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Blepharitis Preferred Practice Pattern®

Correspondence:
Andre Ambrus, MLIS, American Academy of Ophthalmology, P. O. Box 7424, San Francisco, CA 94120-7424. E-mail: aambrus@aao.org.

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 2022–2023
Amy Lin, MD
Sumayya Ahmad, MD, Methodologist
Guillermo Amescua, MD
Albert Y. Cheung, MD
Daniel S. Choi, MD
Vishal Jhanji, MD, FRCS, FRCOphth
Shahzad I. Mian, MD
Michelle K. Rhee, MD
Elizabeth T. Viriya, MD
Francis S. Mah, MD, Co-chair
Divya M. Varu, MD, Co-chair

The **Preferred Practice Patterns Committee** members reviewed and discussed the document during a meeting in June 2023. The document was edited in response to the discussion and comments.

Preferred Practice Patterns Committee 2023
David K. Wallace, MD, MPH, Chair
Christina J. Flaxel, MD
Steven J. Gedde, MD
Deborah S. Jacobs, MD
Francis S. Mah, MD
Kevin M. Miller, MD
Thomas A. Oetting, MD
Divya M. Varu, MD
David C. Musch, PhD, MPH, Methodologist

The Blepharitis PPP was sent for review in July 2023 to improve the quality of the guideline, to gather feedback on the draft recommendations, and to assess feasibility for and applicability to the target audience, including assessing the facilitators and barriers to implementing recommendations (e.g., U.S. ophthalmologists and other important groups, including patients, other physicians, international ophthalmologists, research organizations, ophthalmological organizations, and experts in the field). The PPP was sent for review to the following patient organizations to solicit the views and preferences of patients and the public: Consumers United for Evidence-Based Healthcare, American Foundation for the Blind, Foundation Fighting Blindness, Lighthouse Guild, National Federation of the Blind, and Prevent Blindness. All those who were returning comments were required to provide disclosure of relevant relationships with industry to have their comments considered (indicated with an asterisk below). Members of the Cornea/External Disease Preferred Practice Pattern Panel reviewed these comments and determined revisions to the document.

<u>Academy Reviewers</u>
Board of Trustees and Committee of Secretaries Council
General Counsel*
Ophthalmic Technology Assessment Committee
Cornea/External Disease Panel
Basic and Clinical Science Course Section 8 Subcommittee*
Practicing Ophthalmologists Advisory Committee for Education*

<u>Invited Reviewers</u>
American College of Surgeons, Advisory Council for Ophthalmic Surgery
American Foundation for the Blind
American Ophthalmological Society*
American Society of Cataract & Refractive Surgery

American Uveitis Society*
Asia Cornea Society*
Association for Research in Vision and Ophthalmology
Association of University Professors of Ophthalmology
Canadian Ophthalmological Society
Consumers United for Evidence-Based Health Care
Cornea Society*
Foundation Fighting Blindness
International Council of Ophthalmology
International Society of Refractive Surgery
Lighthouse Guild
National Eye Institute
National Federation of the Blind
National Medical Association, Ophthalmology Section
Ocular Microbiology and Immunology Group
Prevent Blindness
Women in Ophthalmology
Robert S. Feder, MD*
Jeanine Baqai, MD

This guideline will be formally re-evaluated and updated on a 5-year cycle in 2028. A Summary Benchmark is a resource to facilitate application of the guideline and to provide criteria that could be used to measure the application of recommendations, which will be available to all at www.aao.org/ppp.

FINANCIAL DISCLOSURES

There is no external funding, including industry/commercial support, for the development of this PPP or for the distribution of the guidelines. The Academy has fully funded the development of this PPP, and the views or interests of the Academy have not influenced the final recommendations, which are based on evidence from systematic reviews. All those individuals significantly involved in the guideline development process, including guideline panel members, PPP Committee members, Secretary for Quality of Care, and Academy Staff, have declared competing/financial interests through a financial interest disclosure process as well as an assessment of the Open Payments website (available at https://openpaymentsdata.cms.gov/). The interests of the guideline panel members are provided at the beginning of each meeting, and those with competing interests in a guideline topic do not participate in voting on areas of disagreement. In compliance with the Council of Medical Specialty Societies' Code for Interactions with Companies (available at https://cmss.org/code-for-interactions-with-companies/), relevant relationships with industry are listed. As per CMSS code, direct financial relationships with companies do not include food and beverages, research funds paid to the institution, and relationships outside of the topic of the PPP. The Academy has Relationship with Industry Procedures to comply with the Code (available at www.aao.org/about-preferred-practice-patterns). A majority (64%) of the members of the Cornea/External Disease Preferred Practice Pattern Panel 2022–2023 had no direct financial relationships to disclose.

Cornea/External Disease Preferred Practice Pattern Panel 2022–2023
Amy Lin, MD: Kala Pharmaceuticals—Consultant/Advisor
Sumayya Ahmad, MD: No financial relationships to disclose
Guillermo Amescua, MD: No financial relationships to disclose
Daniel S. Choi, MD: No financial relationships to disclose
Albert Y. Cheung, MD: Sight Sciences, Inc.—Consultant/Advisor
Vishal Jhanji, MD, FRCS, FRCOphth: No financial relationships to disclose
Shahzad I. Mian, MD: No financial relationships to disclose
Michelle K. Rhee, MD: NovaBay Pharmaceuticals—Consultant/Advisor
Elizabeth T. Viriya, MD: No financial relationships to disclose
Francis S. Mah, MD: Alcon Laboratories, Aperta Biosciences, Azura Ophthalmics, Bausch + Lomb, Johnson & Johnson Vision, Novartis Pharmaceuticals, NuLids, Ocular Science, Sun Pharma, Tarsus, Thea Pharmaceuticals—Consultant/Advisor; Bausch + Lomb, Novartis Pharmaceuticals, Sun Pharma—Lecture Fees
Divya M. Varu, MD: No financial relationships to disclose

Preferred Practice Patterns Committee 2023
David K. Wallace, MD, MPH: No financial relationships to disclose
Christina J. Flaxel, MD: No financial relationships to disclose
Steven J. Gedde, MD: No financial relationships to disclose
Deborah S. Jacobs, MD: Novartis Pharmaceuticals—Consultant/Advisor
Francis S. Mah, MD: Alcon Laboratories, Aperta Biosciences, Azura Ophthalmics, Bausch + Lomb, Johnson & Johnson Vision, Novartis Pharmaceuticals, NuLids, Sun Pharma, Ocular Science, Tarsus, Thea Pharmaceuticals—Consultant/Advisor; Bausch + Lomb, Novartis Pharmaceuticals, Sun Pharma—Lecture Fees
Kevin M. Miller, MD: Alcon Laboratories, Johnson & Johnson Vision—Consultant/Advisor
Thomas A. Oetting, MD: No financial relationships to disclose
Divya M. Varu, MD: No financial relationships to disclose
David C. Musch, PhD, MPH: No financial relationships to disclose

Secretary for Quality of Care
Roy S. Chuck, MD, PhD: No financial relationships to disclose

Academy Staff
Andre Ambrus, MLIS: No financial relationships to disclose
Meghan Daly: No financial relationships to disclose
Susan Garratt: No financial relationships to disclose
Flora C. Lum, MD: No financial relationships to disclose

The disclosures of relevant relationships to industry of other reviewers of the document from January to October 2023 are available online at www.aao.org/ppp.

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OBJECTIVES OF PREFERRED PRACTICE PATTERN® GUIDELINES

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

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

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

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

References to certain drugs, instruments, and other products are made for illustrative purposes only and are not intended to constitute an endorsement of such. Such material may include information on applications that are not considered community standard, that reflect indications not included in approved US 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 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 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 on March 3, 2022 and June 7, 2023 in the PubMed database. Complete details of the literature searches are available at www.aao.org/ppp.

- Recommendations are based on systematic reviews, as per the Institute of Medicine (Clinical Practice Guidelines We Can Trust, 2011). In formulating the recommendations, the health benefits, side effects/harms/risks, and the balance of benefits and risks are reviewed and considered. Final decisions are arrived at through informal consensus techniques. If there are areas of disagreement, a vote will be conducted among the members of the guideline panel. If there are individuals with direct financial relationships in the area of disagreement, these individuals will refrain from the vote.

HIGHLIGHTED FINDINGS AND RECOMMENDATIONS FOR CARE

In the management of ocular surface disease, it is helpful to distinguish anterior and posterior (meibomian gland dysfunction [MGD]) blepharitis from aqueous deficient dry eye. Anterior blepharitis affects the lash line and includes posterior blepharitis, which is defined as meibomian gland involvement. Worsening of symptoms in the morning is typical of blepharitis, whereas worsening of the symptoms later in the day are typical of aqueous deficient dry eye.

Blepharitis is typically a chronic condition that cannot be permanently cured. It is important for patients to understand that successful management depends on their compliance with a treatment regimen.

Topical antibiotic drops or ointments with or without corticosteroids and/or oral antibiotics can be effective in the treatment of blepharitis. Although azithromycin is used as a treatment for blepharitis, it may produce cardiac arrhythmias when used orally in patients with cardiovascular problems.

