PREFERRED PRACTICE PATTERN®

Blepharitis

AMERICAN ACADEMY® OF OPHTHALMOLOGY
The Eye M.D. Association

Approved by: Board of Trustees
September 21, 2013

This document should be cited as follows:
American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern® Guidelines. Blepharitis. San Francisco, CA: American Academy of Ophthalmology; 2013. Available at: www.aao.org/ppp.

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.

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

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

Cornea/External Disease Preferred Practice Pattern Panel 2012–2013
Robert S. Feder, MD, Co-chair
Stephen D. McLeod, MD, Co-chair
Esen K. Akpek, MD, Cornea Society Representative
Steven P. Dunn, MD
Francisco J. Garcia-Ferrer, MD
Amy Lin, MD
Francis S. Mah, MD
Audrey R. Talley-Rostov, MD
Divya M. Varu, MD
David C. Musch, PhD, MPH, Methodologist

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

Preferred Practice Patterns Committee 2013
Stephen D. McLeod, MD, Chair
David F. Chang, MD
Robert S. Feder, MD
Timothy W. Olsen, MD
Bruce E. Prum, Jr., MD
C. Gail Summers, MD
David C. Musch, PhD, MPH, Methodologist

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

Academy Reviewers
Board of Trustees and Committee of Secretaries
Council
General Counsel
Ophthalmic Technology Assessment Committee
    Cornea and Anterior Segment Disorders Panel
Basic and Clinical Science Course Subcommittee
Practicing Ophthalmologists Advisory Committee
    for Education

Invited Reviewers
AARP
Asia Cornea Society
Cornea Society
National Eye Institute
Ocular Microbiology and Immunology Group
Dan B. Jones, MD
James P. McCulley, MD, FACS
Ronald E. Smith, MD

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 http://one.aao.org/CE/PracticeGuidelines/PPP.aspx). A majority (70%) of the members of the Cornea/External Disease Preferred Practice Pattern Panel 2012–2013 had no financial relationship to disclose.

Cornea/External Disease Preferred Practice Pattern Panel 2012–2013
Esen K. Akpek, MD: No financial relationships to disclose
Steven P. Dunn, MD: No financial relationships to disclose
Robert S. Feder, MD: No financial relationships to disclose
Francisco J. Garcia-Ferrer: No financial relationships to disclose
Amy Lin, MD: No financial relationships to disclose
Francis S. Mah, MD: Alcon Laboratories, Inc. – Consultant/Advisor; Allergan, Inc. – Consultant/Advisor, Lecture fees; ForeSight – Consultant/Advisor; Ista Pharmaceuticals – Consultant/Advisor; Nicox – Consultant/Advisor; Omeros – Consultant/Advisor
Stephen D. McLeod, MD: No financial relationships to disclose
David C. Musch, PhD, MPH: Abbott Laboratories – Consultant fees (member of Independent Data Monitoring Committee); ClinReg Consulting Services, Inc. – Consultant/Advisor
Audrey R. Talley-Rostov, MD: Addition Technology – Lecture fees; Allergan, Inc. – Lecture fees
Divya M. Varu, MD: No financial relationships to disclose

Preferred Practice Patterns Committee 2013
David F. Chang, MD: Abbott Medical Optics – Consultant/Advisor; Allergan, Inc. – Lecture fees; SLACK, Inc. – Patent/Royalty
Robert S. Feder, MD: No financial relationships to disclose
Stephen D. McLeod, MD: No financial relationships to disclose
David C. Musch, PhD, MPH: Abbott Laboratories – Consultant fees (member of Independent Data Monitoring Committee); ClinReg Consulting Services, Inc. – Consultant/Advisor
Timothy W. Olsen, MD: A Tissue Support Structure – Patents/Royalty; Scleral Depressor – Patents/Royalty
Bruce E. Prum, Jr., MD: Pfizer Ophthalmics – Lecture fees
C. Gail Summers, MD: No financial relationships to disclose

Secretary for Quality of Care
Anne L. Coleman, MD, PhD: Allergan, Inc. – Consultant/Advisor; Pfizer Ophthalmics – Consultant/Advisor

Academy Staff
Nicholas P. Emptage, MAE: No financial relationships to disclose
Nancy Collins, RN, MPH: No financial relationships to disclose
Susan Garratt, Medical Editor: No financial relationships to disclose
Flora C. Lum, MD: No financial relationships to disclose
Doris Mizuiri: No financial relationships to disclose
Jessica Ravetto: No financial relationships to disclose

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

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 http://one.aao.org/CE/PracticeGuidelines/PPP.aspx) to comply with the Code.

Appendix 2 contains the International Statistical Classification of Diseases and Related Health Problems (ICD) codes for the disease entities that this PPP covers. The intended users of the Blepharitis 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 Policy, 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. To locate ratings for specific recommendations, see Appendix 3 for additional information.
- Literature searches to update the PPP were undertaken in June 2012 and January 2013 in PubMed and the Cochrane Library. Complete details of the literature search are available at www.aao.org/ppp.

HIGHLIGHTED FINDINGS AND RECOMMENDATIONS FOR CARE

In the management of ocular surface disease, it is helpful to distinguish blepharitis and meibomian gland dysfunction (MGD) from aqueous deficient dry eye. Worsening of symptoms in the morning is typical of blepharitis, whereas symptoms that are worse later in the day are typical of aqueous deficient dry eye.

Blepharitis is typically a chronic condition that cannot be permanently cured, and successful management is dependent on patient compliance with a treatment regimen. This should be explained to the affected patient.

Attempts should be made to treat moderate to severe blepharitis with eyelid hygiene and topical antibiotics prior to intraocular surgery, if in the surgeon's judgment the eyelid condition has increased the load of ocular surface bacteria, even if the patient is asymptomatic, in order to reduce the risk of endophthalmitis.

Costly new technologies (including devices using thermal pulsation) are available, but the current evidence is not sufficient to support their use in the treatment of blepharitis.

Topical antibiotic ointments with or without corticosteroids or oral antibiotics can be used effectively in the treatment of blepharitis. Although azithromycin is used as a treatment for blepharitis, it may be hazardous when used orally in patients with cardiovascular problems. In March 2013, the FDA issued a warning that oral azithromycin may lead to abnormalities in the electrical activity of the heart, with the potential to create serious irregularities in heart rhythm.

In patients with chronic blepharitis that does not respond to therapy, the possibility of carcinoma should be considered, particularly if associated with a loss of eyelashes. Early diagnosis and appropriate treatment can prevent disfigurement and may be lifesaving.

INTRODUCTION

DISEASE DEFINITION

This PPP focuses on chronic blepharitis, which is a chronic ocular inflammation that involves the eyelid margin primarily and is a common cause of chronic ocular irritation.

PATIENT POPULATION

The patient population includes individuals of all ages who present with symptoms and signs suggestive of blepharitis, such as eyelid and ocular irritation and redness.

CLINICAL OBJECTIVES

- Establish the diagnosis of blepharitis, differentiating it from other causes of irritation and redness
- Identify the type of blepharitis
- Establish appropriate therapy
- Relieve discomfort and pain
- Prevent complications
- Educate and engage the patient in the management of this potentially chronic disease

BACKGROUND

Blepharitis can be classified according to anatomic location: anterior blepharitis affects the eyelid skin, base of the eyelashes and the eyelash follicles, and posterior blepharitis affects the meibomian glands and gland orifices. Blepharitis has traditionally been clinically subcategorized as staphylococcal, seborrheic, meibomian gland dysfunction (MGD), or a combination thereof.[4] Staphylococcal and seborrheic blepharitis involve mainly the anterior eyelid and can each be referred to as anterior blepharitis. Meibomian gland dysfunction, as defined by the International Workshop on Meibomian Gland Dysfunction (www.tearfilm.org/mgdworkshop/index.html), is a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion. It may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease. Meibomian gland dysfunction is further subcategorized into hyposecretory, obstructive, and hypersecretory forms.[5] This PPP covers the three clinical subcategories of chronic blepharitis.[6]

There is considerable overlap of symptoms of all types of blepharitis. Blepharitis frequently leads to associated ocular surface inflammation, including conjunctivitis, functional tear deficiency, and keratitis. Blepharitis may also exacerbate symptoms of coexisting ocular surface disease, including allergy and aqueous tear deficiency. The chronic nature of blepharitis, the uncertain etiology, and the frequent coexistence of ocular surface disease make blepharitis difficult to manage.

Staphylococcal blepharitis is characterized by scaling, crusting, and erythema of the eyelid margin with collarette formation at the base of the cilia. Chronic inflammation may be punctuated by acute exacerbations that lead to the development of ulcerative blepharitis. Loss of eyelashes and corneal involvement, including punctate epithelial erosions, marginal infiltrates, and neovascularization, may occur.

