PREFERRED PRACTICE PATTERN®

Dry Eye Syndrome

Limited Revision

AMERICAN ACADEMY OF OPHTHALMOLOGY
The Eye M.D. Association

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

The Preferred Practice Pattern® (PPP) 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.

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Innovation in medicine is essential to assure 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 PPPs 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 To ensure that all PPPs are current, each is valid for 5 years from the "approved by" date unless superseded by a revision.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 before publication.

The intended users of the Dry Eye Syndrome Preferred Practice Pattern guideline are ophthalmologists.

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INTRODUCTION

The Preferred Practice Pattern® (PPP) guidelines have been written on the basis of three principles.

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

In the process of revising this document, a detailed literature search of articles in the English language was conducted in December 2007 in PubMed and the Cochrane Library on the subject of dry eye for the years 2002 to 2007. To complete this limited revision, PubMed and the Cochrane Library were searched on January 27, 28, February 4, 11, and 15, 2011 on the subject of dry eye, limited to English language and publication date from 2008 to the date of the search. Details of the literature search are available at www.aao.org/ppp. The results were reviewed by the Cornea/External Disease Panel and used to prepare the recommendations, which they rated in two ways.

The panel first rated each recommendation according to its importance to the care process. This "importance to the care process" rating represents care that the panel thought would improve the quality of the patient's care in a meaningful way. The ratings of importance are divided into three levels.

- Level A, defined as most important
- Level B, defined as moderately important
- Level C, defined as relevant but not critical

The panel also rated each recommendation on the strength of evidence in the available literature to support the recommendation made. The "ratings of strength of evidence" also are divided into three levels.

- Level I includes evidence obtained from at least one properly conducted, well-designed, randomized controlled trial. It could include meta-analyses of randomized controlled trials.
- Level II includes evidence obtained from the following:
  - Well-designed controlled trials without randomization
  - Well-designed cohort or case-control analytic studies, preferably from more than one center
  - Multiple-time series with or without the intervention
- Level III includes evidence obtained from one of the following:
  - Descriptive studies
  - Case reports
  - Reports of expert committees/organizations (e.g., PPP panel consensus with external peer review)

The evidence cited is that which supports the value of the recommendation as something that should be performed to improve the quality of care. The panel believes that it is important to make available the strength of the evidence underlying the recommendation. In this way, readers can appreciate the degree of importance the panel attached to each recommendation and they can understand what type of evidence supports the recommendation.

The ratings of importance and the ratings of strength of evidence are given in bracketed superscripts after each recommendation. For instance, "[A:II]" indicates a recommendation with high importance to clinical care [A], supported by sufficiently rigorous published evidence, though not by a randomized controlled trial [II].

The sections entitled Orientation and Background do not include recommendations; rather, they are designed to educate and provide summary background information and rationale for the recommendations that are presented in the Care Process section. A summary of the major recommendations for care is included in Appendix 2.

ORIENTATION

ENTITY

Dry eye syndrome (ICD-9 #375.15)

DISEASE DEFINITION

For the purpose of this Preferred Practice Pattern, dry eye syndrome refers to a group of disorders of the tear film that are due to reduced tear production or excessive tear evaporation that is associated with ocular discomfort and/or visual symptoms and may cause disease of the ocular surface. This group of disorders is usually referred to as dry eye.

ACTIVITY

Diagnosis and management of the patient with dry eye.

PATIENT POPULATION

The patient population includes individuals of all ages who present with symptoms and signs suggestive of dry eye, such as irritation, redness, fluctuating vision, and decreased tear meniscus.

PURPOSE

The purpose of diagnosing and managing patients with dry eye is to preserve and/or improve vision, prevent or minimize structural damage to the ocular surface, and improve patient comfort.

GOALS

- Establish the diagnosis of dry eye, differentiating it from other causes of irritation and redness
- Identify the causes of dry eye
- Establish appropriate therapy
- Relieve discomfort
- Prevent complications, such as loss of visual function, infection, and structural damage
- Educate and involve the patient in the management of this disease

BACKGROUND

Dry eye, either alone or in combination with other conditions, is a frequent cause of ocular irritation that leads patients to seek ophthalmologic care.[1] While these symptoms often improve with treatment, the disease usually is not curable, which may be a source of patient and physician frustration. Dry eye can be a cause of visual morbidity and may compromise results of corneal, cataract, and refractive surgery.