In-office procedures targeting the meibomian glands have shown efficacy in some studies, but there is a lack of independent, randomized controlled studies demonstrating superiority of any one of these treatments over another.

In patients with blepharitis who do not respond to therapy, the possibility of carcinoma or immune-mediated diseases should be considered, particularly if the blepharitis is associated with loss of eyelashes and/or conjunctival cicatricial changes. Early diagnosis and appropriate treatment can prevent vision loss and disfigurement, and it may be lifesaving.

INTRODUCTION

DISEASE DEFINITION

Blepharitis 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, whereas posterior blepharitis affects the meibomian glands. 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 blepharitis, which include: staphylococcal, seborrheic, and MGD.[6]

There is considerable overlap of symptoms in all types of blepharitis. Blepharitis frequently leads to 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. In children, blepharoconjuncitivitis is fairly common and may lead to chronically inflamed lids, induced astigmatism, keratopathy, amblyopia, vision loss, or corneal perforation.

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 include acute exacerbations that lead to the development of ulcerative blepharitis. Loss of eyelashes and corneal involvement, including punctate epithelial erosions, marginal infiltrates, peripheral corneal and epithelial defects, and corneal neovascularization, may occur.

Although coagulase-negative staphylococcus is isolated with great frequency from eyelids of both normal subjects and patients with blepharitis (in 89% to 100% of cases), *Staphylococcus aureus* is isolated with greater frequency from eyelids of patients with clinical diagnoses of staphylococcal blepharitis.[4, 7] 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;[8] however, other studies have found no association between toxin production of *S. aureus* isolates and the presence of clinical disease.[9] 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.[10] Cell-mediated immunologic mechanisms have also been implicated in the development of keratitis associated with staphylococcal blepharitis.[11] Staphylococcal antigens themselves can initiate an inflammatory reaction by attaching to bacterial antigen-binding receptors that are present on the corneal epithelium.[12, 13] One study showed no difference in the incidence of staphylococcus in patients with and without clinically significant MGD/ocular surface disease.[14] 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 and fibrosis of the meibomian glands. Patients with MGD frequently are noted to have coexisting rosacea or seborrheic dermatitis.[4, 15] Alterations in the biochemical composition of meibomian gland secretions have been documented in patients with MGD blepharitis when compared with normal subjects.[16] The result of MGD is decreased availability of normal meibum to the lid margin and tear film. This, in turn, may result in hyperosmolarity and instability of the tear film, increased bacterial growth on the lid margin, evaporative dry eye, and ocular surface inflammation and damage.[17]

PREVALENCE

Although blepharitis is one of the most common ocular disorders, epidemiologic 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.[17] Compared with patients who have other forms of blepharitis, patients who have staphylococcal blepharitis were found to be relatively younger (42 years old) and most were female (80%).[4, 18] In younger, active duty military personnel (mean age, 23.2 years), 5.3% were diagnosed with meibomian gland inflammation compared with 71.1% of older military veterans (mean age, 68.1 years).[19]

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. A survey of ophthalmologists and optometrists reported that blepharitis was commonly seen in clinical practice in 37% and 47% of their patients, respectively.

Meibomian gland dysfunction is considered to be the most common cause of evaporative dry eye disease.[20] The prevalence of clinically diagnosed MGD varies widely (from 3.5% to almost 70%) in the published world literature,[17] with a suggestion that MGD is significantly more common among Asian populations than Caucasian populations. However, there was significant variation in how the disease was defined and in the age of the study groups.[21-25]

Blepharoconjuctivitis in children is fairly common and often under-recognized. A retrospective case series reported that 15% of children referred to a U.S. pediatric cornea clinic had a diagnosis of blepharoconjuctivitis.[26]

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.[27] 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.[11]

  Twenty-five percent to 40% of patients with seborrheic blepharitis and MGD,[4] and 37% to 52% of patients with ocular rosacea[15] 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.[28,29] Low levels of tear film phospholipids have been found to be associated with the presence of dry eye in patients with chronic blepharitis.[30]

- Dermatologic conditions

  Dermatologic conditions associated with seborrheic blepharitis and MGD may share common etiologies and predisposing factors. In one study of 99 chronic blepharitis patients and 33 age- and

sex-matched controls, 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, 17] Atopic dermatitis is found in both children and adults, and it is highly associated with blepharitis.[31] Psoriasis can also be associated with blepharitis.[32, 33]

- Demodicosis

  Demodex folliculorum has been found in 30% to 68% of patients with chronic blepharitis (especially older patients), but this mite has also been found in a significant percentage of patients without blepharitis.[34-38] Both *Demodex folliculorum* and *Demodex brevis* have been found in 12% of healthy children, but the children did not have a greater incidence of ocular discomfort compared with those who did not have mites.[39] However, patients with recalcitrant blepharitis have responded to therapy directed at decreasing or eradicating the *Demodex* mites.[38] Eyelashes with cylindrical dandruff or sleeves at the eyelash base are reported to be a sign of ocular *Demodex* infestation.[40] Studies have shown that the severity of ocular surface discomfort has a strong positive correlation with the number of *Demodex* per cilia.[41]

- Pediculosis palpebrarum

  Pediculosis palpebrarum (*Phthirus pubis*) can cause unilateral or bilateral follicular conjunctivitis. Adult lice are found at the base of the eyelashes, nits (eggs) are adherent to the eyelash shafts, and blood-tinged debris may be noted on the eyelashes and eyelids. Blepharitis and conjunctivitis persists until treatment is initiated. Pediculosis palpebrarum is typically sexually transmitted and may be associated with pubic lice or other sexually transmitted diseases. In children, these findings may be an indication of sexual abuse.[42]

- Rosacea

  Rosacea is a disease of the skin and eye that is observed more frequently in fair-skinned individuals,[43] but it can occur in people of all races and both sexes. 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.[44,45] The *Demodex* mite may play a role in the pathogenesis of rosacea. The *Demodex* load is increased in individuals with rosacea.[46]

  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.[47] Although rosacea is more prevalent in women, it can be more severe when it occurs in men.[48, 49] 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, phlyctenules, punctate erosions, keratitis, MGD, or recurrent chalazia and have subtle signs of rosacea.[50]

  Children with ocular rosacea often present with corneal involvement, asymmetry of ocular disease, and the potential for visual impairment such as corneal melting/perforation.[51] Facial rosacea is less frequent in children, and associated atopy is common.[52, 53] Children with a history of styes have an increased risk of developing adult rosacea.[54]

- Medications

  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.[55] Discontinuation of the medication leads to improvement in most cases.[55-58]

  Dupilumab is a subcutaneous injection used for the treatment of atopic dermatitis, which is associated with conjunctivitis, keratitis, and blepharitis in 32% to 55% of patients.[59, 60]

- Giant papillary conjunctivitis

  Patients with contact lens-associated giant papillary conjunctivitis have an increased frequency of MGD.[61] The severity of giant papillary conjunctivitis may correlate with the severity of MGD.[61]

- Metabolic syndrome

  There is some evidence that components of metabolic syndrome may be associated with a higher risk for blepharitis. One study showed that patients with increased waist circumference and systolic blood pressure, higher glucose, higher total cholesterol and low density lipoprotein cholesterol, and higher triglycerides were more likely to have a diagnosis of blepharitis.[62] Another population-based study found that use of statins was associated with a lower risk of

blepharitis.[63] Further research is needed to examine the relationship between cholesterol and blepharitis.

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

TABLE 1 OTHER CONDITIONS ASSOCIATED WITH EYELID INFLAMMATION

Condition	Entity
Bacterial infections	• Impetigo (due primarily to *Staphylococcus aureus*) • Erysipelas (due primarily to *Streptococcus pyogenes*) • Angular blepharitis (*Moraxella*)
Viral infections	• Herpes simplex virus • Molluscum contagiosum • Varicella zoster virus • Papillomavirus • Vaccinia
Parasitic infestations	• *Demodex folliculorum*, Pediculosis palpebrarum (*Phthirus pubis*)

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

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

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.[26, 50] Severe staphylococcal blepharitis may eventually lead to eyelash loss, eyelid scarring with trichiasis, and corneal scarring and neovascularization.[10] Patients with seborrheic blepharitis and MGD are generally older and have a longer history of ocular symptoms (range, 6.5 to 11.6 years).[11] Eyelid margin telangiectasia and meibomian gland orifice narrowing and pouting may occur in asymptomatic older patients.[64] Meibomian gland dysfunction can also occur in the absence of inflammation.[5]

Patients with severe ocular rosacea and blepharitis may develop superficial punctate keratopathy, corneal neovascularization, and scarring.[43] Although ulceration and perforation can rarely occur in blepharitis, the incidence of these complications is greater in children.[65]

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.[66, 67] The diagnosis of blepharitis is usually based on a typical patient history and characteristic slit-lamp biomicroscopic findings. Ancillary testing such as taking microbiologic cultures of the eyelid and conjunctiva, dynamic meibomian gland imaging, and eyelash epilation for examination by light microscopy for identification/confirmation of *Demodex* infestation 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, and recurrent hordeolum)
- Time of day when symptoms are worse (worsening of the symptoms in the morning is typical of blepharitis, whereas worsening of the symptoms later in the day is 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, aqueous tear deficiency)
- Symptoms and signs related to systemic diseases (e.g., rosacea, atopy, psoriasis, and graft-versus-host disease [GVHD])
- Current and previous systemic and topical medications (e.g., antihistamines or drugs with anticholinergic effects, or drugs used in the past such as isotretinoin that might have an effect on the ocular surface)
- Recent exposure to an infected individual (e.g., pediculosis palpebrarum [*P. pubis*])

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 hordeola and/or chalazia is common in patients with posterior blepharitis.

