and increases resource utilization regardless of the severity of nasal symptoms.[261] Another cross-sectional study looked at patients diagnosed with allergic conjunctivitis in 16 ophthalmology departments in Portugal. It found that 59% of patients had year-round symptoms, and that 46% had significant impairment in their quality of life during an acute episode.[262] Chronic allergic rhinitis/conjunctivitis is also a common disease among children.[264] Among students with nasal and ocular symptoms, 42%, 24%, 36%, and 28% reported moderate to severe interference of daily activities, at least 1 day of absence from school, a visit to a health care professional, and drug usage for rhinitis, respectively. The total number of prescriptions written for ocular allergy has increased by 20% per year, and current expenditure on treatment is approximately $1 billion, a 25% increase per year.[269] In the United States, the direct and indirect costs are estimated to be at least $6 billion a year.[265] Similar decreases in quality of life and progressively increasing economic costs for seasonal allergic conjunctivitis were also found in Spain and Oxfordshire, England.[270] Treatment options that address ocular symptoms may have a large beneficial impact on quality of life and decrease direct and indirect costs associated with allergic rhinitis.[261]

Vernal keratoconjunctivitis is a chronic form of allergic conjunctivitis that is more common in children and young adults and is more prevalent in hot, dry climates.[271] A population-based case-control study conducted on 3049 children in Rwanda identified hot climates, male gender, and higher socioeconomic status as risk factors.[271] The authors hypothesize that there may be differing immunologic and environmental mechanisms present in urban settings compared with rural settings that account for this socioeconomic finding, and they suggest that further study is warranted. In the Rwandan study, 36% of children with VKC missed 1 or more days of school in the last 3 months for an ocular reason.[272] Topical cyclosporine and tacrolimus have been shown to be effective treatments, but cost may limit their use in the developing world.[61] One study reported that during active flare-ups of adult KVC, productivity was reduced by 26% and social activities by 31%.[22]

Bacterial Conjunctivitis

The economic impact of bacterial conjunctivitis is also substantial. A study was performed on a single outbreak of pneumococcal conjunctivitis at Dartmouth College in 2002 that affected 698 students.[5] Even though the course of the disease was very short

and there were no long-term ocular sequelae, the estimated cost, including doctors' visits, cultures, and antibiotics, ranged from $66,468 to $120,583. Another study looked at the entire country using data from the medical literature, existing national databases, and Current Procedural Terminology codes.[4] The estimated number of cases of bacterial conjunctivitis in the United States in 2005 was 4 million, and the total direct and indirect cost of treating patients with bacterial conjunctivitis was $589 million. Data on costs associated with missed work or school, as well as the economic impact of untreated bacterial conjunctivitis, are not available.

Adenoviral Conjunctivitis

Antibiotics are not indicated in the treatment of adenoviral conjunctivitis yet are frequently prescribed. In one retrospective study, 60% of patients diagnosed with adenoviral conjunctivitis filled antibiotic prescriptions, and one of five of these were for antibiotic-steroid combination drops, which are contraindicated in acute conjunctivitis. Compared to ophthalmologists, prescriptions were given more often if an optometrist, urgent care physician, or primary care provider versus an ophthalmologist made the initial diagnosis. Antibiotic prescriptions were also more likely to be filled by white, affluent, and/or educated patients.[273] These practices contribute to avoidable increased health care costs and may promote antibiotic resistance.

Even though adenoviral conjunctivitis is a common condition that often results in several missed days of work/school and can lead to painful and visually debilitating keratoconjunctivitis, there are not any published studies yet on its overall economic impact in the general population. A single outbreak of adenoviral keratoconjunctivitis in a long-term care facility, which affected 41 residents, resulted in hospital costs of $29,527 ($1085 for medical costs, $8210 for investigative costs, $3048 for preventive measures, and $17,184 for lost productivity).[274] Preventive infection-control measures can be extremely cost-effective if such an outbreak is avoided. There are quick point-of-care tests for adenovirus. The cost per case using one system for adenoviral conjunctivitis is $111.56 with no rapid test (including the cost of unnecessary antibiotic therapy), and it is $40.25 with the test, implying a cost savings of $71.31 per case.[53] If these costs are extrapolated to include the entire US population, it is estimated that nearly $430 million in unnecessary medical care could be saved and that over 1 million cases of unnecessary antibiotic treatment could be avoided.