Although coagulase negative staphylococcus is isolated with great frequency (in 89% to 100% of cases) from eyelids of both normal subjects and patients with blepharitis, *Staphylococcus aureus* is isolated with greater frequency from eyelids of patients with clinical diagnoses of staphylococcal blepharitis.[4] Both coagulase negative staphylococcus and *S. aureus* are believed to play a role in the development of staphylococcal blepharitis, but the mechanisms of pathophysiology remain poorly understood. Toxin production has been reported to correlate with the presence of blepharoconjunctivitis[7]; however, other studies have found no correlation between toxin production of *S. aureus* isolates and the presence of clinical disease.[8] Immunologic mechanisms have been documented. Enhanced cell-mediated immunity to *S. aureus* has been detected in 40% of patients with chronic blepharitis but not among normal subjects.[9] Cell-mediated immunologic mechanisms have also been implicated in the development of keratitis associated with staphylococcal

blepharitis.[10] Staphylococcal antigens themselves can initiate an inflammatory reaction by attaching to bacterial antigen-binding receptors that are present on the corneal epithelium.[11,12]

Patients with seborrheic blepharitis have greasy scaling of the anterior eyelid, and they frequently have seborrheic dermatitis of the eyebrows and scalp as well.

Eyelid manifestations of MGD include prominent blood vessels crossing the mucocutaneous junction, frothy discharge along the eyelid margin, pouting or plugging of meibomian orifices, expression of meibomian secretions that range from turbid fluid to thick cheese-like material, thickening and scalloping of the eyelid margin, trichiasis, and chalazion. These changes can lead to eventual atrophy of meibomian glands and cicatrization. Patients with MGD frequently are noted to have coexisting rosacea or seborrheic dermatitis.[4,13] Alterations in the biochemical composition of meibomian gland secretions have been documented in patients with MGD blepharitis when compared with normal subjects.[14] The result of MGD is decreased availability of normal meibum to the lid margin and tear film. This, in turn, may result in an increase in tear evaporation, hyperosmolarity and instability of the tear film, increased bacterial growth on the lid margin, evaporative dry eye, and ocular surface inflammation and damage.[15]

PREVALENCE

Although blepharitis is one of the most common ocular disorders, epidemiological information on its incidence or prevalence within defined populations is lacking. One single-center study of 90 patients with chronic blepharitis noted that the mean age of patients was 50 years.[15] Compared with patients with other forms of blepharitis, patients with staphylococcal blepharitis were found to be relatively younger (42 years old) and most were female (80%).[4] A survey of a representative sample of U.S. adults (n = 5000) revealed that typical symptoms associated with blepharitis are quite common, and that younger people report more frequent symptoms than older individuals. In another study in the same report, ophthalmologists and optometrists reported that blepharitis was commonly seen in clinical practice in 37% and 47% of their patients, respectively. Meibomian gland dysfunction was considered to be the most common cause of evaporative dry eye disease.[16]

The prevalence of clinically diagnosed MGD varies widely in the published world literature,[15] with a suggestion that MGD is significantly more common among Asian populations than Caucasian populations. However, there is significant variation in how the disease was defined and in the age of the study groups.[17-21]

RISK FACTORS AND ASSOCIATED CONDITIONS

- Dry eye

  Dry eye has been reported to be present in 50% of patients with staphylococcal blepharitis.[4] Conversely, in a series of 66 patients with dry eye, 75% had staphylococcal conjunctivitis or blepharitis.[22] It is possible that a decrease in local lysozyme and immunoglobulin levels associated with tear deficiency may alter resistance to bacteria, predisposing to the development of staphylococcal blepharitis.[10]

  Twenty-five percent to 40% of patients with seborrheic blepharitis and MGD,[4] and 37% to 52% of patients with ocular rosacea[13] also have aqueous tear deficiency. This may result from increased tear film evaporation due to a deficiency in the lipid component of the tears as well as reduced ocular surface sensation.[23,24] Low levels of tear film phospholipids have been found to correlate with the presence of dry eye in patients with chronic blepharitis.[25]

- Dermatologic conditions

  Dermatologic conditions associated with seborrheic blepharitis and MGD may share common etiologies and predisposing factors. In one study, 95% of patients with seborrheic blepharitis also had seborrheic dermatitis.[4] In patients with a subset of MGD called primary (diffuse) meibomitis, 74% had a seborrheic dermatitis and 51% had rosacea (acne rosacea).[4,15]

- Demodicosis

  Demodex folliculorum has been found in 30% of patients with chronic blepharitis, but it has also been found with nearly the same prevalence in patients without blepharitis.[26] However, patients with recalcitrant blepharitis have responded to therapy directed at eradicating the Demodex mites.[26] Eyelashes with cylindrical dandruff or sleeves are reported to be pathognomonic for ocular Demodex infestation.[27]

- Rosacea

  Rosacea is a disease of the skin and eye that is observed more frequently in fair-skinned individuals,[28] but it can occur in people of all races. Characteristic facial skin findings include erythema, telangiectasia, papules, pustules, prominent sebaceous glands, and rhinophyma. Rosacea is also associated with epithelial basement membrane abnormalities and recurrent corneal epithelial erosions.[29,30]

  Rosacea may be difficult to diagnose in patients with darker skin tones because of the difficulty in visualizing telangiectasia or facial flushing. Rosacea is typically seen in middle age and occurs more often in women.[31] While rosacea is more prevalent in women, it can be more severe when it occurs in men.[32,33] Because many patients exhibit only mild signs, such as telangiectasia and a history of easy facial flushing, the diagnosis of rosacea is often overlooked, especially in children who may present with chronic recurrent keratoconjunctivitis, punctate erosions, keratitis, MGD, or recurrent chalazia and have subtle signs of rosacea.[34] Children with ocular rosacea often present with corneal involvement, asymmetry of ocular disease, and the potential for sight-threatening visual impairment. Facial rosacea is less frequent in children, and associated atopy is common.[35,36] Children with a history of styes have an increased risk of developing adult rosacea.[37]

- Isotretinoin

  Isotretinoin, an oral medication that is used to treat severe cystic acne, is associated with a significant increase in colonization of the conjunctiva with *S. aureus*, blepharitis, and a disruption in tear function.[38] Discontinuation of the medication leads to improvement in most cases.[38-41]

- Giant papillary conjunctivitis

  Patients with contact-lens-associated giant papillary conjunctivitis (GPC) have an increased frequency of MGD.[42] The severity of GPC may correlate with the severity of MGD.[42]

  Table 1 lists other entities that produce inflammation of the eyelid margin.

NATURAL HISTORY

Blepharitis is a chronic condition that has periods of exacerbation and remission. Although onset usually occurs in middle-aged adults, it can begin in childhood.[34,43] Staphylococcal blepharitis may become less problematic with time. Severe staphylococcal blepharitis may eventually lead to eyelash loss, eyelid scarring with trichiasis, and corneal scarring and neovascularization.[9] Patients with seborrheic blepharitis and MGD are generally older and have a longer history of ocular symptoms (range 6.5 to 11.6 years).[10] Eyelid margin telangiectasia and meibomian gland orifice narrowing and pouting may occur in asymptomatic older patients.[44] Meibomian gland dysfunction can also occur in the absence of inflammation.[5]

Patients with severe ocular rosacea may develop superficial punctate keratopathy, corneal neovascularization, and scarring.[28] However, these findings can occur with blepharitis in the absence of rosacea. Ulceration and perforation can occur rarely.

Blepharitis PPP:
Risk Factors and Associated Conditions

TABLE 1 OTHER CONDITIONS ASSOCIATED WITH EYELID INFLAMMATION

Condition	Entity
Bacterial infections	• Impetigo (due primarily to *Staphylococcus aureas*) • Erysipelas (due primarily to *Streptococcus pyogenes*)
Viral infections	• Herpes simplex virus • Molluscum contagiosum • Varicella zoster virus • Papillomavirus • Vaccinia
Parasitic infection	• Pediculosis palpebrarum (*Phthirus pubis*)

Immunologic conditions	• Atopic dermatitis
	• Contact dermatitis
	• Erythema multiforme
	• Pemphigus foliaceus
	• Ocular mucous membrane pemphigoid (OMMP)
	• Stevens-Johnson syndrome
	• Connective tissue disorders
	  • Discoid lupus
	  • Dermatomyositis
	• Graft-versus-host disease (GVHD)
	• Crohn disease

Dermatoses	• Psoriasis • Ichthyosis • Exfoliative dermatitis • Erythroderma
Benign eyelid tumors	• Pseudoepitheliomatous hyperplasia • Actinic keratosis • Squamous cell papilloma • Sebaceous gland hyperplasia • Hemangioma • Pyogenic granuloma
Malignant eyelid tumors	• Basal cell carcinoma • Squamous cell carcinoma • Sebaceous carcinoma • Melanoma • Kaposi sarcoma • Mycosis fungoides
Trauma	• Chemical • Thermal • Radiation • Mechanical • Surgical
Toxic conditions	• Medicamentosa

CARE PROCESS

PATIENT OUTCOME CRITERIA

Outcome criteria for managing blepharitis include the following:

- Reduce the symptoms and signs of blepharitis
- Minimize structural damage
- Prevent loss of visual function

DIAGNOSIS

The initial evaluation of a patient with symptoms and signs suggestive of blepharitis should include the relevant aspects of the comprehensive medical eye evaluation.[45,46] The diagnosis of blepharitis is usually based on a typical patient history and characteristic slit-lamp biomicroscopic findings. Ancillary testing such as conjunctival cultures may be helpful.