The medical history may also include information about dermatologic 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. 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), incomplete eyelid closure (i.e., lagophthalmos), blink response, and/or eyelid laxity
  - Loss, breakage, or misdirection of eyelashes
  - Vascularization or hyperemia of eyelid margins
  - Abnormal deposits/sleeves 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 on the eyelid margin
  - Debris in the tear film
- Anterior eyelid margin
  - Hyperemia
  - Telangiectasia
  - Scarring
  - Pigmentary changes
  - Keratinization
  - Ulceration
  - Vesicles
  - Blood-tinged debris
  - Pediculosis palpebrarum (*P. pubis*)
  - Presence of lesion
- Eyelashes
  - Malposition or misdirection
  - Loss or breakage
  - Pediculosis palpebrarum (*P. 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[68]
  - Character of meibomian secretions such as expressibility, thickness, turbidity, and color
  - Vascularization, keratinization, nodularity
  - Thickening
  - Scarring/fibrosis
- 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
- Cicatricial changes: subepithelial fibrosis, fornix foreshortening, symblepharon formation

- Bulbar conjunctiva
  - Hyperemia
  - Phlyctenules, follicles
  - Conjunctival chalasis
  - Punctate staining with fluorescein, rose bengal, or lissamine green (generally fluorescein is used for cornea; rose bengal and lissamine green are used for conjunctiva)
- Cornea
  - Epithelial defect, punctate staining with fluorescein, rose bengal, or lissamine green
  - Edema, infiltrates, ulcers, and/or scars (small subepithelial or superficial stromal, circumferential, in midperipheral cornea typically with a clear zone between the infiltrate and the limbus, usually without overlying fluorescein staining)
  - Vascularization, scarring, including pannus
  - Phlyctenules

Diagnostic Tests

Microbiologic testing can be performed in certain instances of blepharitis. 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. Lash collarettes in the setting of persistent blepharitis is suspicious for *Demodex* infestation. Microscopic evaluation of epilated eyelashes may reveal *Demodex* mites. This can be performed by placing the explanted eyelashes on a glass slide, adding a drop of fluorescein, and placing a cover slip.[69] Evaluation for mites can even be performed on the glass slide using a slit lamp and a 90 Diopter condensing lens.[70]

The possibility of carcinoma should be considered in patients with chronic blepharitis unresponsive to therapy, especially when only one eye is involved. Often such patients will have a degree of conjunctival cicatricial changes in the affected eye. 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.[71] 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.

It is also very important to do a complete ocular surface exam on patients with chronic blepharitis that has been unresponsive to standard medical treatment to look for any signs of conjunctival cicatricial changes. If there are any signs of cicatrizing disease, such as forniceal foreshortening, clinicians should be suspicious about the possibility of ocular mucous membrane pemphigoid (OMMP) and the proper workup should be initiated, including immunofluorescence studies of the biopsy specimen. (See the Conjunctivitis PPP.[72])

An important diagnostic tool for MGD is the assessment of lid margin changes and expression of the meibomian glands. This may be performed by applying pressure to the lower eyelids with either fingers or a cotton tipped applicator. Interferometry technology provides a more detailed analysis of the lipid layer by evaluating the tear film lipid-layer thickness and blink dynamics, and by capturing images of the meibomian gland structure. Patients with low interferometry values of lipid-layer thickness report more dry eye symptoms.[73, 74]

Clinical features 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 aqueous deficiency can present with similar clinical features.

TABLE 2 CLINICAL FEATURES OF BLEPHARITIS BY CATEGORY

	Anterior Eyelid		Posterior Eyelid
Feature	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 and superior 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, 2023. Table 3-11. San Francisco: American Academy of Ophthalmology, 2023.

* Also consider herpes simplex virus.

MANAGEMENT

Detection

Detection and appropriate treatment can reduce signs and symptoms of blepharitis, and in severe cases it can prevent permanent structural damage and possible vision loss. This is particularly important in children, in whom chronic blepharokeratoconjunctivitis is often unrecognized and can be more severe. It should be suspected in a child with recurrent conjunctivitis, keratitis, neovascularization, eyelid inflammation, hordeolum, chalazia, corneal opacification, and amblyopia.[26, 50, 52, 53, 75] The presentation can be asymmetric and is often confused with herpetic disease.

Tear film break-up time using fluorescein is significantly shorter in patients with MGD, even if aqueous tear production is normal.[76] 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

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%], *S. aureus* [6.8%], and *Streptococcus* species [8.2%]).[79] 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. There are studies demonstrating that blepharitis is a risk factor in the development of endophthalmitis after intravitreal injection[80] and in bleb-related infection.[81] However, long-term antibiotic treatment may result in the development of resistant organisms.[82]

Treatment

The patient must understand that a cure is usually not possible, but continual daily treatment can significantly improve symptoms. Treatments that may be helpful include the following:

- Warm compresses
- Artificial tears
- Eyelid cleansing, including eyelid massage in cases of MGD to express the meibomian glands
- Topical perfluorohexyloctane
- Antibiotics (topical and/or systemic)
- Antiparasitic medication (metronidazole, ivermectin, lotilaner)
- Topical anti-inflammatory agents (e.g., corticosteroids, cyclosporine)
- In-office procedural treatments (e.g., vectored thermal pulsation, microblepharoexfoliation)

These treatment options are often used in combination. Eyelid hygiene may provide symptomatic relief for both anterior and posterior blepharitis. Eyelid cleansing is especially useful for anterior blepharitis, whereas warm compresses are especially helpful for posterior blepharitis/MGD. The optimal treatment regimen often requires persistence and a trial-and-error approach. An initial step in treating patients who have blepharitis is to recommend warm compresses and eyelid cleansing,[83] 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 washcloth, over-the-counter heat pack, or homemade bean/rice bag that can be heated 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. Eye cleaners with hypochlorous acid at 0.01% have a strong antimicrobial effect which has been used for the treatment of both anterior and posterior blepharitis.[84] 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. Although some efficacy has been demonstrated for several types of eyelid wipes, there remains a lack of robust evidence to support their routine recommendation. Long-term costs and potential adverse effects should not be overlooked. There is not enough evidence to suggest superiority of one option over others.[85] *(I-, Insufficient, Discretionary)* The ophthalmologist should consider the patient's ability to perform this treatment and tailor the therapeutic plan accordingly. Proper counseling of patients with neurotrophic corneas is important in order to avoid injury to corneal epithelium. A schedule of regularly performed eyelid cleansing, daily or several times weekly, often blunts the symptoms of chronic blepharitis.[86]

Once- or twice-daily warm 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,[87] but it must be performed with care. Frequent manipulation of the eyelid may lead to

mechanically induced irritation. In addition, patients who have advanced glaucoma, with or without a history of a glaucoma filtering procedure, should be advised to not place pressure on the lids aggressively, because it may subsequently increase eye pressure. Patients should be advised that warm compress and eyelid cleansing treatment may be required long term, because the symptoms often recur when treatment is discontinued.

There are several topical treatments available for blepharitis. Topical perfluorohexyloctane was FDA approved in 2023 and is a prescription treatment that prevents tear evaporation and was shown to improve symptoms and corneal staining in patients with dry eye disease after 8 weeks of treatment.[88]

Selenium sulfide is a compound utilized in dermatology. It is reported to induce sebum production and to possess keratolytic and keratostatic effects. It has been explored for use for MGD. The hypothesis is that it breaks disulfide bonds, causing proteins to disaggregate, potentially unblocking the meibomian gland orifices and decreasing meibum viscosity. In a phase 2 clinical trial in MGD patients, treatment resulted in significant improvements in glands secreting meibum as well as in a mean Ocular Surface Disease Index score compared with vehicle.[89]

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. 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. 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.[90-93] Topical administration of loteprednol etabonate 0.5%/tobramycin 0.3% suspension can improve blepharoconjunctivitis in adults,[94] and it has been shown to be a safer medication compared with dexamethasone due to less risk of intraocular pressure rise[95] *(I-, Insufficient, Strong)* or cataract progression.