EPIDEMIOLOGY

Epidemiological information on dry eye syndrome has been limited by lack of uniformity in its definition and the inability of any single diagnostic test or set of diagnostic tests to confirm or rule out the condition. There is no doubt, however, that dry eye syndrome is a common condition that causes varying degrees of discomfort and disability. While clinic-based studies confirm its frequency (17% of 2127 consecutive new outpatients were diagnosed with dry eye following comprehensive examination), such studies may not reflect the overall population.[2] In a population-based sample of 2520 elderly (65 years old or older) residents of Salisbury, Maryland, 14.6% were symptomatic, which was defined as reporting one or more dry eye symptoms often or all the time.[1] The combination of being symptomatic and having a low Schirmer test (≤5 mm with anesthesia) or a high rose bengal score (≥5) was seen in 3.5% of the residents.[1] Depending on which of these two

percentages is used, extrapolating to the U.S. population aged 65 to 84 years yields estimates of approximately 1 million to 4.3 million people who have dry eye. A population-based study of dry eye conducted in Melbourne, Australia, using different diagnostic criteria reported higher percentages of the 926 participants aged 40 to 97 years with a low Schirmer test (16.3% ≤8 mm) or a high rose bengal score (10.8% ≥4).[3] The prevalence of self-reported dry eye in 3722 participants of the Beaver Dam (Wisconsin) Eye Study varied from 8.4% of subjects younger than 60 to 19.0% in those older than 80, with an overall prevalence of 14.4%.[4] Estimates of dry eye prevalence based on treatment-derived data yield much lower percentages. A study evaluating medical claims data for nearly 10 million enrollees in managed care plans found that dry eye was diagnosed or treated with punctal occlusion in 0.4% to 0.5% of the enrollees.[5]

Many risk factors for dry eye have been proposed (see Table 1). Older age and female gender have been identified as risk factors for dry eye.[3-8] A Japanese study found an increased prevalence of dry eye disease among Japanese office workers using visual display terminals.[9] Concurrent use of benzalkonium chloride (BAK)-containing glaucoma medications was also shown to be a risk factor in glaucoma patients.[10,11] Arthritis was evaluated as a risk factor in two studies and found to be associated with an increased risk of dry eye in both.[3,4] The Beaver Dam Eye Study found that after controlling for age and gender, smoking and multivitamin use were associated with an increased risk of dry eye, whereas caffeine use was associated with a decreased risk.[4] An update to the Beaver Dam Study[8] found that additional risk factors for dry eye included the use of antihistamines, antidepressant and antianxiety medications, and oral corticosteroids. Angiotensin converting enzyme inhibitors were associated with a lower risk. Within the 25,665 postmenopausal women in the Women's Health Study, Schaumberg et al reported that hormone replacement therapy, and, in particular, estrogen use alone, was associated with an increased risk of clinically diagnosed dry eye syndrome or severe symptoms.[12]

TABLE 1 RISK FACTORS FOR DRY EYE

Level of Evidence		
Mostly consistent*	**Suggestive†**	**Unclear‡**
• Older age	• Asian ethnicity	• Cigarette smoking
• Female gender	• Medications Tricyclic antidepressants Selective serotonin reuptake inhibitors Diuretics Beta-blockers	• Hispanic ethnicity
• Postmenopausal estrogen therapy	• Diabetes mellitus	• Medications Anticholinergics Anxiolytics Antipsychotics
• Low dietary intake of omega-3 fatty acids	• HIV/HTLV1 infection	• Alcohol use
• Medications Antihistamines	• Systemic chemotherapy	• Menopause
• Connective tissue disease	• Large-incision ECCE and penetrating keratoplasty	• Botulinum toxin injection
• LASIK and refractive excimer laser surgery	• Isotretinoin	• Acne
• Radiation therapy	• Low-humidity environments	• Gout
• Hematopoietic stem cell transplantation	• Sarcoidosis	• Oral contraceptives
• Vitamin A deficiency	• Ovarian dysfunction	• Pregnancy
• Hepatitis C infection		
• Androgen deficiency		

ECCE = extracapsular cataract extraction; HIV = human immunodeficiency virus; HTLV = human T-lymphotropic virus

* Mostly consistent evidence implies the existence of at least one adequately powered and otherwise well-conducted study published in a peer-reviewed journal, along with the existence of a plausible biological rationale and corroborating basic research or clinical data.

† Suggestive evidence implies the existence of either: 1) inconclusive information from peer-reviewed publication or 2) inconclusive or limited information to support the association, but either not published or published somewhere other than in a peer-reviewed journal.