History

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

- Symptoms and signs (e.g., redness, irritation, burning, tearing, itching, crusting of eyelashes, loss of eyelashes, eyelid sticking, blurring or fluctuating vision, contact lens intolerance, photophobia, increased frequency of blinking)
- Time of day when symptoms are worse (worsening of the symptoms in the morning is typical of blepharitis, whereas symptoms that worsen later in the day are typical of aqueous deficient dry eye)
- Duration of symptoms
- Unilateral or bilateral presentation
- Exacerbating conditions (e.g., smoke, allergens, wind, contact lenses, low humidity, retinoids, diet and alcohol consumption, eye makeup)
- Symptoms and signs related to systemic diseases (e.g., rosacea, allergy)
- Current and previous systemic and topical medications (e.g., antihistamines or drugs with anticholinergic effects, or drugs used in the past such as isotretinoin that might have an effect on the ocular surface)
- Recent exposure to an infected individual (e.g., pediculosis palpebrarum [*Phthirus pubis*])

The ocular history may include details about previous intraocular and eyelid surgery as well as local trauma, including mechanical, thermal, chemical, and radiation injury. A history of cosmetic blepharoplasty is important to obtain because increased surface exposure may increase tear evaporation. A history of styes and/or chalazia is common in patients with blepharitis.

The medical history may also include information about dermatological diseases such as rosacea, atopic dermatitis, and herpes zoster ophthalmicus.

Examination

Examination of the eye and adnexa includes measurement of visual acuity, an external examination, slit-lamp biomicroscopy, and measurement of intraocular pressure (IOP). The external examination should be performed in a well-lighted room with particular attention to the following:

- Skin
  - Changes consistent with rosacea such as rhinophyma, erythema, telangiectasia, papules, pustules, and hypertrophic sebaceous glands in malar areas
- Eyelids
  - Abnormal eyelid position (i.e., ectropion and entropion), eyelid closure (i.e., lagophthalmos), or blink response
  - Loss, breakage, or misdirection of eyelashes
  - Vascularization or hyperemia of eyelid margins
  - Abnormal deposits at the base of the eyelashes
  - Ulceration

- Vesicles
- Scaling, hyperkeratosis
- Chalazion/hordeolum
- Scarring

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

- Tear film
  - Tear meniscus
  - Tear film break-up time and pattern
  - Foamy discharge
  - Debris in the tear film
- Anterior eyelid margin
  - Hyperemia
  - Telangiectasia
  - Scarring
  - Pigmentary changes
  - Keratinization
  - Ulceration
  - Vesicles
  - Blood-tinged debris
  - Pediculosis palpebrarum (*Phthirus pubis*)
  - Presence of lesion
- Eyelashes
  - Malposition or misdirection
  - Loss or breakage
  - Pediculosis palpebrarum (*Phthirus pubis*) nits
  - Cylindrical sleeves (demodicosis or seborrhea)
  - Cosmetic deposits and collarettes
- Posterior eyelid margin
  - Abnormalities of meibomian orifices such as capping, pouting, retroplacement, metaplasia, and obliteration[47]
  - Character of meibomian secretions such as expressibility, thickness, turbidity, and color
  - Vascularization, keratinization, nodularity
  - Thickening
  - Scarring
- Tarsal conjunctiva (everting eyelids)
  - Appearance of meibomian glands and ducts such as dilation and inflammation
  - Chalazia
  - Erythema
  - Scarring
  - Keratinization
  - Papillary/follicular reaction
  - Lipid exudation/inspissation/concretions
- Bulbar conjunctiva
  - Hyperemia
  - Phlyctenules, follicles
  - Punctate staining with fluorescein, rose bengal, or lissamine green (generally fluorescein is used for cornea and lissamine green for conjunctiva)
- Cornea
  - Epithelial defect, punctate staining with fluorescein, rose bengal, or lissamine green (generally, fluorescein is used for cornea and lissamine for conjunctiva)
  - Edema, infiltrates, ulcers, and/or scars (small subepithelial or superficial stromal, circumferential, in midperipheral cornea, usually without overlying fluorescein staining)
  - Vascularization, scarring, including pannus
  - Phlyctenules

Diagnostic Tests

There are no specific clinical diagnostic tests for blepharitis. However, cultures of the eyelid margins may be indicated for patients who have recurrent anterior blepharitis with severe inflammation as well as for patients who are not responding to therapy. Microscopic evaluation of epilated eyelashes may reveal Demodex mites, which have been implicated in some cases of chronic blepharoconjunctivitis. This can be performed by placing the explanted eyelashes on a glass slide, adding a drop of fluorescein, and placing a cover slip.[48] Demodex infestation is associated with cylindrical dandruff or sleeves on the eyelashes and has been described in patients with MGD, conjunctival inflammation, and ocular rosacea. It has also been described in patients with corneal signs such as marginal infiltrate, phlyctenule, superficial vascularization, superficial opacities, and nodular scarring.[27,49] Since the presence of Demodex is common, its role as an etiologic agent in the cases of blepharoconjunctivitis has not been well established.

The possibility of carcinoma should be considered in patients with chronic blepharitis unresponsive to therapy, especially when only one eye is involved. A biopsy of the eyelid may be indicated to exclude the possibility of carcinoma in cases of marked asymmetry, resistance to therapy, or unifocal recurrent chalazia that do not respond well to therapy.[50] Additional signs of concern may include loss of normal eyelid margin and conjunctival anatomy, and focal lash loss (ciliary madarosis). Before obtaining a biopsy for suspected sebaceous carcinoma, consultation with a pathologist is recommended to discuss the potential need for frozen sections and mapping of the conjunctiva to search for pagetoid spread. Fresh tissue may be needed to detect lipids using special dyes such as oil red-O.

Clinical findings that may aid in the differential diagnosis of staphylococcal, seborrheic, and MGD blepharitis are summarized in Table 2. Features of these forms of blepharitis often overlap. In addition, patients with associated conditions such as dry eye can present with similar clinical features.

TABLE 2 DESCRIPTION OF CLINICAL FEATURES OF BLEPHARITIS BY CATEGORY

Feature	Anterior Eyelid		Posterior Eyelid
	Staphylococcal	Seborrheic	Meibomian Gland Dysfunction
Eyelash loss	Frequent	Rare	(—)
Eyelash misdirection	Frequent	Rare	May occur with long-standing disease
Eyelid deposits	Matted, hard scales/collarettes	Oily or greasy	Excess lipid, foamy discharge
Eyelid ulceration*	With severe exacerbations	(—)	(—)
Eyelid scarring	May occur	(—)	May occur with long-standing disease
Chalazia	Rare	Rare	Occasional to frequent, sometimes multiple
Hordeolum	May occur	(—)	(—)
Conjunctiva	Mild to moderate injection; phlyctenules may occur	Mild injection	Mild to moderate injection; papillary reaction of tarsal conjunctiva
Aqueous tear deficiency	Frequent	Frequent	Frequent
Cornea	Inferior punctate epithelial erosions, peripheral/marginal infiltrates (typically at 10, 2, 4, or 8 o'clock), scarring, neovascularization and pannus, thinning, phlyctenules	Inferior punctate epithelial erosions	Inferior punctate epithelial erosions, fine infiltrates superiorly and inferiorly, scarring, neovascularization and pannus, ulceration
Dermatologic disease	Atopy rarely	Seborrheic dermatitis	Rosacea

NOTE: A dash (—) in the column indicates that the feature is not found for the specific type of blepharitis.

Adapted with permission from the American Academy of Ophthalmology Basic and Clinical Science Course Subcommittee. Basic Clinical and Science Course. External Disease and Cornea: Section 8, 2013-2014. Table 3-9. San Francisco: American Academy of Ophthalmology, 2013.

* Also consider herpes simplex virus.

MANAGEMENT

Detection

Detection and appropriate treatment can reduce signs and symptoms of blepharitis, and in severe cases, prevent permanent structural damage and possible vision loss. This is particularly important in children, in whom chronic blepharokeratoconjunctivitis is often unrecognized. It should be suspected in a child with recurrent conjunctivitis, keratitis, neovascularization, eyelid inflammation, hordeolae, and chalazia.[34-36,43,51]

Tear film break-up time using fluorescein is significantly shorter in patients with MGD, even if aqueous tear production is normal.[52] This suggests that meibomian gland secretions are important in maintaining a stable preocular tear film. The overlap of clinical features of the various forms of chronic blepharitis and the variable association of all forms with tear dysfunction[4] underscore the complexity of the relationship between blepharitis and tear dysfunction as well as the need for customized treatment approaches for patients with complaints of ocular irritation.