Oral tetracyclines and topical antibiotics may be helpful for patients with MGD, whose chronic symptoms and signs are not adequately controlled by eyelid cleansing or meibomian gland expression. Doxycycline, minocycline, or tetracycline can be given daily and tapered after clinical improvement is noted.[96, 97] To avoid using tetracyclines in women of childbearing age and in children, oral erythromycin or azithromycin may be used. One suggested dosing regimen for erythromycin in children is 30 to 40 mg/kg divided over 3 doses for 3 weeks, then twice daily for 4 to 6 weeks.[50] A pediatric dosing regimen for azithromycin of 5 mg/kg daily for 2 months was shown to be helpful for clinical improvement in a small case series.[98] However, a Cochrane systematic review reported uncertainty with respect to indications and effectiveness of both topical and systemic treatments for blepharokeratoconjunctivitis in children due to the lack of high-quality evidence.[99] More clinical trials are necessary to establish safety and efficacy for the proper treatment of blepharokeratoconjunctivitis in children.[99-101] Tetracyclines and macrolide antibiotics also have anti-inflammatory activity.[102] Treatments can be intermittently discontinued and reinstated, based on the severity of the patient's blepharitis and tolerance for the medication.

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[103] and improving tear break-up time in patients with rosacea and MGD.[104] The tetracyclines decrease lipase production in both *S. epidermidis* and *S. aureus*.[105, 106] Tetracyclines can cause photosensitization, gastrointestinal upset, vaginitis, and, rarely, azotemia. Tetracyclines have been implicated in cases of pseudotumor cerebri,[107, 108] 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 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,[109] since staining of teeth may occur; however, oral erythromycin or azithromycin may be substituted.[50, 98, 110] There are case reports of doxycycline-

induced Stevens-Johnson syndrome.[96, 97] Tetracyclines can sensitize the skin to the sun and result in greater likelihood of sunburn with exposure. Minocycline has been reported to stain skin, nails, sclera, teeth, conjunctiva, tongue, and bone.[111-113]

Oral azithromycin (off label) has been used successfully in the management of acne rosacea as an alternative to oral tetracyclines and can be combined with 0.1% topical tacrolimus.[114, 115] 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.[116] Another acceptable dosing regimen for pulsed oral azithromycin in adults is 1 g per week for 3 weeks.[117] Another study found efficacy with topical azithromycin as well as systemic azithromycin in both the signs and symptoms of posterior blepharitis.[118] Importantly, a Medicaid cohort in Tennessee showed a small but absolute increase in cardiovascular deaths (hazard ratio, 2.88; 95% confidence interval, 1.79–4.63; $P < 0.001$), 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.[119] 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.[120] However, the use of oral azithromycin for 5 days may actually be more efficacious with fewer side effects than 30 days of doxycycline.[121] A Cochrane study showed a small benefit of oral doxycycline in improving clinical signs, but may cause more adverse events.[122] More studies are necessary to evaluate the efficacy of oral antibiotics in blepharitis.

Currently, there is only high-quality evidence to support topical azelaic acid, topical ivermectin,[123, 124] brimonidine, doxycycline, and isotretinoin as effective treatments for patients with systemic rosacea. Additional studies must be performed to determine the effectiveness of topical metronidazole, oral tetracycline, low-dose minocycline, or topical cyclosporine for ocular rosacea.[125]

A brief course of topical corticosteroids may be helpful for eyelid or ocular surface inflammation, including 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 used, 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 intraocular pressure 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 phosphate. Guidelines for maintenance therapy should be discussed. Topical cyclosporine may be helpful in some patients with posterior blepharitis.[126]

Diet modification has been a traditional (though not well-documented) way of managing acne rosacea. The role of dietary supplementation with essential fatty acids in the management of blepharitis was evaluated in a 1-year study in which patients took two 1000-mg capsules of essential fatty acids 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.[127] A prospective, multicenter, double-blind clinical trial funded by the National Eye Institute and National Institutes of Health, studied the use of oral omega-3 supplements by patients with moderate to severe dry eye disease. Patients who were randomly assigned to receive supplements containing 3000 mg of omega-3 fatty acids for 12 months did not have significantly better outcomes than patients assigned to receive placebo (olive oil).[128] These two conflicting outcomes may indicate differences in patient population, formulations of the supplements, dosing, and/or the disease process being examined (i.e., blepharitis vs. moderate to severe dry eye disease). There may be a treatment effect of the olive oil placebo, which could explain the lack of significant benefit of omega-3 fatty acids in the multicenter trial. One review showed a benefit of oral omega-3 supplementation in MGD.[129] More studies are needed to clearly define the role of omega-3 supplements in ocular surface disease.

Artificial tears, especially those containing oil or lipid-based products, can be helpful for posterior blepharitis. Because many blepharitis patients have tear film instability, 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, lifitegrast, nasal neurostimulation, and/or punctal plugs may also be helpful in managing coexisting aqueous tear deficiency. (See the Dry Eye Syndrome PPP for more information on topical cyclosporine.[130])

Demodicosis can be considered in patients who do not improve using the above treatments.[131] According to reports, local application of tea tree oil is an effective treatment method for controlling *Demodex* blepharitis.[132] The most effective component in tea tree oil is 4-terpineol.[133] Improvement in symptoms and signs was reported in a small case series in which weekly 50% tea tree oil eyelid scrubs and daily tea-tree-oil shampoo scrubs were used for a minimum of 6 weeks in a group of patients who failed the above treatment methods.[41, 134, 135] During the treatment process, it is important to be cautious of the potential effects of tea tree oil on the corneal epithelium. Tharmarajah et al reported a case of corneal epithelial defect in a patient with blepharitis who used a 50% tea tree oil solution topically, which exceeded the recommended concentration.[136] Oral ivermectin has also been reported to be of benefit in some cases of recalcitrant *Demodex* blepharitis.[137, 138] Studies have shown that topical and systemic ivermectin have successfully reduced or eliminated the number of *D. folliculorum* found in the epilated lashes of patients with blepharitis or ocular rosacea.[113] Topical ivermectin cream weekly was shown to significantly improve symptoms, ocular surface staining, eyelid debris, redness/swelling, and telangiectasias compared with eyelid hygiene alone.[124] Another study showed that hypochlorous acid 0.01% spray had minimal effect on *Demodex*.[139] A Cochrane review showed uncertainty in the benefits of topical tea tree oil in the treatment of *Demodex* blepharitis.[140] In addition to the aforementioned medications, local application of lotilaner ophthalmic solution 0.25% has been found to be effective and safe in the treatment of *Demodex* blepharitis.[141]

Topical lotilaner was recently FDA approved for the treatment of *Demodex* blepharitis. It was shown to significantly reduce collarettes, decrease or eradicate mites, and reduce eyelid erythema after 6 weeks of twice daily use.[142, 143]

There are several in-office procedural treatments available that may improve the inspissated meibomian gland orifices using intense pulsed light (IPL) or theoretically unclog the meibomian glands by mechanical means (e.g., microblepharoexfoliation of the eyelid margin, meibomian gland probing, and/or devices using thermal pulsation). Although there have been industry-sponsored studies, independent, randomized clinical trials have yet to be performed to assess efficacy or superiority of any one of these treatments over another.[144] *(I-, Moderate, Discretionary)*

- Meibomian gland probing is a procedure that can be performed at the slit lamp or in a minor-procedure room. This is a relatively safe procedure but is invasive and requires proper anesthesia of the area. An industry-associated retrospective review of 25 consecutive patients demonstrated that intraductal probing of meibomian glands provided lasting and rapid symptom relief in patients with obstructed meibomian glands.[145]
- Vectored thermal pulsation therapy for meibomian glands is a technology designed to transfer heat and actively express the meibomian gland contents. This commercially available device applies heat (42.5° C/108.5° F) to the inner eyelid surface while protecting the cornea, and pulsating pressure is applied to the outer eyelid surface. Industry-sponsored studies have demonstrated that a single vectored thermal pulsation treatment can be effective at improving meibomian gland function and reducing dry eye symptoms for a year or more post-procedure.[146, 147]
- Another commercially available in-office procedure combines the application of heat to the eyelids with manual meibomian gland expression. This treatment was found to improve the signs and symptoms of MGD and was noninferior to vectored thermal pulsation.[148]
- Microblepharoexfoliation can be performed in the office with using a commercially available device that consists of a hand-held electromechanical unit and a disposable microsponge that spins rapidly to provide debridement and exfoliation at the lid margin. Limited, primarily industry-sponsored reports are available comparing this with conventional manual scrub techniques. Murphy et al reported that eyelid hygiene using tea tree oil with combination microblepharoexfoliation was of comparable benefit to hypochlorous acid scrubs or tea tree oil alone in patients with blepharitis secondary to *Demodex* infestation.[149] Another study demonstrated that microblepharoexfoliation

combined with tea tree oil scrubs or sham scrubs significantly decreased Demodex levels but it was indeterminate in clinical significance.[150]

- Intense pulsed light is a noncoherent polychromatic light source with a broad wavelength spectrum of 500 to 1200 nm that has been widely used for aesthetic or therapeutic purposes in the dermatology field. This is also a therapy for MGD because the photothermal effect helps decrease inflammation of the gland, but the exact mechanism of action is still unclear. Several groups have reported that IPL improved meibomian gland function and gland macrostructure and microstructure, with secondary improvement of dry eye symptoms. There has been one small independent 28-patient study showing improved symptoms and tear quality in a contralateral eye study. This treatment is not covered by insurance, is relatively costly, and has to be repeated in order to obtain, theoretically, long-lasting effects.[151, 152] Intense pulsed light should be used with caution for more darkly pigmented individuals (above Fitzpatrick skin type IV) because the increased melanin can attract more light and cause burns and could also lead to changes in pigmentation level.[153] In one study, IPL has been shown to have a high *Demodex* eradication rate and improved Ocular Surface Disease Index score, tear break-up time, and meibum quality compared with topical in-office treatment of tea tree oil 30 and 60 days post-treatment.[154] Intense pulsed light plus meibomian gland expression was found to be superior to meibomian gland expression alone in patients with moderate-to-severe blepharoconjunctivitis signs and symptoms.[155] Low-energy IPL treatment has also been found to be effective and safe for treating moderate to severe blepharitis in children.[156] Furthermore, there are retrospective reports indicating that IPL with meibomian gland expression can be used as a nonsurgical treatment option for recurrent multiple chalazia.[157] Although there is insufficient evidence to determine the effectiveness of this therapy in patients with rosacea,[125] one small study did show clinical benefit and improvement of some signs of rosacea-associated MGD.[158]

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.[159] 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 in the same location.