‡ Unclear evidence implies either directly conflicting information in peer-reviewed publications or inconclusive information but with some basis for a biological rationale.

Reproduced with permission from Smith JA (Chair). Epidemiology Subcommittee of the International Dry Eye Workshop. The epidemiology of dry eye disease: report of the Epidemiology Subcommittee of the International Dry Eye Workshop (2007). Ocul Surf 2007;5:99.

A study of dry eye and quality of life found decreased quality of life for all severity levels of dry eye syndrome, with an effect on quality of life for severe dry eye comparable with that reported for moderate angina.[13] A study of anxiety and depression among patients found a high correlation in dry eye patients.[14] Another study found that patients with dry eye syndrome of any severity level reported more limitations due to physical problems and more pain when compared with general population norms for the Medical Outcomes Study Short Form-36 (SF-36) Health Survey.[15,16] Patients with severe dry eye reported lower scores than the norms across all scales of the SF-36.[15] In a study of patients with glaucoma, dry eye syndrome negatively influenced patient's quality of life.[11]

PATHOGENESIS

It is now recognized that the ocular surface and tear-secreting glands function as an integrated unit to maintain the tear supply and to clear used tears.[17] Disease or dysfunction of this functional unit results in an unstable and poorly maintained tear film that causes ocular irritation symptoms and the epithelial disease called keratoconjunctivitis sicca (KCS). Dysfunction of this integrated unit may develop from aging, a decrease in supportive factors (such as androgen hormones), systemic inflammatory diseases (such as rheumatoid arthritis), ocular surface diseases (such as herpes simplex virus keratitis) or surgeries that disrupt the trigeminal afferent sensory nerves (e.g., LASIK), and systemic diseases or medications that disrupt the efferent cholinergic nerves that stimulate tear secretion.[18] Decreased tear secretion and clearance initiates an inflammatory response on the ocular surface that involves both soluble and cellular mediators.[19,20] Clinical and basic research suggests that this inflammation plays a role in the pathogenesis of KCS (see Figure 1).[21,22]

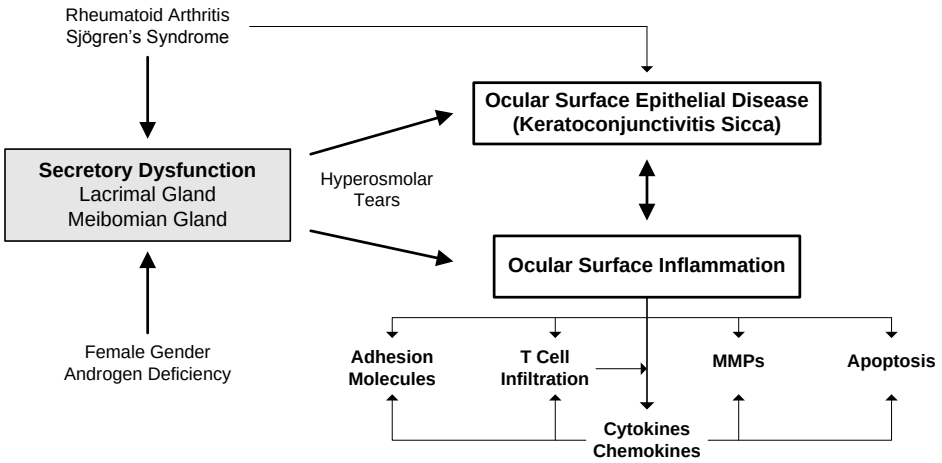

FIGURE 1. INFLAMMATORY MEDIATORS IN KERATOCONJUNCTIVITIS SICCA

MMPs = matrix metalloproteinases

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ASSOCIATED CONDITIONS

Symptoms caused by dry eye may be exacerbated by the use of systemic medications such as diuretics, antihistamines, anticholinergics, antidepressants, and systemic retinoids (e.g., isotretinoin).[4,8,10,23-27] Instillation of any eye medications, especially when they are instilled frequently (e.g., more than four drops a day), may prevent the normal maintenance of the tear film and cause dry eye symptoms. In addition, environmental factors, such as reduced humidity and increased wind, drafts, air conditioning, or heating may exacerbate the ocular discomfort of patients with dry eye. Exogenous irritants and allergens, although not believed to be causative of dry eye, may exacerbate the symptoms.