Discoid lupus erythematosus can masquerade as blepharoconjunctivitis, and ulcerative blepharitis can be an early presentation of Crohn disease.[53,54] Recognizing the association of eyelid inflammation with these systemic diseases can lead to prompt and effective treatment. In cases where carcinoma masquerades as blepharitis, early diagnosis and appropriate treatment can prevent disfigurement and may be lifesaving.

Postoperative endophthalmitis is a feared complication following intraocular surgery. In a large retrospective study at a tertiary care center, the causative microorganisms of acute postoperative endophthalmitis following clear corneal cataract surgery included the usual ocular surface pathogens that are commonly associated with blepharitis (coagulase-negative *Staphylococcus* [68.4%], *Staphylococcus aureus* [6.8%], and *Streptococcus* species [8.2%]).[55] Therefore, it may be helpful to address moderate to severe blepharitis with topical antibiotics and eyelid hygiene so that symptoms and signs are controlled prior to an intraocular surgical procedure. Opinions vary regarding when and how aggressively to treat blepharitis prior to surgery. There is no evidence proving that such treatment will prevent endophthalmitis. The long-term antibiotic treatment may result in the development of resistant organisms.

Treatment

Topical antibiotics have been shown to provide some symptomatic relief, and they have been effective in decreasing bacteria from the eyelid margin in cases of anterior blepharitis. Eyelid hygiene may provide symptomatic relief for both anterior and posterior blepharitis. Evidence on the effectiveness of other treatments for blepharitis, such as topical corticosteroids or oral antibiotics, has been shown to be inconclusive.[56] The patient must understand that a cure is usually not possible. Treatments that may be helpful include the following:

- Warm compresses
- Eyelid cleansing, including eyelid massage in cases of MGD to express the meibomian glands
- Antibiotics (topical and/or systemic)
- Topical anti-inflammatory agents (e.g., corticosteroids, cyclosporine)

These treatment options are often used in combination. Eyelid cleansing is especially useful for anterior blepharitis, while warm compresses are especially helpful for posterior blepharitis and MGD. The optimal treatment regimen often requires a trial-and-error approach. An initial step in treating patients who have blepharitis is to recommend warm compresses and eyelid cleansing,[57] which may be accomplished in several ways.

One regimen is to apply warm compresses to the eyelids for several minutes to soften adherent scurf and scales or discharge and/or warm the meibomian secretions. Sustained warmth can be achieved by using hot tap water on a clean wash cloth or by heating a gel pack or bag of rice in the microwave. It is very important to instruct patients to avoid using compresses that are so hot that they burn the skin.

Eyelid cleansing can be accomplished by brief, gentle massage of the eyelids. Vertical eyelid massage can be performed to express meibomian secretions. Rubbing the eyelid margins from side to side removes crusting from the eyelashes. Cleaning the eyelid can be safely

accomplished by having the patient gently rub the base of the eyelashes using either diluted baby shampoo or commercially available eyelid cleaner on a pad, cotton ball, cotton swab, or clean fingertip. Cleaning the eyelid using any of the above devices and/or digital massage potentially can be dangerous if the patient lacks manual dexterity or the necessary skill or judgment to perform the task safely. The ophthalmologist should consider the patient's ability to perform this treatment and tailor the therapeutic plan accordingly. A schedule of regularly performed eyelid cleansing, daily or several times weekly, often blunts the symptoms of chronic blepharitis.

Once- or twice-daily compresses and massage, at a time most convenient for the patient, is generally adequate. Expression of the meibomian glands may be particularly helpful in cases of MGD. Frequent manipulation of the eyelid may lead to mechanically induced irritation. Some patients find it useful to repeat the warm compress and eyelid cleansing treatment more frequently during the day. Patients should be advised that warm compress and eyelid cleansing treatment, if effective, may be required long term, because the symptoms often recur if treatment is discontinued. There are also several expensive, in-office procedural treatments available to unclog the inspissated gland orifices using intense pulsed light or mechanical means (e.g., meibomian gland probing or devices using thermal pulsation). Randomized, masked clinical trials have yet to be performed to assess efficacy of these treatments.

A topical antibiotic ointment such as bacitracin or erythromycin can be prescribed and applied on the eyelid margins one or more times daily or at bedtime for a few weeks. Topical antibiotic treatment can be repeated on an intermittent basis using different kinds of medications with different mechanisms of action to prevent the development of resistant organisms. Metronidazole gel applied to the eyelid skin is an alternate treatment in cases unresponsive to antibiotic ointments, particularly in demodicosis (off-label).[58] The frequency and duration of treatment should be guided by the severity of the blepharitis and response to treatment. The clinical efficacy of topical tobramycin/dexamethasone ophthalmic suspension and azithromycin in a sustained release system has been evaluated in uncontrolled (off-label), manufacturer-sponsored studies, and these topical treatments appear to reduce some of the signs and symptoms of blepharitis.[59-61]

For patients with MGD, whose chronic symptoms and signs are not adequately controlled by eyelid cleansing or meibomian gland expression, oral tetracyclines and topical antibiotics may be helpful. Doxycycline or minocycline 100 mg or tetracycline 1000 mg in divided doses can be given daily, to be tapered to doxycycline or minocycline 40 to 50 mg or tetracycline 250 to 500 mg daily after clinical improvement is noted (usually 2 to 6 weeks). Alternatively, oral erythromycin (250 to 500 mg daily) or azithromycin (250 to 500 mg, one to three times a week, or 1 g per week, for 3 weeks) can be used. Macrolide antibiotics (e.g., erythromycin, azithromycin) also have anti-inflammatory activity.[62] Treatments can be intermittently discontinued and reinstated, based on the severity of the patient's blepharitis and tolerance for the medication, and to allow recolonization of normal flora.

The rationale for the use of tetracyclines is based in part on small clinical trials that report efficacy of the drugs in improving symptoms in patients with ocular rosacea[63] and improving tear break-up time in patients with rosacea and MGD.[64] The tetracyclines decrease lipase production in both *S. epidermidis* and *S. aureus*.[65,66] Tetracyclines can cause photosensitization, gastrointestinal upset, vaginitis, and, rarely, azotemia. Tetracyclines have been implicated in cases of pseudotumor cerebri,[67,68] and their metabolism may alter the effectiveness of certain medications (e.g., decrease the effectiveness of oral contraceptives and potentiate the effect of warfarin). A sustained-release 40-mg preparation of doxycycline can be used to reduce side effects. Tetracyclines are contraindicated in pregnancy, for nursing women, and for patients with a history of hypersensitivity to tetracyclines. Tetracyclines also should not be used in children under 8 years of age,[69] since staining of teeth may occur; however, oral erythromycin may be substituted.[70] Minocycline has been reported to stain skin, thyroid, nails, sclera, teeth, conjunctiva, tongue, and bone.[71-73]

Oral azithromycin (off-label) has been used successfully in the management of acne rosacea as an alternative to oral tetracyclines, particularly in combination with 0.1% topical tacrolimus.[74,75] Similarly, oral azithromycin 500 mg per day for 3 days in three cycles with 7-day intervals yielded good clinical improvement in 13 patients with blepharitis in an open-label single-center prospective case series.[76] Importantly, a Medicaid cohort in Tennessee showed a small but

absolute (hazard ratio, 2.88; 95% confidence interval [CI], 1.79 to 4.63; $P<0.001$) increase in cardiovascular deaths, which was most pronounced among patients who had a high baseline risk of cardiovascular disease and were treated with a 5-day oral azithromycin therapy.[77] In March 2013, the FDA issued a warning that oral azithromycin may lead to abnormalities in the electrical activity of the heart, with the potential to create serious irregularities in heart rhythm.[78]

A brief course of topical corticosteroids may be helpful for eyelid or ocular surface inflammation such as severe conjunctival infection, marginal keratitis, or phlyctenules. Corticosteroid eye drops or ointments are typically applied several times daily to the eyelids or ocular surface. Once the inflammation is controlled, the corticosteroid can be tapered and discontinued and then used intermittently to maintain patient comfort. The minimal effective dose of corticosteroids should be utilized, and long-term corticosteroid therapy should be avoided if possible. Patients should be informed of the potential adverse effects of corticosteroid use, including the risk for developing increased IOP and cataract. These adverse effects may be minimized by using a site-specific corticosteroid such as loteprednol etabonate and corticosteroids with limited ocular penetration, such as fluorometholone. Guidelines for maintenance therapy should be discussed. Topical cyclosporine 0.05% may be helpful in some patients with posterior blepharitis.[79]

Diet modification has been a traditional (though not well documented) way of managing acne rosacea. The role of omega-3 dietary supplementation in the management of blepharitis was evaluated in a 1-year study in which patients took two 1000-mg capsules of omega 3-fatty acid three times a day. Those receiving the supplement demonstrated an improvement in the tear film break-up time, dry eye symptoms, and meibum score, suggesting a potential benefit for this treatment in some blepharitis patients.[80]

Because many blepharitis patients have evaporative and aqueous tear deficiency, artificial tears may improve symptoms when used as an adjunct to eyelid cleansing and medications. If artificial tears are used more than four times per day, nonpreserved tears should be used to avoid preservative toxicity. Topical cyclosporine and/or punctal plugs may also be helpful in managing coexisting aqueous tear deficiency.