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 co-morbid 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 intraocular pressure, 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, particularly children, with blepharitis should be evaluated by an ophthalmologist in any of the following circumstances:

- 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. It is important for patients to understand that successful management is dependent on their compliance with a treatment regimen. Patients with an inflammatory eyelid lesion that appears suspicious for malignancy should be referred to an appropriate specialist.

SOCIOECONOMIC CONSIDERATIONS

The economic impact of blepharitis as a separate entity has not been adequately evaluated. One study reported the eye-related Medicare costs between 1995 and 1999 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.[160] The economic burden of blepharitis is magnified by its prevalence, and additional studies are needed to characterize its financial impact.

Although there is no strong evidence of 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. In-office procedures, such as microblepharoexfoliation, thermal pulsation of meibomian glands, and IPL are not well covered by insurance and can incur significant cost to the patient. 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]

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

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

	ICD-10 CM
Ulcerative	H01.01-
Squamous	H01.02-
Stye	H00.01-
Meibomitis	H01.02-
Abscess of eyelid	H00.03-
Parasitic infestation of eyelid	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:

- 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

LITERATURE SEARCHES FOR THIS PPP

Literature searches of the PubMed database were conducted on March 3, 2022; the search strategies are listed below. Specific limited update searches were conducted on June 7, 2023. The searches had added filters for human, English-language randomized controlled trials and systematic reviews and date limiters to capture literature published since June 27, 2018. The panel analyzed 240 studies, of which 47 were included in the PPP. The literature searches with the disease condition and the search term, patient values and patient preferences didn't yield results. The literature searches for economic evaluation and treatment cost yielded 6 studies, 6 of which were provided to the panel, none of which merited inclusion in the PPP.

All: ("blepharitis"[mh] OR "blepharitis")

Epidemiology: "blepharitis/epidemiology"[mh]

Risk Factors: ("blepharitis"[MeSH Terms]) AND (("risk factors"[MeSH Terms]) OR ("cost of illness"[MeSH Terms]) OR ("cost benefit analysis"[MeSH Terms]) OR ("quality of life"[MeSH Terms]))

Rosacea: ("blepharitis"[MeSH Terms]) AND (rosacea[MeSH Terms])

Drug Therapy: (("blepharitis/drug therapy"[MAJR]) OR ("blepharitis/therapy"[MAJR]) OR ("blepharitis/prevention and control"[MAJR]))

Etiology: ("blepharitis/etiology"[MAJR])

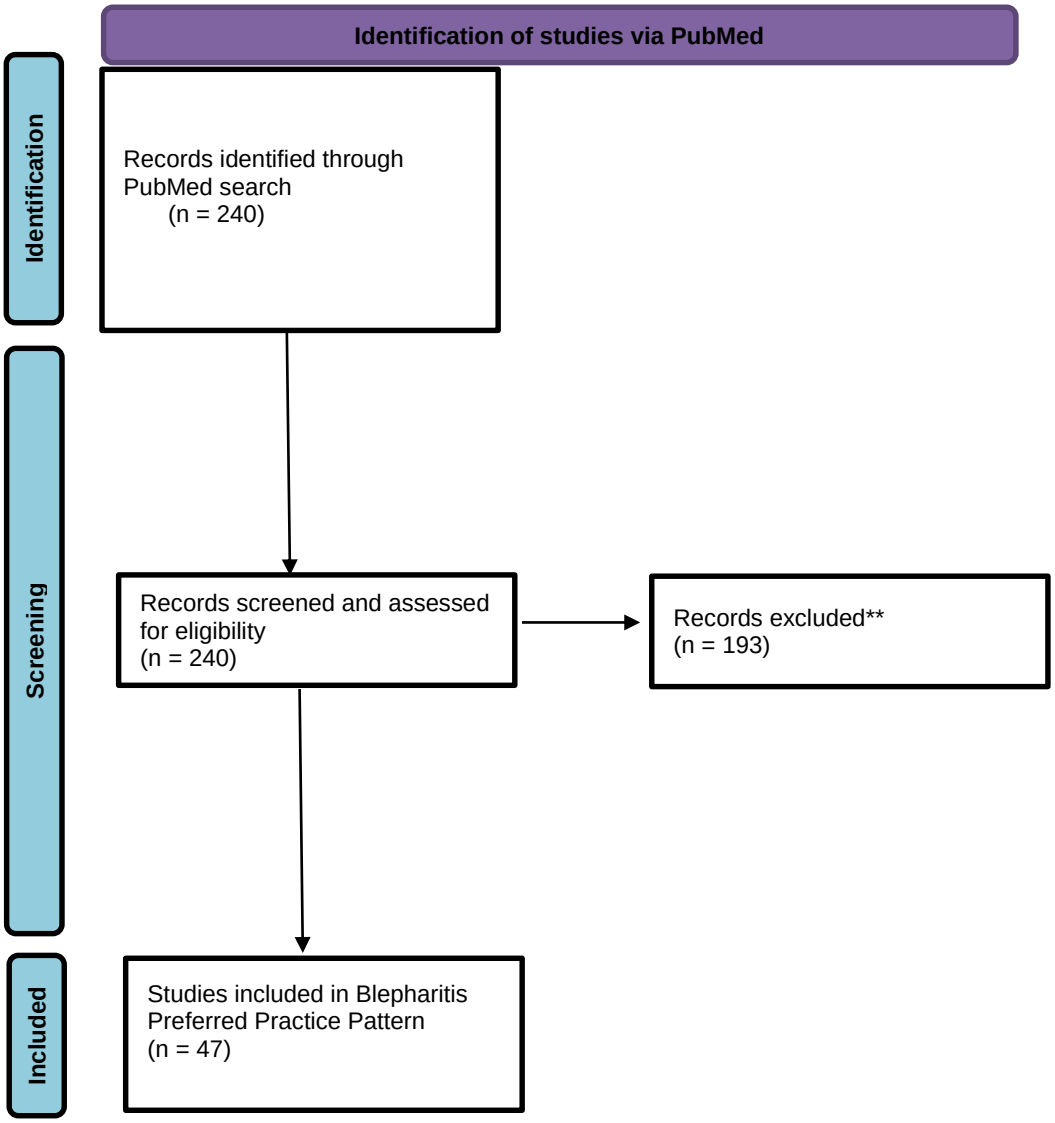
Pathology, Physiology: ("blepharitis/physiopathology"[MeSH Terms]) OR ("blepharitis/physiology"[MeSH Terms]) OR ("blepharitis/pathology"[MeSH Terms])

Disease Progression: (blepharitis[MeSH Terms]) AND ("disease progression"[MeSH Terms])

Blepharoconjunctivitis: ("blepharitis"[tiab] OR blepharoconjunctivitis[tiab] OR blepharokeratoconjunctivitis[tiab])

Diagnosis: "blepharitis/diagnosis"[MeSH Terms]

Patient Values: blepharitis[tiab] AND (patient values[tiab] OR patient preferences[tiab])



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

RELATED ACADEMY MATERIALS

Basic and Clinical Science Course
External Disease and Cornea (Section 8, 2023–2024)

Patient Education Brochure
Blepharitis (2022)

Preferred Practice Pattern® Guidelines – Free download available at www.aao.org/ppp**.**
Comprehensive Adult Medical Eye Evaluation (2020)
Pediatric Eye Evaluations (2022)