Blepharitis associated with meibomitis was noted in 3.6% of 2520 subjects aged 65 years and older in the population-based study of residents of Salisbury, Maryland.[1] Those patients were twice as likely to have dry eye symptoms as those without signs of meibomitis. A recent study in Spain indicated that nearly half of patients with dry eye have meibomian gland dysfunction.[28] In addition,

hyposecretory meibomian gland dysfunction may be a precursor to obstructive meibomian gland dysfunction and may play a role in the pathogenesis of dry eye disease.[29]

Associated systemic diseases include Sjögren syndrome, in which an inflammatory cellular infiltration of the lacrimal gland leads to tear-production deficiency, and rosacea, which is associated with posterior blepharitis with increased tear evaporation (see Appendix 3). Aqueous tear deficiency may develop in conditions that result in infiltration of the lacrimal gland and replacement of the secretory acini such as lymphoma, sarcoidosis,[30,31] hemochromatosis, and amyloidosis.[32] Dry eye may develop in patients with systemic viral infections; it has been reported in patients infected by the retroviruses, human T-cell lymphotropic virus type 1, and human immunodeficiency virus (HIV).[33] Dry eye was diagnosed in 21% of a group of patients with AIDS[34] and a condition known as diffuse infiltrative lymphadenopathy syndrome has been reported in patients with HIV infection, most of whom were children.[33] Decreased tear secretion, reduced tear volume, and reduced tear concentrations of lactoferrin have been reported in patients with hepatitis C.[35,36] Lacrimal gland swelling, dry eye, and Sjögren syndrome have been associated with primary and persistent Epstein-Barr virus infections.[37-40] Severe dry eye has been reported to occur in recipients of allogenic bone marrow or stem cell transplants with or without the development of graft-versus-host disease (GVHD).[41,42] In chronic GVHD, there is infiltration and fibrosis of the lacrimal glands as a result of T-cell interaction with fibroblasts.[41,43,44] Diseases such as ocular mucous membrane pemphigoid and Stevens-Johnson syndrome produce tear deficiency due to inflammation, scarring, and destruction of the conjunctival goblet cells. Atopy may produce dry eye due to blepharitis, conjunctival scarring, or antihistamine use.

Local conditions associated with dry eye include eyelid malposition, lagophthalmos, and blepharitis as well as neuromuscular disorders that affect blinking (e.g., Parkinson disease, Bell palsy).[45] Local trauma, including orbital surgery, radiation, and injury, may also cause dry eye.

NATURAL HISTORY

Dry eye syndrome varies in severity, duration, and etiology.[46] In the majority of patients, the condition is not sight-threatening and is characterized by troublesome symptoms of irritation and intermittently blurred vision. In some individuals, exacerbating factors such as systemic medications that decrease tear production or environmental conditions that increase tear evaporation may lead to an acute increase in the severity of symptoms. Elimination of such factors often leads to marked improvement and may even be curative. In other patients in whom the dry eye condition is caused by a nonreversible deficiency of tear production or a chronic condition leading to increased evaporation such as blepharitis, the disease may exhibit chronicity, characterized by fluctuating severity of symptoms and/or a gradual increase in symptom severity with time.

Reversible conjunctival squamous metaplasia and punctate epithelial erosions of the conjunctiva and cornea develop in many patients who have moderate to severe dry eye. Rarely, patients with severe dry eye will develop complications such as ocular surface keratinization; corneal scarring, thinning, or neovascularization; microbial or sterile corneal ulceration with possible perforation; and severe visual loss.[47]

CARE PROCESS

PATIENT OUTCOME CRITERIA

Outcome criteria for treating dry eye include the following:

- Reducing or alleviating signs and symptoms of dry eye
- Maintaining and improving visual function
- Reducing or preventing structural damage

DIAGNOSIS

Many ocular surface diseases produce symptoms that are similar to those associated with dry eye, including foreign body sensation, mild itching, irritation, and soreness. Identifying characteristics of

the causative factors, such as adverse environments (e.g., air travel, sitting near an air conditioner vent, low humidity), prolonged visual efforts (e.g., reading, computer use), or ameliorating circumstances (symptomatic relief with the use of artificial tears) is helpful in diagnosing dry eye. Supporting clinical observations and tests are used to confirm the diagnosis. A diagnostic classification scheme adapted from the 2007 Report of the International Dry Eye Workshop is shown in Figure 2. Participants in the workshop agreed that the two major factors, deficient aqueous tear production and increased evaporative loss, may cause dry eyes independently, but they may also be present together and both contribute to dry eye symptoms and signs. Most patients have multiple factors contributing to dry eye. Many conditions, such as neurotrophic keratitis after herpes simplex virus infection or LASIK, include aspects of decreased tear production and increased evaporative loss.