An eyelid tumor should be suspected in patients with atypical eyelid-margin inflammation or disease not responsive to medical therapy, and these patients should be carefully re-evaluated. The presence of features such as nodular mass, ulceration, extensive scarring, lash loss, localized crusting and scaling of the dermis, or yellow conjunctival nodules surrounded by intense inflammation may suggest the presence of an eyelid tumor. Basal cell carcinoma and squamous cell carcinoma are the most frequently encountered malignant tumors involving the eyelids. Melanoma and sebaceous carcinoma are the next most frequently diagnosed malignant tumors of the eyelid.[81] Sebaceous carcinoma may have a multicentric origin and may induce severe conjunctival inflammation due to pagetoid spread, and it may be difficult to diagnose. Sebaceous carcinoma should be considered in elderly patients who have unresponsive, chronic, unilateral blepharitis or conjunctivitis, or recurrent chalazia.

Demodicosis should be considered in patients who did not improve with the above treatments. Improvement in symptoms and signs were recently reported in a small case series when weekly 50% tea-tree-oil eyelid scrubs and daily tea-tree-oil shampoo scrubs when used for a minimum of 6 weeks in a group of patients who failed the above treatment methods.[49] Oral ivermectin has also been reported to be of benefit in some cases of recalcitrant Demodex blepharitis.[82,83]

Follow-Up

Patients with mild blepharitis should be advised to return to their ophthalmologist if their condition worsens. Visit intervals for patients are dictated by the severity of symptoms and signs, the current therapy, and comorbid factors such as glaucoma in patients who have been treated with corticosteroids. Patients with planned intraocular surgery should have a follow-up visit after initiating treatment to reassess the control of the eyelid inflammation prior to surgery. The follow-up visit should consist of an interval history, measurement of visual acuity, external examination, and slit-lamp biomicroscopy. If corticosteroid therapy is prescribed, patients should be re-evaluated within a few weeks to determine the response to therapy, measure IOP, and assess treatment compliance.

PROVIDER AND SETTING

The diagnosis and management of blepharitis requires broad medical skills and experience because of the potential association of systemic conditions, including cancer, with eyelid inflammation. At times, a multidisciplinary approach with a dermatologist, allergist, or oculoplastics specialist can be helpful. Patients with blepharitis who are evaluated by non-ophthalmologist health care providers should be promptly referred to an ophthalmologist if any of the following occurs:

- Visual loss
- Moderate or severe pain
- Severe or chronic redness
- Orbital involvement
- Recurrent episodes
- Lack of response to therapy

COUNSELING AND REFERRAL

One of the most important aspects of caring for patients with blepharitis is educating them about the chronicity and recurrence of the disease process. Patients should be informed that symptoms can frequently be improved but are rarely eliminated. Patients with an inflammatory eyelid lesion that appears suspicious for malignancy should be referred to an appropriate specialist.

SOCIOECONOMIC CONSIDERATIONS

The economics of blepharitis alone has not been adequately evaluated. One study reported the eye-related Medicare costs of a random sample of beneficiaries with diagnostic codes for at least one of the following: blepharitis (373.0x), chronic conjunctivitis (372.1x), or blepharoconjunctivitis (372.2x) to be a median of $658 and a mean of $1428 ± $1752 over a 5-year period.[84] The economic burden of blepharitis is magnified by its prevalence, and additional studies are needed to characterize its financial impact.

Multiple studies are available on the economic impact of dry eye. The link between MGD and aqueous tear deficiency, as well as between MGD and staphylococcal and seborrheic blepharitis, is well established.[85-88] Furthermore, this relationship is commonly understood by U.S. eye professionals, as illustrated in a survey in which 74% to 94% agreed or strongly agreed that MGD is the most common cause of evaporative dry eye and 96% to 97% agreed that they were comorbidities.[16]

The impact of blepharitis alone on the quality of life has not been studied, but the burden of dry eye has been shown to profoundly impact daily tasks.[89,90] Given the established relationship between blepharitis and dry eye, it is possible that patients with blepharitis suffer a similar impact on their quality of life and difficulties with common activities of daily living. Additional studies need to be conducted to assess the impact of blepharitis on patients in order to address their needs and provide adequate resources.

While there is no strong evidence that there is an effective cure for chronic blepharitis, there is evidence that certain treatment modalities may provide symptomatic relief. Improved signs and symptoms of blepharitis may lead to decreased office visits and increased productivity, which may result in a decrease in direct and indirect costs, and an increase in quality of life. Conversely, new technologies such as devices using thermal pulsation are available for the treatment of blepharitis, but the evidence supporting their use in this population is not sufficient, and the high cost of these technologies suggests limited economic value. The cost effectiveness and the impact on quality of life of the treatment options for blepharitis need to be further investigated.

To study the socioeconomic impact of blepharitis effectively, an improved understanding of the disease is needed, and a uniform classification system and accurate prevalence data must be utilized. The International Workshop on Meibomian Gland Dysfunction has endeavored to do just this (www.tearfilm.org/mgdworkshop/index.html), and the results of its work were published in 2011.[5] Similar to available studies of dry eye syndrome, additional studies should consider the consumption of health care dollars, including office visits and therapeutic remedies; the indirect costs, including lost time and productivity; and the intangible costs, including quality of life. Blepharitis likely is a significant public health burden, and additional studies are needed to accurately assess its socioeconomic impact.

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.

Reviewed by: Council
Approved by: Board of Trustees
October 12, 1988

2nd Printing: January 1991
3rd Printing: August 2001
4th Printing: July 2005

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

Blepharitis, which includes entities with the following ICD-9 and ICD-10 classifications:

	ICD-9 CM	ICD-10 CM
Ulcerative	373.01	H01.01-
Squamous	373.02	H01.02-
Stye	373.11	H00.01-
Meibomitis	373.12	H01.02-
Abscess of eyelid	373.13	H00.03-
Parasitic infestation of eyelid	373.60*	B89

CM = Clinical Modification used in the United States; (–) = 1, right upper eyelid; 2, right lower eyelid; 4, left upper eyelid; 5, left lower eyelid

* Code first underlying disease, as leishmaniasis (085.0–085.9), loiasis (125.2), onchocerciasis (125.3), or pediculosis (132.0)

Additional information for ICD-10 codes:

- 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 upper eyelid is always 1
  - Right lower eyelid is always 2
  - Left upper eyelid is always 4
  - Left lower eyelid is always 5

APPENDIX 3. PREFERRED PRACTICE PATTERN RECOMMENDATION GRADING

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

Highlighted Findings and Recommendations for Care

Page 4: In the management of ocular surface disease, it is helpful to distinguish blepharitis and meibomian gland dysfunction from aqueous deficient dry eye: III; Good; Strong

Page 4: Blepharitis is typically a chronic condition that cannot be permanently cured, and successful management is dependent on patient compliance with a treatment regimen; this should be explained to the affected patient: III; Good; Strong

Page 4: Attempts should be made to address moderate to severe blepharitis prior to intraocular surgery, even if the patient is asymptomatic, in order to reduce the risk of endophthalmitis: III; Moderate; Strong

Page 4: Costly new technologies are available, but the current evidence is not sufficient to support their use in the treatment of blepharitis: III; Insufficient; Discretionary

Page 4: Topical antibiotic ointments with or without corticosteroids or oral antibiotics can be used in treatment: I-; Moderate; Discretionary

Page 4: In patients with chronic blepharitis that does not respond to therapy, the possibility of carcinoma should be considered, particularly if it is associated with a loss of eyelashes: III; Good; Strong

Care Process – Diagnosis

Page 9: The initial evaluation of a patient with symptoms and signs suggestive of blepharitis should include the relevant aspects of the comprehensive medical eye evaluation: II++; Good; Strong

Page 9: Ancillary testing such as conjunctival cultures may be helpful: III; Insufficient; Discretionary

Page 9: The ocular history may include details about previous intraocular and eyelid surgery, as well as local trauma, including mechanical, thermal, chemical, and radiation injury: III; Good; Strong

Page 9: A history of cosmetic blepharoplasty is important to obtain because increased surface exposure may increase tear evaporation: III; Good; Strong

Page 9: The medical history may also include information about dermatological diseases such as rosacea, atopic dermatitis, and herpes zoster ophthalmicus: III; Good; Strong