REFERENCES

1. Scottish Intercollegiate Guidelines Network (SIGN). *SIGN 50: A guideline developer's handbook.* Edinburgh: SIGN; 2015. (SIGN publication no. 50). [November 2015]. Available from url: http://www.sign.ac.uk.
2. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. *BMJ.* 2008;336:924-926.
3. GRADE working group. Organizations that have endorsed or that are using grade. http://www.gradeworkinggroup.org/. Accessed November 17, 2023.
4. McCulley JP, Dougherty JM, Deneau DG. Classification of chronic blepharitis. *Ophthalmology.* 1982;89:1173-1180.
5. Nichols KK, Foulks GN, Bron AJ, et al. The international workshop on meibomian gland dysfunction: Executive summary. *Invest Ophthalmol Vis Sci.* 2011;52:1922-1929.
6. American Academy of Ophthalmology Basic and Clinical Science Course Subcommittee. Basic and clinical science course. External disease and cornea: Section 8, 2021-2022. San Francisco, CA: American Academy of Ophthalmology.
7. de Paula A, Oliva G, Barraquer RI, de la Paz MF. Prevalence and antibiotic susceptibility of bacteria isolated in patients affected with blepharitis in a tertiary eye centre in Spain. *Eur J Ophthalmol.* 2020;30:991-997.
8. Valenton MJ, Okumoto M. Toxin-producing strains of staphylococcus epidermidis (albus). Isolates from patients with staphylococcic blepharoconjunctivitis. *Arch Ophthalmol.* 1973;89:186-189.
9. Seal D, Ficker L, Ramakrishnan M, Wright P. Role of staphylococcal toxin production in blepharitis. *Ophthalmology.* 1990;97:1684-1688.
10. Ficker L, Ramakrishnan M, Seal D, Wright P. Role of cell-mediated immunity to staphylococci in blepharitis. *Am J Ophthalmol.* 1991;111:473-479.
11. Bowman RW, Dougherty JM, McCulley JP. Chronic blepharitis and dry eyes. *Int Ophthalmol Clin.* 1987;27:27-35.
12. Aderem A, Ulevitch RJ. Toll-like receptors in the induction of the innate immune response. *Nature.* 2000;406:782-787.
13. 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;42:2867-2877.
14. Nattis A, Perry HD, Rosenberg ED, Donnenfeld ED. Influence of bacterial burden on meibomian gland dysfunction and ocular surface disease. *Clin Ophthalmol.* 2019;13:1225-1234.
15. Lemp MA, Mahmood MA, Weiler HH. Association of rosacea and keratoconjunctivitis sicca. *Arch Ophthalmol.* 1984;102:556-557.
16. McCulley JP, Shine WE. Meibomian secretions in chronic blepharitis. *Adv Exp Med Biol.* 1998;438:319-326.
17. 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.
18. Yeotikar NS, Zhu H, Markoulli M, et al. Functional and morphologic changes of meibomian glands in an asymptomatic adult population. *Invest Ophthalmol Vis Sci.* 2016;57:3996-4007.
19. Stanek S. Meibomian gland status comparison between active duty personnel and U.S. veterans. *Mil Med.* 2000;165:591-593.
20. Lemp MA, Nichols KK. Blepharitis in the United States 2009: A survey-based perspective on prevalence and treatment. *Ocul Surf.* 2009;7:S1-S14.
21. Schein OD, Munoz B, Tielsch JM, et al. Prevalence of dry eye among the elderly. *Am J Ophthalmol.* 1997;124:723-728.
22. 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;110:1096-1101.
23. 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.
24. Jie Y, Xu L, Wu YY, Jonas JB. Prevalence of dry eye among adult Chinese in the Beijing eye study. *Eye (Lond).* 2009;23:688-693.
25. McCarty CA, Bansal AK, Livingston PM, et al. The epidemiology of dry eye in Melbourne, Australia. *Ophthalmology.* 1998;105:1114-1119.

26. Hammersmith KM, Cohen EJ, Blake TD, et al. Blepharokeratoconjunctivitis in children. *Arch Ophthalmol.* 2005;123:1667-1670.
27. Baum J. Clinical manifestations of dry eye states. *Trans Ophthalmol Soc U K.* 1985;104 (Pt 4):415-423.
28. Stern ME, Beuerman RW, Fox RI, et al. The pathology of dry eye: The interaction between the ocular surface and lacrimal glands. *Cornea.* 1998;17:584-589.
29. Mathers WD. Ocular evaporation in meibomian gland dysfunction and dry eye. *Ophthalmology.* 1993;100:347-351.
30. Shine WE, McCulley JP. Keratoconjunctivitis sicca associated with meibomian secretion polar lipid abnormality. *Arch Ophthalmol.* 1998;116:849-852.
31. Hsu JI, Pflugfelder SC, Kim SJ. Ocular complications of atopic dermatitis. *Cutis.* 2019;104:189-193.
32. Demerdjieva Z, Mazhdrakova I, Tsankov N. Ocular changes in patients with psoriasis. *Clin Dermatol.* 2019;37:663-667.
33. Constantin MM, Ciurduc MD, Bucur S, et al. Psoriasis beyond the skin: Ophthalmological changes (review). *Exp Ther Med.* 2021;22:981.
34. Murphy O, O'Dwyer V, Lloyd-McKernan A. Ocular demodex folliculorum: Prevalence and associated symptoms in an Irish population. *Int Ophthalmol.* 2019;39:405-417.
35. Cheng AM, Hwang J, Dermer H, Galor A. Prevalence of ocular demodicosis in an older population and its association with symptoms and signs of dry eye. *Cornea.* 2021;40:995-1001.
36. Rabensteiner DF, Aminfar H, Boldin I, et al. Demodex mite infestation and its associations with tear film and ocular surface parameters in patients with ocular discomfort. *Am J Ophthalmol.* 2019;204:7-12.
37. Biernat MM, Rusiecka-Ziolkowska J, Piatkowska E, et al. Occurrence of demodex species in patients with blepharitis and in healthy individuals: A 10-year observational study. *Jpn J Ophthalmol.* 2018;62:628-633.
38. Kemal M, Sumer Z, Toker MI, et al. The prevalence of demodex folliculorum in blepharitis patients and the normal population. *Ophthalmic Epidemiol.* 2005;12:287-290.
39. Zhang N, Liu Y, Wen K, et al. Prevalence of ocular demodex infestation in children: An epidemiological survey in South China. *Eye Contact Lens.* 2021;47:60-64.
40. Gao YY, Di Pascuale MA, Li W, et al. High prevalence of demodex in eyelashes with cylindrical dandruff. *Invest Ophthalmol Vis Sci.* 2005;46:3089-3094.
41. Koo H, Kim TH, Kim KW, et al. Ocular surface discomfort and demodex: Effect of tea tree oil eyelid scrub in demodex blepharitis. *J Korean Med Sci.* 2012;27:1574-1579.
42. Ryan MF. Phthiriasis palpebrarum infection: A concern for child abuse. *J Emerg Med.* 2014;46:e159-162.
43. Browning DJ, Proia AD. Ocular rosacea. *Surv Ophthalmol.* 1986;31:145-158.
44. Jenkins MS, Brown SI, Lempert SL, Weinberg RJ. Ocular rosacea. *Am J Ophthalmol.* 1979;88:618-622.
45. Akpek EK, Merchant A, Pinar V, Foster CS. Ocular rosacea: Patient characteristics and follow-up. *Ophthalmology.* 1997;104:1863-1867.
46. Deeks ED. Ivermectin: A review in rosacea. *Am J Clin Dermatol.* 2015;16:447-452.
47. American Academy of Ophthalmology Basic and Clinical Science Course Subcommittee. Basic and clinical science course. External disease and cornea: Section 8, 2021-2022. San Francisco, CA: American Academy of Ophthalmology.
48. Berg M, Liden S. An epidemiological study of rosacea. *Acta Derm Venereol.* 1989;69:419-423.
49. Chalmers DA. Rosacea: Recognition and management for the primary care provider. *Nurse Pract.* 1997;22:18, 23-18, 30.
50. Viswalingam M, Rauz S, Morlet N, Dart JK. Blepharokeratoconjunctivitis in children: Diagnosis and treatment. *Br J Ophthalmol.* 2005;89:400-403.
51. Tavassoli S, Wong N, Chan E. Ocular manifestations of rosacea: A clinical review. *Clin Exp Ophthalmol.* 2021;49:104-117.
52. Cetinkaya A, Akova YA. Pediatric ocular acne rosacea: Long-term treatment with systemic antibiotics. *Am J Ophthalmol.* 2006;142:816-821.
53. Donaldson KE, Karp CL, Dunbar MT. Evaluation and treatment of children with ocular rosacea. *Cornea.* 2007;26:42-46.
54. Bamford JT, Gessert CE, Renier CM, et al. Childhood stye and adult rosacea. *J Am Acad Dermatol.* 2006;55:951-955.
55. Bozkurt B, Irkec MT, Atakan N, et al. Lacrimal function and ocular complications in patients treated with systemic isotretinoin. *Eur J Ophthalmol.* 2002;12:173-176.
56. Mathers WD, Shields WJ, Sachdev MS, et al. Meibomian gland morphology and tear osmolarity: Changes with accutane therapy. *Cornea.* 1991;10:286-290.