Ocular Surface Squamous Neoplasia

Outcomes of medical versus surgical treatment in patients with ocular surface squamous neoplasia (OSSN) have been found to be equally efficacious.[275,276] Socioeconomic considerations do play a role in treatment decision making. One study reviewed the cost of medical treatment with interferon (IFN-α2b) and found that it involved more time and a higher level of compliance over surgical treatment. Hospital billing charges were higher in the surgical group compared with the interferon group (the surgery group's average cost was $17,598 vs. the interferon group's average cost of $4986). For uninsured patients, medical treatment may be more financially appealing. The Medicare allowable charges were comparable between the two groups (surgical allowable charges were $705.60 vs. medical treatment of $566.20, or 20% of allowable charges).[277]

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 respond in an adequate and timely manner.
  - 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

Conjunctivitis includes entities with the following ICD-10 classifications:

	ICD-10 CM
Conjunctivitis, other diseases of conjunctiva caused by viruses	Code first underlying virus or chemical and intent H10.011 – H10.813 (approximately 65 codes in this range)
Chlamydia and ophthalmia neonatorum caused by gonococcus	A74.0, B30.0 – B30.9 A54.31
Blepharoconjunctivitis	H10.50-, H10.51-, H10.53-
Zika virus	A92.5
Ligneous	H10.51-
Measles	B05.81
Seasonal allergic conjunctivitis	H10.45
Vernal conjunctivitis	H10.44
Atopic conjunctivitis	H10.1-
Giant papillary conjunctivitis (GPC), which also has a mechanical component	H10.41-
Superior limbic keratoconjunctivitis (SLK)	H16.29-
Contact lens–related keratoconjunctivitis	H12.89
Floppy eyelid syndrome	H02.89
Giant fornix syndrome	H16.29_ (other keratoconjunctivitis)
Pediculosis palpebrarum (*Phthirus pubis*)	H44.52-
Medication-induced keratoconjunctivitis	H10.40_ (unspecified chronic conjunctivitis)
Conjunctival chalasis	H11.82-
Adenoviral conjunctivitis	B30.1
Herpes simplex virus (HSV) conjunctivitis	B00.53
Varicella (herpes) zoster virus (VZV) conjunctivitis	B02.31
Molluscum contagiosum	B08.1
Bacterial conjunctivitis (including nongonococcal and gonococcal)	H10.89
Chlamydial conjunctivitis	A74.0
Ocular mucous membrane pemphigoid (OMMP)	L12.1
Graft-versus-host disease (GVHD)	D89.810, D89.811, D89.812
Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN)	L51.3

CM = Clinical Modification used in the United States; ICD = International Classification of Diseases; (–) = 1, right eye; 2, left eye; 3, bilateral

Additional information:

- Certain ICD-10 CM categories have applicable 7th characters. The applicable 7th character is required for all codes within the category, or as the notes in the Tabular List instruct. The 7th character must always be the 7th character in the data field. If a code that requires a 7th 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., 4th digit, 5th digit, or 6th digit):
    - Right is always 1
    - Left is always 2
    - Bilateral is always 3

APPENDIX 3. OCULAR SURFACE DYE STAINING

Fluorescein, rose bengal, or lissamine green dyes may be used to assess the ocular surface.

Fluorescein dye stains areas of the corneal and conjunctival epithelium where there is sufficient disruption of intercellular junctions to allow the dye to permeate into the tissue.[278] Saline-moistened fluorescein strips or 1% to 2% sodium fluorescein solution are used to stain the tear film. After instilling the dye, the ocular surface is examined through a biomicroscope using a cobalt blue filter. Staining may become more apparent after 1 to 2 minutes. Staining is more intense when it is observed using a yellow filter. Mild fluorescein staining can be observed in normal eyes and may be more prominent in the morning. Exposure-zone punctate or blotchy fluorescein staining is observed in dry eye, and staining is more easily visualized on the cornea than on the conjunctiva.

Rose bengal dye stains ocular surface cells that lack a mucous coating as well as debris in the tear film,[278] and this staining may be easier to observe with a red-free filter (green filter). Rose bengal staining of the tear film may be performed using a saline-moistened strip or 1% solution. (Patients should be informed that the drop might irritate the eye.) The saline drop used to moisten the strip should remain in contact with the strip for at least a minute to achieve an adequate concentration of rose bengal to stain the ocular surface. Rose bengal staining is more intense on the conjunctiva than on the cornea. Rose bengal has antiviral properties and may affect herpes simplex virus-1 (HSV-1) culture results. It is also helpful when delineating the margins of ocular surface neoplasms.[279]

Lissamine green dye has a staining profile similar to that of rose bengal[280] and may cause less ocular irritation.[280] It is not recommended for evaluating corneal epithelial disease; it is more useful for observing conjunctival staining.

Diffuse corneal and conjunctival staining is commonly seen in viral keratoconjunctivitis and medicamentosa. Staining of the inferior cornea and bulbar conjunctiva is typically observed in patients with staphylococcal blepharitis, meibomian gland dysfunction (MGD), lagophthalmos, and exposure, whereas staining of the superior bulbar conjunctiva is typically seen in superior limbic keratoconjunctivitis. A pattern of exposure zone (interpalpebral) corneal and bulbar conjunctival staining is typically seen with dry eye disease.[281,282]

LITERATURE SEARCHES FOR THIS PPP

Literature searches of the PubMed and Cochrane databases were conducted in March 2017; the search strategies were as follows. Specific limited update searches were conducted after June 2018.