Page 9: Examination of the eye and adnexa includes measurement of visual acuity, an external examination, slit-lamp biomicroscopy, and measurement of intraocular pressure (IOP): III; Good; Strong

Page 9: The external examination should be performed in a well-lighted room: III; Good; Strong

Page 10: The slit-lamp biomicroscopy should include evaluation of tear film, anterior and posterior eyelid margin, eyelashes, tarsal and bulbar conjunctiva, and cornea: III; Good; Strong

Page 11: Cultures of the eyelid margins may be indicated for patients with recurrent anterior blepharitis with severe inflammation as well as for patients who are not responding to therapy: III: Insufficient; Discretionary

Page 11: Microscopic evaluation of epilated eyelashes may reveal Demodex mites, which have been implicated in cases of chronic blepharoconjunctivitis: III; Insufficient; Discretionary

Page 11: The possibility of carcinoma should be considered in patients with chronic blepharitis unresponsive to therapy: III; Good; Strong

Page 11: A biopsy of the eyelid may be indicated to exclude the possibility of carcinoma in cases of marked asymmetry, resistance to therapy, or unifocal recurrent chalazia that do not respond well to therapy: III; Insufficient; Discretionary

Page 11: Before obtaining a biopsy for suspected sebaceous carcinoma, consultation with a pathologist is recommended to discuss the potential need for frozen sections and mapping of the conjunctiva to search for pagetoid spread: III; Good; Strong

Care Process – Management

Page 12: Chronic blepharokeratoconjunctivitis should be suspected in a child with recurrent conjunctivitis, keratitis, neovascularization, eyelid inflammation, hordeolae, and chalazia: II-; Moderate; Strong

Page 12: Recognizing the association of eyelid inflammation with these systemic diseases can lead to prompt and effective treatment: III; Insufficient; Discretionary

Page 12: It may be helpful to address the blepharitis with topical antibiotics and eyelid hygiene, so that symptoms are controlled prior to any intraocular surgical procedure: III; Good; Strong

Page 12: Topical antibiotics have been shown to provide some symptomatic relief, and have been effective in eradicating bacteria from the eyelid margin for anterior blepharitis: I+; Good; Strong

Page 12: Eyelid hygiene may provide symptomatic relief for anterior and posterior blepharitis: III; Insufficient; Discretionary

Page 12: Treatments that may be helpful include warm compresses, eyelid cleansing, antibiotics, and topical anti-inflammatory agents: III; Insufficient; Discretionary

Page 12: Treatment options are often used in combination: III; Insufficient; Discretionary

Page 12: An initial step in treating patients with blepharitis is to recommend warm compresses and eyelid cleansing: II-; Insufficient; Discretionary

Page 12: One regimen is to apply warm compresses to the eyelids for several minutes to soften adherent scurf and scales or discharge and/or warm the meibomian secretions: III; Insufficient; Discretionary

Page 12: It is very important to instruct patients to avoid using compresses that are so hot that they burn the skin: III; Good; Strong

Page 12: Eyelid cleansing can be accomplished by brief, gentle massage of the eyelids: III; Insufficient; Discretionary

Page 13: The ophthalmologist should consider the patient’s ability to perform this treatment and tailor the therapeutic plan accordingly: III; Good; Strong

Page 13: A schedule of regularly performed eyelid cleansing, daily or several times weekly, often blunts the symptoms of chronic blepharitis: III; Insufficient; Discretionary

Page 13: Once- or twice-daily compresses and massage, at a time most convenient for the patient, is generally adequate: III; Insufficient; Discretionary

Page 13: Patients should be advised that warm compress and eyelid cleansing treatment may be required long term: III; Good; Strong

Page 13: A topical antibiotic ointment such as bacitracin or erythromycin can be prescribed and applied on the eyelid margins one or more times daily or at bedtime for a few weeks: III; Insufficient; Discretionary

Page 13: Topical antibiotic treatment can be repeated on an intermittent basis using different kinds of medications with different mechanisms of action to prevent the development of resistant organisms: III; Insufficient; Discretionary

Page 13: Metronidazole gel applied to the eyelid skin is an alternate treatment in cases unresponsive to antibiotic ointments, particularly in demodicosis (off-label): II-; Insufficient; Discretionary

Page 13: The frequency and duration of treatment should be guided by the severity of the blepharitis and response to treatment: III; Good; Strong

Page 13: Topical tobramycin/dexamethasone ophthalmic suspension and azithromycin in a sustained release system appear to reduce some of the signs and symptoms of blepharitis: I-; Moderate; Discretionary

Page 13: For patients with MGD, whose chronic symptoms and signs are not adequately controlled by eyelid cleansing, oral tetracyclines and topical antibiotics may be helpful: III; Insufficient; Discretionary

Page 13: Treatments can be intermittently discontinued and reinstated, based on the severity of the patient's blepharitis and tolerance for the medication, and to allow recolonization of normal flora: III; Insufficient; Discretionary

Page 13: A sustained-release 40-mg preparation of doxycycline can be used to reduce side effects: III; Insufficient; Discretionary

Page 13: Tetracyclines are contraindicated in pregnancy, for nursing women, and for patients with a history of hypersensitivity to tetracyclines: III; Good; Strong

Page 13: Tetracyclines also should not be used in children under 10 years of age: III; Good; Strong

Page 13: Oral erythromycin may be substituted for tetracyclines: III; Insufficient; Discretionary

Page 13: Oral azithromycin (off-label) has been used successfully in the management of acne rosacea as an alternative to oral tetracyclines: I-; Moderate; Discretionary

Page 13: Oral azithromycin (off-label) has been used successfully in the management of acne rosacea, particularly in combination with 0.1% topical tacrolimus: III; Insufficient; Discretionary

Page 13: Oral azithromycin 500 mg per day for 3 days in three cycles with 7-day intervals yielded good clinical improvement in 13 patients with blepharitis in an open-label single-center prospective case series: III; Insufficient; Discretionary

Page 14: A brief course of topical corticosteroids may be helpful for eyelid or ocular surface inflammation such as severe conjunctival injection, marginal keratitis, or phlyctenules: III; Insufficient; Discretionary

Page 14: Corticosteroid eye drops or ointments are typically applied several times daily to the eyelids or ocular surface: III; Insufficient; Discretionary

Page 14: Once the inflammation is controlled, the corticosteroid can be tapered and discontinued and then used intermittently to maintain patient comfort: III; Insufficient; Discretionary

Page 14: The minimal effective dose of corticosteroids should be utilized, and long-term corticosteroid therapy should be avoided if possible: III; Good; Strong

Page 14: Patients should be informed of the potential adverse effects of corticosteroid use, including the risk for developing increased IOP and cataract: III; Good; Strong

Page 14: Guidelines for maintenance therapy should be discussed: III; Good; Strong

Page 14: Diet modification has been a traditional (though not well documented) way of managing acne rosacea: I-; Moderate; Discretionary

Page 14: Artificial tears may improve symptoms when used as an adjunct to eyelid cleansing and medications: III; Insufficient; Discretionary

Page 14: If artificial tears are used more than four times per day, nonpreserved tears should be used to avoid preservative toxicity: III; Good; Strong

Page 14: Topical cyclosporine and/or punctal plugs may also be helpful in managing coexisting aqueous tear deficiency: III; Insufficient; Discretionary

Page 14: An eyelid tumor should be suspected in patients with atypical eyelid-margin inflammation or disease not responsive to medical therapy, and these patients should be carefully re-evaluated: III; Good; Strong

Page 14: Sebaceous carcinoma should be considered in elderly patients who have unresponsive, chronic unilateral blepharitis or conjunctivitis, or recurrent chalazia: III; Good; Strong

Page 14: Demodicosis should be considered in patients who did not improve with the above treatments: III; Good; Strong

Page 14: Improvement in symptoms and signs were recently reported with weekly 50% tea-tree-oil eyelid scrubs and daily tea-tree-oil shampoo scrubs when used for a minimum of 6 weeks: III; Insufficient; Discretionary

Page 14: Oral ivermectin has also been reported to be of benefit in some cases of recalcitrant Demodex blepharitis: III; Insufficient; Discretionary

Care Process – Follow-up

Page 14: Patients with mild blepharitis should be advised to return to their ophthalmologist if their condition worsens: III; Good; Strong

Page 14: Patients with planned intraocular surgery should have a follow-up visit after initiating treatment to reassess the control of the eyelid inflammation prior to surgery: III; Good; Strong

Page 14: The follow-up visit should consist of an interval history, measurement of visual acuity, external examination, and slit-lamp biomicroscopy: III; Good; Strong

Page 14: If corticosteroid therapy is prescribed, patients should be re-evaluated within a few weeks to determine the response to therapy, measure IOP, and assess treatment compliance: III; Good; Strong

Provider and Setting

Page 15: A multidisciplinary approach with a dermatologist, allergist, or oculoplastics specialist can be helpful: III; Good; Strong