57. Fraunfelder FT, Fraunfelder FW, Edwards R. Ocular side effects possibly associated with isotretinoin usage. *Am J Ophthalmol.* 2001;132:299-305.
58. 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;73:355-357.
59. Halling AS, Loft N, Silverberg JI, et al. Real-world evidence of dupilumab efficacy and risk of adverse events: A systematic review and meta-analysis. *J Am Acad Dermatol.* 2021;84:139-147.
60. Wu D, Daniel BS, Lai AJX, et al. Dupilumab-associated ocular manifestations: A review of clinical presentations and management. *Surv Ophthalmol.* 2022.
61. Martin NF, Rubinfeld RS, Malley JD, Manzitti V. Giant papillary conjunctivitis and meibomian gland dysfunction blepharitis. *CLAO J.* 1992;18:165-169.
62. Perez-Cano HJ, Rubalcava-Soberanis ML, Velazquez Salgado R. Relationship between blepharitis and components of the metabolic syndrome. *Arch Soc Esp Oftalmol (Engl Ed).* 2018;93:476-480.
63. Feng KM, Chung CH, Chen YH, et al. Statin use is associated with a lower risk of blepharitis: A population-based study. *Front Med (Lausanne).* 2022;9:820119.
64. Hykin PG, Bron AJ. Age-related morphological changes in lid margin and meibomian gland anatomy. *Cornea.* 1992;11:334-342.
65. Daniel MC, O'Gallagher M, Hingorani M, et al. Challenges in the management of pediatric blepharokeratoconjunctivis / ocular rosacea. *Expert Rev Ophthalmol.* 2016;11:299-309.
66. Hutchinson AK, Morse CL, Hercinovic A, et al. Pediatric eye evaluations referred practice pattern. *Ophthalmology.* 2023;130:P222-P270.
67. Chuck RS, Dunn SP, Flaxel CJ, et al. Comprehensive adult medical eye evaluation preferred practice pattern. *Ophthalmology.* 2021;128:P1-P29.
68. Bron AJ, Benjamin L, Snibson GR. Meibomian gland disease. Classification and grading of lid changes. *Eye.* 1991;5 (Pt 4):395-411.
69. 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.
70. Man Peles I, Zahavi A, Chemodanova E, Vardizer Y. Novel in-office technique for visual confirmation of demodex infestation in blepharitic patients. *Cornea.* 2020;39:858-861.
71. Gilberg S, Tse D. Malignant eyelid tumors. *Ophthalmol Clin North Am.* 1992;5:261-285.
72. American Academy of Ophthalmology Cornea/External Disease Panel. Preferred practice pattern®. Conjunctivitis. San Francisco, CA: American Academy of Ophthalmology; 2023. www.aao.org/ppp. Accessed November 17, 2023.
73. Finis D, Pischel N, Schrader S, Geerling G. Evaluation of lipid layer thickness measurement of the tear film as a diagnostic tool for meibomian gland dysfunction. *Cornea.* 2013;32:1549-1553.
74. Blackie CA, Solomon JD, Scaffidi RC, et al. The relationship between dry eye symptoms and lipid layer thickness. *Cornea.* 2009;28:789-794.
75. Jones SM, Weinstein JM, Cumberland P, et al. Visual outcome and corneal changes in children with chronic blepharokeratoconjunctivitis. *Ophthalmology.* 2007;114:2271-2280.
76. 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.
77. Acharya N, Pineda R, 2nd, Uy HS, Foster CS. Discoid lupus erythematosus masquerading as chronic blepharoconjunctivitis. *Ophthalmology.* 2005;112:e19-23.
78. 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;138:292-294.
79. 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;115:473-476.
80. Lyall DA, Tey A, Foot B, et al. Post-intravitreal anti-VEGF endophthalmitis in the United Kingdom: Incidence, features, risk factors, and outcomes. *Eye (Lond).* 2012;26:1517-1526.
81. Rai PA, Barton K, Murdoch IE. Risk factors for bleb-related infection following trabeculectomy surgery: Ocular surface findings-a case-control study. *Br J Ophthalmol.* 2017;101:868-873.
82. Miller KM, Oetting TA, Tweeten JP, et al. Cataract in the adult eye preferred practice pattern. *Ophthalmology.* 2022;129:P1-P126.
83. Key JE. A comparative study of eyelid cleaning regimens in chronic blepharitis. *CLAO J.* 1996;22:209-212.
84. Stroman DW, Mintun K, Epstein AB, et al. Reduction in bacterial load using hypochlorous acid hygiene solution on ocular skin. *Clin Ophthalmol.* 2017;11:707-714.

85. Gostimir M, Allen LH. Is there enough evidence for the routine recommendation of eyelid wipes? A systematic review of the role of eyelid wipes in the management of blepharitis. *Can J Ophthalmol.* 2020;55:424-436.
86. Olson MC, Korb DR, Greiner JV. Increase in tear film lipid layer thickness following treatment with warm compresses in patients with meibomian gland dysfunction. *Eye Contact Lens.* 2003;29:96-99.
87. Thode AR, Latkany RA. Current and emerging therapeutic strategies for the treatment of meibomian gland dysfunction (MGD). *Drugs.* 2015;75:1177-1185.
88. Tauber J, Berdy GJ, Wirta DL, et al. NOV03 for dry eye disease associated with meibomian gland dysfunction: Results of the randomized phase 3 GOBI study. *Ophthalmology.* 2023;130:516-524.
89. Watson SL, Jones LW, Stapleton F, et al. Efficacy and safety of AZR-MD-001 selenium sulfide ophthalmic ointment in adults with meibomian gland dysfunction: A vehicle-controlled, randomized clinical trial. *Ocul Surf.* 2023;29:537-546.
90. Arita R, Fukuoka S. Efficacy of azithromycin eyedrops for individuals with meibomian gland dysfunction-associated posterior blepharitis. *Eye Contact Lens.* 2021;47:54-59.
91. 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;27:171-178.
92. 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;29:871-877.
93. Foulks GN, Borchman D, Yappert M, et al. Topical azithromycin therapy for meibomian gland dysfunction: Clinical response and lipid alterations. *Cornea.* 2010;29:781-788.
94. Mah FS, Karpecki PM. Review of loteprednol etabonate 0.5%/tobramycin 0.3% in the treatment of blepharokeratoconjunctivitis. *Ophthalmol Ther.* 2021;10:859-875.
95. Zhao L, Sun YJ, Pan ZQ. Topical steroids and antibiotics for adult blepharokeratoconjunctivitis (BKC): A meta-analysis of randomized clinical trials. *J Ophthalmol.* 2021;2021:3467620.
96. Cac NN, Messingham MJ, Sniezek PJ, Walling HW. Stevens-Johnson syndrome induced by doxycycline. *Cutis.* 2007;79:119-122.
97. Lau B, Mutyala D, Dhaliwal D. A case report of doxycycline-induced Stevens-Johnson syndrome. *Cornea.* 2011;30:595-597.
98. Choi DS, Djalilian A. Oral azithromycin combined with topical anti-inflammatory agents in the treatment of blepharokeratoconjunctivitis in children. *J AAPOS.* 2013;17:112-113.
99. O'Gallagher M, Bunce C, Hingorani M, et al. Topical treatments for blepharokeratoconjunctivitis in children. *Cochrane Database Syst Rev.* 2017;2:CD011965.
100. Lindsley K, Matsumura S, Hatef E, Akpek EK. Interventions for chronic blepharitis. *Cochrane Database Syst Rev.* 2012:CD005556.
101. O'Gallagher M, Banteka M, Bunce C, et al. Systemic treatment for blepharokeratoconjunctivitis in children. *Cochrane Database Syst Rev.* 2016:CD011750.
102. Ianaro A, Ialenti A, Maffia P, et al. Anti-inflammatory activity of macrolide antibiotics. *J Pharmacol Exp Ther.* 2000;292:156-163.
103. 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.
104. Zengin N, Tol H, Gunduz K, et al. Meibomian gland dysfunction and tear film abnormalities in rosacea. *Cornea.* 1995;14:144-146.
105. 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;32:2970-2975.
106. Shine WE, McCulley JP, Pandya AG. Minocycline effect on meibomian gland lipids in meibomianitis patients. *Exp Eye Res.* 2003;76:417-420.
107. Quinn AG, Singer SB, Buncic JR. Pediatric tetracycline-induced pseudotumor cerebri. *J AAPOS.* 1999;3:53-57.
108. Chiu AM, Chuenkongkaew WL, Cornblath WT, et al. Minocycline treatment and pseudotumor cerebri syndrome. *Am J Ophthalmol.* 1998;126:116-121.
109. American Academy of Ophthalmology Basic and Clinical Science Course Subcommittee. Basic and clinical science course. Update on general medicine: Section 1, 2021-2022. San Francisco, CA: American Academy of Ophthalmology.
110. Meisler DM, Raizman MB, Traboulsi EI. Oral erythromycin treatment for childhood blepharokeratitis. *J AAPOS.* 2000;4:379-380.