General:

(conjunctivitis[majr:noexp] OR conjunctivitis, allergic[majr:noexp] OR conjunctivitis, bacterial[majr:noexp] OR conjunctivitis, viral[majr:noexp] OR keratoconjunctivitis[majr:noexp] OR conjunctivitis[tiab] OR keratoconjunctivitis[tiab])

Epidemiology:

(conjunctivitis/epidemiology[majr:noexp] OR conjunctivitis, allergic/epidemiology[majr:noexp] OR conjunctivitis, bacterial/epidemiology[majr:noexp] OR conjunctivitis, viral/epidemiology[majr:noexp] OR keratoconjunctivitis/epidemiology[majr:noexp])

Risk Factors:

(conjunctivitis[majr:noexp] OR conjunctivitis, allergic[majr:noexp] OR conjunctivitis, bacterial[majr:noexp] OR conjunctivitis, viral[majr:noexp] OR keratoconjunctivitis[majr:noexp]) AND (risk factors[MeSH Terms])

Contact Lenses:

(conjunctivitis[mh:noexp] OR conjunctivitis, allergic[mh:noexp] OR conjunctivitis, bacterial[mh:noexp] OR conjunctivitis, viral[mh:noexp] OR keratoconjunctivitis[mh:noexp])

Etiology:

(conjunctivitis/etiology[majr:noexp] OR conjunctivitis, allergic/etiology[majr:noexp] OR conjunctivitis, bacterial/etiology[majr:noexp] OR conjunctivitis, viral/etiology[majr:noexp] OR keratoconjunctivitis/etiology[majr:noexp])

Pathology/Physiology/Physiopathology:

(conjunctivitis/pathology[majr:noexp] OR conjunctivitis/physiology[majr:noexp] OR conjunctivitis/physiopathology[majr:noexp] OR conjunctivitis, allergic/pathology[majr:noexp] OR conjunctivitis, allergic/physiopathology[majr:noexp] OR conjunctivitis, allergic/physiology[mh] OR conjunctivitis, bacterial/pathology[majr:noexp] OR conjunctivitis, bacterial/physiopathology[majr:noexp] OR conjunctivitis, bacterial/physiology[mh] OR conjunctivitis, viral/pathology[majr:noexp] OR conjunctivitis, viral/physiopathology[majr:noexp] OR conjunctivitis, viral/physiology[mh] OR keratoconjunctivitis/pathology[majr:noexp] OR keratoconjunctivitis/physiology[majr:noexp] OR keratoconjunctivitis/physiopathology[majr:noexp])

Economics:

(conjunctivitis/economics[mh:noexp] OR conjunctivitis, allergic/economics[mh:noexp] OR conjunctivitis, bacterial/economics[mh:noexp] OR conjunctivitis, viral/economics[mh:noexp] OR keratoconjunctivitis/economics[mh:noexp])

Cost of Illness:

(conjunctivitis[majr:noexp] OR conjunctivitis, allergic[majr:noexp] OR conjunctivitis, bacterial[majr:noexp] OR conjunctivitis, viral[majr:noexp] OR keratoconjunctivitis[majr:noexp]) AND (cost of illness[MeSH Terms] OR Cost-Benefit Analysis[MeSH Terms])

Quality of Life:

(conjunctivitis[majr:noexp] OR conjunctivitis, allergic[majr:noexp] OR conjunctivitis, bacterial[majr:noexp] OR conjunctivitis, viral[majr:noexp] OR keratoconjunctivitis[majr:noexp]) AND (Quality of Life[MeSH Terms])

Disease Progression:

(conjunctivitis[majr:noexp] OR conjunctivitis, allergic[majr:noexp] OR conjunctivitis, bacterial[majr:noexp] OR conjunctivitis, viral[majr:noexp] OR keratoconjunctivitis[majr:noexp]) AND (disease progression[MeSH terms])

Ganciclovir:

("ganciclovir"[MeSH Terms] OR ganciclovir[tiab]) AND (keratitis[tiab] OR conjunctivitis[tiab] OR keratoconjunctivitis[tiab])

Diagnosis:

(conjunctivitis/diagnosis[majr:noexp] OR conjunctivitis, allergic/diagnosis[majr:noexp] OR conjunctivitis, bacterial/diagnosis[majr:noexp] OR conjunctivitis, viral/diagnosis[majr:noexp] OR keratoconjunctivitis/diagnosis[majr:noexp]) AND (“2012/06/15”[dp]: “3000”[dp]) = 53 references

RELATED ACADEMY MATERIALS

Basic and Clinical Science Course

External Disease and Cornea (Section 8, 2018–2019)

Focal Points

Chronic Conjunctivitis, Part 1 and Part 2 (2012)

Patient Education Brochure

Conjunctivitis (2014)

Preferred Practice Pattern® Guidelines – Free download available at www.aao.org/ppp**.**

Comprehensive Adult Medical Eye Evaluation (2015)

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