Page 15: Patients with blepharitis who are evaluated by non-ophthalmologist health care providers should be promptly referred to an ophthalmologist if visual loss, moderate or severe pain, severe or chronic redness, orbital involvement, recurrent episodes or lack of response to therapy occurs: III; Good; Strong

Counseling and Referral

Page 15: Patients should be informed that symptoms can frequently be improved but are rarely eliminated: III; Good; Strong

Page 15: Patients with an inflammatory eyelid lesion that appears suspicious for malignancy should be referred to an appropriate specialist: III; Good; Strong

RELATED ACADEMY MATERIALS

Basic and Clinical Science Course
External Disease and Cornea (Section 8, 2013–2014)

Patient Education Brochure
Eyelid Margin Disease Including Blepharitis (2011)

Preferred Practice Pattern® Guidelines – Free download available at www.aao.org/ppp.
Comprehensive Adult Medical Eye Evaluation (2010)

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

REFERENCES

1. Scottish Intercollegiate Guidelines Network. Annex B: key to evidence statements and grades of recommendations. In: SIGN 50: A Guideline Developer's Handbook. Available at: www.sign.ac.uk/guidelines/fulltext/50/annexb.html. Accessed October 2, 2012
2. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924-6.
3. GRADE Working Group. Organizations that have endorsed or that are using GRADE. Available at: www.gradeworkinggroup.org/society/index.htm. Accessed October 2, 2012.
4. McCulley JP, Dougherty JM, Deneau DG. Classification of chronic blepharitis. Ophthalmology 1982;89:1173-80.
5. Nichols KK, Foulks GN, Bron AJ, et al. The International Workshop on Meibomian Gland Dysfunction: executive summary. Invest Ophthalmol Vis Sci 2011;52:1922-9.
6. American Academy of Ophthalmology Basic and Clinical Science Course Subcommittee. Basic and Clinical Science Course. External Disease and Cornea: Section 8, 2013-2014. San Francisco, CA: American Academy of Ophthalmology; 2013:61.
7. Valenton MJ, Okumoto M. Toxin-producing strains of Staphylococcus epidermidis (albus). Isolates from patients with staphylococcic blepharoconjunctivitis. Arch Ophthalmol 1973;89:186-9.
8. Seal D, Ficker L, Ramakrishnan M, Wright P. Role of staphylococcal toxin production in blepharitis. Ophthalmology 1990;97:1684-8.
9. Ficker L, Ramakrishnan M, Seal D, Wright P. Role of cell-mediated immunity to staphylococci in blepharitis. Am J Ophthalmol 1991;111:473-9.
10. Bowman RW, Dougherty JM, McCulley JP. Chronic blepharitis and dry eyes. Int Ophthalmol Clin 1987;27:27-35.
11. Aderem A, Ulevitch RJ. Toll-like receptors in the induction of the innate immune response. Nature 2000;406:782-7.
12. Song PI, Abraham TA, Park Y, et al. The expression of functional LPS receptor proteins CD14 and toll-like receptor 4 in human corneal cells. Invest Ophthalmol Vis Sci 2001;42:2867-77.
13. Lemp MA, Mahmood MA, Weiler HH. Association of rosacea and keratoconjunctivitis sicca. Arch Ophthalmol 1984;102:556-7.
14. McCulley JP, Shine WE. Meibomian secretions in chronic blepharitis. Adv Exp Med Biol 1998;438:319-26.
15. Schaumberg DA, Nichols JJ, Papas EB, et al. The International Workshop on Meibomian Gland Dysfunction: report of the subcommittee on the epidemiology of, and associated risk factors for, MGD. Invest Ophthalmol Vis Sci 2011;52:1994-2005.

16. Lemp MA, Nichols KK. Blepharitis in the United States 2009: a survey-based perspective on prevalence and treatment. Ocul Surf 2009;7:S1-S14.
17. Schein OD, Munoz B, Tielsch JM, et al. Prevalence of dry eye among the elderly. Am J Ophthalmol 1997;124:723-8.
18. Lin PY, Tsai SY, Cheng CY, et al. Prevalence of dry eye among an elderly Chinese population in Taiwan: the Shihpai Eye Study. Ophthalmology 2003;110:1096-101.
19. Uchino M, Dogru M, Yagi Y, et al. The features of dry eye disease in a Japanese elderly population. Optom Vis Sci 2006;83:797-802.
20. Jie Y, Xu L, Wu YY, Jonas JB. Prevalence of dry eye among adult Chinese in the Beijing Eye Study. Eye (Lond) 2009;23:688-93.
21. McCarty CA, Bansal AK, Livingston PM, et al. The epidemiology of dry eye in Melbourne, Australia. Ophthalmology 1998;105:1114-9.
22. Baum J. Clinical manifestations of dry eye states. Trans Ophthalmol Soc U K 1985;104 (Pt 4):415-23.
23. Stern ME, Beuerman RW, Fox RI, et al. The pathology of dry eye: the interaction between the ocular surface and lacrimal glands. Cornea 1998;17:584-9.
24. Mathers WD. Ocular evaporation in meibomian gland dysfunction and dry eye. Ophthalmology 1993;100:347-51.
25. Shine WE, McCulley JP. Keratoconjunctivitis sicca associated with meibomian secretion polar lipid abnormality. Arch Ophthalmol 1998;116:849-52.
26. Kemal M, Sumer Z, Toker MI, et al. The prevalence of Demodex folliculorum in blepharitis patients and the normal population. Ophthalmic Epidemiol 2005;12:287-90.
27. Gao YY, Di Pascuale MA, Li W, et al. High prevalence of Demodex in eyelashes with cylindrical dandruff. Invest Ophthalmol Vis Sci 2005;46:3089-94.
28. Browning DJ, Proia AD. Ocular rosacea. Surv Ophthalmol 1986;31:145-58.
29. Jenkins MS, Brown SI, Lempert SL, Weinberg RJ. Ocular rosacea. Am J Ophthalmol 1979;88:618-22.
30. Akpek EK, Merchant A, Pinar V, Foster CS. Ocular rosacea: patient characteristics and follow-up. Ophthalmology 1997;104:1863-7.
31. American Academy of Ophthalmology Basic and Clinical Science Course Subcommittee. Basic and Clinical Science Course. External Disease and Cornea: Section 8, 2013-2014. San Francisco, CA: American Academy of Ophthalmology; 2013:58-9.
32. Berg M, Liden S. An epidemiological study of rosacea. Acta Derm Venereol 1989;69:419-23.
33. Chalmers DA. Rosacea: recognition and management for the primary care provider. Nurse Pract 1997;22:18, 23-8, 30.
34. Viswalingam M, Rauz S, Morlet N, Dart JK. Blepharokeratoconjunctivitis in children: diagnosis and treatment. Br J Ophthalmol 2005;89:400-3.
35. Cetinkaya A, Akova YA. Pediatric ocular acne rosacea: long-term treatment with systemic antibiotics. Am J Ophthalmol 2006;142:816-21.
36. Donaldson KE, Karp CL, Dunbar MT. Evaluation and treatment of children with ocular rosacea. Cornea 2007;26:42-6.
37. Bamford JT, Gessert CE, Renier CM, et al. Childhood stye and adult rosacea. J Am Acad Dermatol 2006;55:951-5.
38. Bozkurt B, Irkec MT, Atakan N, et al. Lacrimal function and ocular complications in patients treated with systemic isotretinoin. Eur J Ophthalmol 2002;12:173-6.
39. Mathers WD, Shields WJ, Sachdev MS, et al. Meibomian gland morphology and tear osmolarity: changes with Accutane therapy. Cornea 1991;10:286-90.
40. Fraunfelder FT, Fraunfelder FW, Edwards R. Ocular side effects possibly associated with isotretinoin usage. Am J Ophthalmol 2001;132:299-305.
41. Egger SF, Huber-Spitzy V, Bohler K, et al. Ocular side effects associated with 13-cis-retinoic acid therapy for acne vulgaris: clinical features, alterations of tearfilm and conjunctival flora. Acta Ophthalmol Scand 1995;73:355-7.
42. Martin NF, Rubinfeld RS, Malley JD, Manzitti V. Giant papillary conjunctivitis and meibomian gland dysfunction blepharitis. CLAO J 1992;18:165-9.