111. Fraunfelder FT, Randall JA. Minocycline-induced scleral pigmentation. *Ophthalmology.* 1997;104:936-938.
112. Bradfield YS, Robertson DM, Salomao DR, et al. Minocycline-induced ocular pigmentation. *Arch Ophthalmol.* 2003;121:144-145.
113. Sanchez AR, Rogers RS, 3rd, Sheridan PJ. Tetracycline and other tetracycline-derivative staining of the teeth and oral cavity. *Int J Dermatol.* 2004;43:709-715.
114. Modi S, Harting M, Rosen T. Azithromycin as an alternative rosacea therapy when tetracyclines prove problematic. *J Drugs Dermatol.* 2008;7:898-899.
115. 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;47:284-288.
116. Igami TZ, Holzchuh R, Osaki TH, et al. Oral azithromycin for treatment of posterior blepharitis. *Cornea.* 2011;30:1145-1149.
117. Greene JB, Jeng BH, Fintelmann RE, Margolis TP. Oral azithromycin for the treatment of meibomitis. *JAMA Ophthalmol.* 2014;132:121-122.
118. Yildiz E, Yenerel NM, Turan-Yardimci A, et al. Comparison of the clinical efficacy of topical and systemic azithromycin treatment for posterior blepharitis. *J Ocul Pharmacol Ther.* 2018;34:365-372.
119. Ray WA, Murray KT, Hall K, et al. Azithromycin and the risk of cardiovascular death. *N Engl J Med.* 2012;366:1881-1890.
120. U.S. Food and Drug Administration. FDA drug safety communication. Azithromycin (zithromax or zmax) and the risk of potentially fatal heart rhythms. www.fda.gov/drugs/drugsafety/ucm341822.htm. Accessed November 17, 2023.
121. De Benedetti G, Vaiano AS. Oral azithromycin and oral doxycycline for the treatment of meibomian gland dysfunction: A 9-month comparative case series. *Indian J Ophthalmol.* 2019;67:464-471.
122. Onghanseng N, Ng SM, Halim MS, Nguyen QD. Oral antibiotics for chronic blepharitis. *Cochrane Database Syst Rev.* 2021;6:CD013697.
123. Sobolewska B, Doycheva D, Deuter CM, et al. Efficacy of topical ivermectin for the treatment of cutaneous and ocular rosacea. *Ocul Immunol Inflamm.* 2021;29:1137-1141.
124. Choi Y, Eom Y, Yoon EG, et al. Efficacy of topical ivermectin 1% in the treatment of demodex blepharitis. *Cornea.* 2022;41:427-434.
125. van Zuuren EJ, Fedorowicz Z, Carter B, et al. Interventions for rosacea. *Cochrane Database Syst Rev.* 2015:CD003262.
126. 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;25:171-175.
127. Macsai MS. The role of omega-3 dietary supplementation in blepharitis and meibomian gland dysfunction (an AOS thesis). *Trans Am Ophthalmol Soc.* 2008;106:336-356.
128. The Dry Eye Assessment and Management Study Research Group. N−3 fatty acid supplementation for the treatment of dry eye disease *N Engl J Med.* 2018;378:1681-1690.
129. Al-Namaeh M. A systematic review of the effect of omega-3 supplements on meibomian gland dysfunction. *Ther Adv Ophthalmol.* 2020;12:2515841420952188.
130. American Academy of Ophthalmology Cornea/External Disease Panel. Preferred practice pattern®. Dry eye syndrome. San Francisco, CA: American Academy of Ophthalmology; 2023. www.aao.org/ppp. Accessed November 17, 2023.
131. Shah PP, Stein RL, Perry HD. Update on the management of demodex blepharitis. *Cornea.* 2022;41:934-939.
132. Capasso L, Abbinante G, Coppola A, et al. Recent evidence of tea tree oil effectiveness in blepharitis treatment. *Biomed Res Int.* 2022;2022:9204251.
133. Tighe S, Gao YY, Tseng SC. Terpinen-4-ol is the most active ingredient of tea tree oil to kill demodex mites. *Transl Vis Sci Technol.* 2013;2:2.
134. Kheirkhah A, Casas V, Li W, et al. Corneal manifestations of ocular demodex infestation. *Am J Ophthalmol.* 2007;143:743-749.
135. Gao YY, Di Pascuale MA, Li W, et al. In vitro and in vivo killing of ocular demodex by tea tree oil. *Br J Ophthalmol.* 2005;89:1468-1473.
136. Tharmarajah B, Coroneo MT. Corneal effects of tea tree oil. *Cornea.* 2021;40:1363-1364.
137. 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;95:893-895.
138. Holzchuh FG, Hida RY, Moscovici BK, et al. Clinical treatment of ocular demodex folliculorum by systemic ivermectin. *Am J Ophthalmol.* 2011;151:1030-1034.

139. Kabat AG. In vitro demodicidal activity of commercial lid hygiene products. *Clin Ophthalmol.* 2019;13:1493-1497.
140. Savla K, Le JT, Pucker AD. Tea tree oil for demodex blepharitis. *Cochrane Database Syst Rev.* 2020;6:CD013333.
141. Gonzalez-Salinas R, Karpecki P, Yeu E, et al. Safety and efficacy of lotilaner ophthalmic solution, 0.25% for the treatment of blepharitis due to demodex infestation: A randomized, controlled, double-masked clinical trial. *Cont Lens Anterior Eye.* 2022;45:101492.
142. Gaddie IB, Donnenfeld ED, Karpecki P, et al. Lotilaner ophthalmic solution 0.25% for demodex blepharitis: Randomized, vehicle-controlled, multicenter, phase 3 trial (Saturn-2). *Ophthalmology.* 2023.
143. Yeu E, Wirta DL, Karpecki P, et al. Lotilaner ophthalmic solution, 0.25%, for the treatment of demodex blepharitis: Results of a prospective, randomized, vehicle-controlled, double-masked, pivotal trial (Saturn-1). *Cornea.* 2023;42:435-443.
144. Cote S, Zhang AC, Ahmadzai V, et al. Intense pulsed light (IPL) therapy for the treatment of meibomian gland dysfunction. *Cochrane Database Syst Rev.* 2020;3:CD013559.
145. Maskin SL. Intraductal meibomian gland probing relieves symptoms of obstructive meibomian gland dysfunction. *Cornea.* 2010;29:1145-1152.
146. Blackie CA, Coleman CA, Holland EJ. The sustained effect (12 months) of a single-dose vectored thermal pulsation procedure for meibomian gland dysfunction and evaporative dry eye. *Clin Ophthalmol.* 2016;10:1385-1396.
147. Greiner JV. Long-term (12-month) improvement in meibomian gland function and reduced dry eye symptoms with a single thermal pulsation treatment. *Clin Exp Ophthalmol.* 2013;41:524-530.
148. Gupta PK, Periman LM, Lain E, et al. Meibomian gland dysfunction: A dermatological perspective on pathogenesis and treatment outlook. *Clin Ophthalmol.* 2021;15:4399-4404.
149. Murphy O, O'Dwyer V, Lloyd-McKernan A. The efficacy of tea tree face wash, 1, 2-octanediol and microblepharoexfoliation in treating demodex folliculorum blepharitis. *Cont Lens Anterior Eye.* 2018;41:77-82.
150. Epstein IJ, Rosenberg E, Stuber R, et al. Double-masked and unmasked prospective study of terpinen-4-ol lid scrubs with microblepharoexfoliation for the treatment of demodex blepharitis. *Cornea.* 2020;39:408-416.
151. Toyos R, McGill W, Briscoe D. Intense pulsed light treatment for dry eye disease due to meibomian gland dysfunction; a 3-year retrospective study. *Photomed Laser Surg.* 2015;33:41-46.
152. Yin Y, Liu N, Gong L, Song N. Changes in the meibomian gland after exposure to intense pulsed light in meibomian gland dysfunction (MGD) patients. *Curr Eye Res.* 2018;43:308-313.
153. Thaysen-Petersen D, Erlendsson AM, Nash JF, et al. Side effects from intense pulsed light: Importance of skin pigmentation, fluence level and ultraviolet radiation-a randomized controlled trial. *Lasers Surg Med.* 2017;49:88-96.
154. Zhang X, Song N, Gong L. Therapeutic effect of intense pulsed light on ocular demodicosis. *Curr Eye Res.* 2019;44:250-256.
155. Ruan F, Zang Y, Sella R, et al. Intense pulsed light therapy with optimal pulse technology as an adjunct therapy for moderate to severe blepharitis-associated keratoconjunctivitis. *J Ophthalmol.* 2019;2019:3143469.
156. Zhai Z, Jiang H, Wu Y, et al. Safety and feasibility of low fluence intense pulsed light for treating pediatric patients with moderate-to-severe blepharitis. *J Clin Med.* 2022;11.
157. Arita R, Fukuoka S. Therapeutic efficacy and safety of intense pulsed light for refractive multiple recurrent chalazia. *J Clin Med.* 2022;11.
158. Seo KY, Kang SM, Ha DY, et al. Long-term effects of intense pulsed light treatment on the ocular surface in patients with rosacea-associated meibomian gland dysfunction. *Cont Lens Anterior Eye.* 2018;41:430-435.
159. 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;116:195-198.
160. Coleman AL, Yu F. Eye-related medicare costs for patients with age-related macular degeneration from 1995 to 1999. *Ophthalmology.* 2008;115:18-25.