43. Hammersmith KM, Cohen EJ, Blake TD, et al. Blepharokeratoconjunctivitis in children. Arch Ophthalmol 2005;123:1667-70.
44. Hykin PG, Bron AJ. Age-related morphological changes in lid margin and meibomian gland anatomy. Cornea 1992;11:334-42.
45. American Academy of Ophthalmology Preferred Practice Patterns Committee. Preferred Practice Pattern® Guidelines. Comprehensive Adult Medical Eye Evaluation. San Francisco, CA: American Academy of Ophthalmology; 2010. Available at: www.aao.org/ppp.
46. American Academy of Ophthalmology Pediatric Ophthalmology/Strabismus Panel. Preferred Practice Pattern® Guidelines. Pediatric Eye Evaluations. San Francisco, CA: American Academy of Ophthalmology; 2012. Available at: www.aao.org/ppp.
47. Bron AJ, Benjamin L, Snibson GR. Meibomian gland disease. Classification and grading of lid changes. Eye 1991;5 (Pt 4):395-411.
48. Kheirkhah A, Blanco G, Casas V, Tseng SC. Fluorescein dye improves microscopic evaluation and counting of demodex in blepharitis with cylindrical dandruff. Cornea 2007;26:697-700.
49. Kheirkhah A, Casas V, Li W, et al. Corneal manifestations of ocular Demodex infestation. Am J Ophthalmol 2007;143:743-9.
50. Gilberg S, Tse D. Malignant eyelid tumors. Ophthalmol Clin North Am 1992;5:261-85.
51. Jones SM, Weinstein JM, Cumberland P, et al. Visual outcome and corneal changes in children with chronic blepharokeratoconjunctivitis. Ophthalmology 2007;114:2271-80.
52. Pflugfelder SC, Tseng SC, Sanabria O, et al. Evaluation of subjective assessments and objective diagnostic tests for diagnosing tear-film disorders known to cause ocular irritation. Cornea 1998;17:38-56.
53. Acharya N, Pineda R 2nd, Uy HS, Foster CS. Discoid lupus erythematosus masquerading as chronic blepharoconjunctivitis. Ophthalmology 2005;112:e19-23.
54. Diaz-Valle D, Benitez del Castillo JM, Fernandez Acenero MJ, et al. Bilateral lid margin ulcers as the initial manifestation of Crohn disease. Am J Ophthalmol 2004;138:292-4.
55. Lalwani GA, Flynn HW Jr, Scott IU, et al. Acute-onset endophthalmitis after clear corneal cataract surgery (1996-2005). Clinical features, causative organisms, and visual acuity outcomes. Ophthalmology 2008;115:473-6.
56. Lindsley K, Matsumura S, Hatef E, Akpek EK. Interventions for chronic blepharitis. Cochrane Database of Syst Revs 2012, Issue 5. Art. No.: CD005556. DOI: 10.1002/14651858.CD005556.pub2.
57. Key JE. A comparative study of eyelid cleaning regimens in chronic blepharitis. CLAO J 1996;22:209-12.
58. Barnhorst DA Jr, Foster JA, Chern KC, Meisler DM. The efficacy of topical metronidazole in the treatment of ocular rosacea. Ophthalmology 1996;103:1880-3.
59. Torkildsen GL, Cockrum P, Meier E, et al. Evaluation of clinical efficacy and safety of tobramycin/dexamethasone ophthalmic suspension 0.3%/0.05% compared to azithromycin ophthalmic solution 1% in the treatment of moderate to severe acute blepharitis/blepharoconjunctivitis. Curr Med Res Opin 2011;27:171-8.
60. Haque RM, Torkildsen GL, Brubaker K, et al. Multicenter open-label study evaluating the efficacy of azithromycin ophthalmic solution 1% on the signs and symptoms of subjects with blepharitis. Cornea 2010;29:871-7.
61. Foulks GN, Borchman D, Yappert M, et al. Topical azithromycin therapy for meibomian gland dysfunction: clinical response and lipid alterations. Cornea 2010;29:781-8.
62. Ianaro A, Ialenti A, Maffia P, et al. Anti-inflammatory activity of macrolide antibiotics. J Pharmacol Exp Ther 2000;292:156-63.
63. Frucht-Pery J, Sagi E, Hemo I, Ever-Hadani P. Efficacy of doxycycline and tetracycline in ocular rosacea. Am J Ophthalmol 1993;116:88-92.
64. Zengin N, Tol H, Gunduz K, et al. Meibomian gland dysfunction and tear film abnormalities in rosacea. Cornea 1995;14:144-6.
65. Dougherty JM, McCulley JP, Silvany RE, Meyer DR. The role of tetracycline in chronic blepharitis. Inhibition of lipase production in staphylococci. Invest Ophthalmol Vis Sci 1991;32:2970-5.
66. Shine WE, McCulley JP, Pandya AG. Minocycline effect on meibomian gland lipids in meibomianitis patients. Exp Eye Res 2003;76:417-20.

67. Quinn AG, Singer SB, Buncic JR. Pediatric tetracycline-induced pseudotumor cerebri. J AAPOS 1999;3:53-7.
68. Chiu AM, Chuenkongkaew WL, Cornblath WT, et al. Minocycline treatment and pseudotumor cerebri syndrome. Am J Ophthalmol 1998;126:116-21.
69. American Academy of Ophthalmology Basic and Clinical Science Course Subcommittee. Basic and Clinical Science Course. Update on General Medicine: Section 1, 2013-2014. San Francisco, CA: American Academy of Ophthalmology; 2013:62.
70. Meisler DM, Raizman MB, Traboulsi EI. Oral erythromycin treatment for childhood blepharokeratitis. J AAPOS 2000;4:379-80.
71. Fraunfelder FT, Randall JA. Minocycline-induced scleral pigmentation. Ophthalmology 1997;104:936-8.
72. Bradfield YS, Robertson DM, Salomao DR, et al. Minocycline-induced ocular pigmentation. Arch Ophthalmol 2003;121:144-5.
73. Sanchez AR, Rogers RS 3rd, Sheridan PJ. Tetracycline and other tetracycline-derivative staining of the teeth and oral cavity. Int J Dermatol 2004;43:709-15.
74. Modi S, Harting M, Rosen T. Azithromycin as an alternative rosacea therapy when tetracyclines prove problematic. J Drugs Dermatol 2008;7:898-9.
75. Akhyani M, Ehsani AH, Ghiasi M, Jafari AK. Comparison of efficacy of azithromycin vs. doxycycline in the treatment of rosacea: a randomized open clinical trial. Int J Dermatol 2008;47:284-8.
76. Igami TZ, Holzchuh R, Osaki TH, et al. Oral azithromycin for treatment of posterior blepharitis. Cornea 2011;30:1145-9.
77. Ray WA, Murray KT, Hall K, et al. Azithromycin and the risk of cardiovascular death. N Engl J Med 2012;366:1881-90.
78. U.S. Food and Drug Administration. FDA Drug Safety Communication. Azithromycin (Zithromax or Zmax) and the risk of potentially fatal heart rhythms. Available at: www.fda.gov/drugs/drugsafety/ucm341822.htm. Accessed April 5, 2013.
79. Perry HD, Doshi-Carnevale S, Donnenfeld ED, et al. Efficacy of commercially available topical cyclosporine A 0.05% in the treatment of meibomian gland dysfunction. Cornea 2006;25:171-5.
80. Macsai MS. The role of omega-3 dietary supplementation in blepharitis and meibomian gland dysfunction (an AOS thesis). Trans Am Ophthalmol Soc 2008;106:336-56.
81. Margo CE, Mulla ZD. Malignant tumors of the eyelid: a population-based study of non-basal cell and non-squamous cell malignant neoplasms. Arch Ophthalmol 1998;116:195-8.
82. Filho PA, Hazarbassanov RM, Grisolia AB, et al. The efficacy of oral ivermectin for the treatment of chronic blepharitis in patients tested positive for Demodex spp. Br J Ophthalmol 2011;95:893-5.
83. Holzchuh FG, Hida RY, Moscovici BK, et al. Clinical treatment of ocular Demodex folliculorum by systemic ivermectin. Am J Ophthalmol 2011;151:1030-4.
84. Coleman AL, Yu F. Eye-related medicare costs for patients with age-related macular degeneration from 1995 to 1999. Ophthalmology 2008;115:18-25.
85. American Academy of Ophthalmology Basic and Clinical Science Course Subcommittee. Basic and Clinical Science Course. External Disease and Cornea: Section 8, 2013-2014. San Francisco, CA: American Academy of Ophthalmology; 2013:46, 60-4.
86. Lemp MA. Report of the National Eye Institute/Industry workshop on Clinical Trials in Dry Eyes. CLAO J 1995;21:221-32.
87. Foulks GN, Bron AJ. Meibomian gland dysfunction: a clinical scheme for description, diagnosis, classification, and grading. Ocul Surf 2003;1:107-26.
88. Bron AJ, Tiffany JM. The contribution of meibomian disease to dry eye. Ocul Surf 2004;2:149-65.
89. Mertzanis P, Abetz L, Rajagopalan K, et al. The relative burden of dry eye in patients' lives: comparisons to a U.S. normative sample. Invest Ophthalmol Vis Sci 2005;46:46-50.
90. Miljanovic B, Dana R, Sullivan DA, Schaumberg DA. Impact of dry eye syndrome on vision-related quality of life. Am J Ophthalmol 2007;143:409-15.

AMERICAN ACADEMY® OF OPHTHALMOLOGY
The Eye M.D. Association

P.O. Box 7424
San Francisco,
California 94120-7424
415.561.8500