All patients should have a comprehensive adult medical eye evaluation at the recommended intervals.[48 [A:III]] The initial evaluation of a patient who presents with symptoms suggestive of dry eye should include those features of the comprehensive adult medical eye evaluation relevant to dry eye.[48 [A:III]]

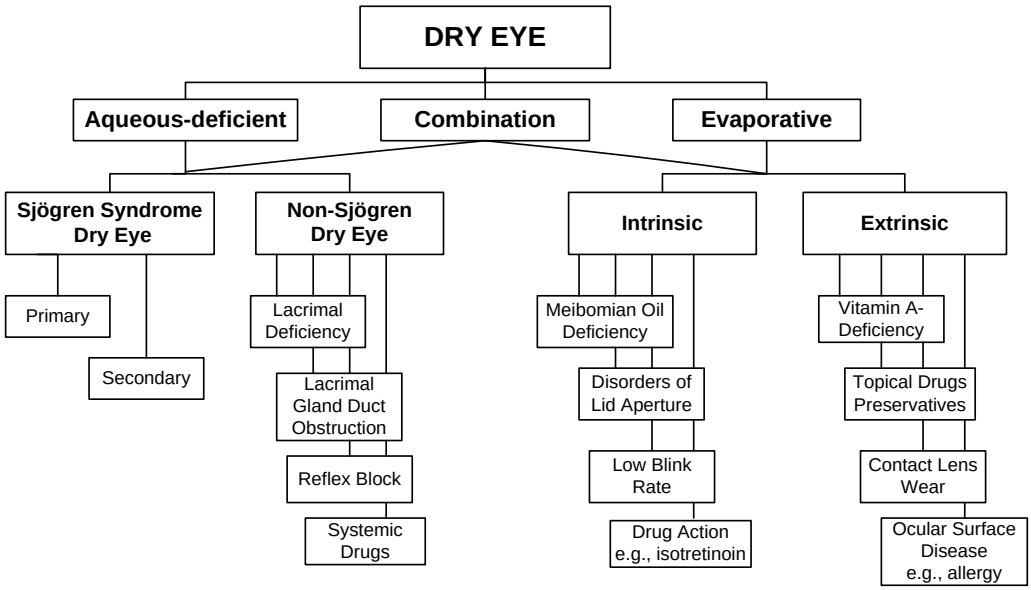

FIGURE 2. MAJOR ETIOLOGICAL CAUSES OF DRY EYE

Adapted with permission from Lemp MA (Chair). Definition and Classification Subcommittee of the International Dry Eye Workshop. The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye Workshop (2007). Ocul Surf 2007;5:77.

Patient History

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

- Symptoms and signs:[A:III] e.g., irritation, tearing, burning, stinging, dry or foreign body sensation, mild itching, photophobia, blurry vision, contact lens intolerance, redness, mucous discharge, increased frequency of blinking, eye fatigue, diurnal fluctuation, symptoms that worsen later in the day
- Exacerbating conditions:[B:III] e.g., wind, air travel, decreased humidity, prolonged visual efforts associated with decreased blink rate such as reading and computer use
- Duration of symptoms[A:III]

The ocular history may include details about the following:

- Topical medications used, their frequency, and their effect on symptoms:[A:III] e.g., artificial tears, “eyewash,” antihistamines, glaucoma medications, vasoconstrictors, corticosteroids
- Contact lens wear, schedule, and care[A:III]

- Allergic conjunctivitis[B:III]
- Ocular surgical history:[A:III] e.g., prior keratoplasty, cataract surgery, keratorefractive surgery
- Ocular surface disease:[A:III] e.g., herpes simplex virus, varicella zoster virus, ocular mucous membrane pemphigoid, Stevens-Johnson syndrome, aniridia, GVHD
- Punctal surgery[A:III]
- Eyelid surgery:[A:III] e.g., prior ptosis repair, blepharoplasty, entropion/ectropion repair
- Bell palsy[A:III]

The medical history may take into account the following elements:

- Smoking or exposure to second-hand smoke[A:III]
- Dermatological diseases:[A:III] e.g., rosacea
- Technique and frequency of facial washing including eyelid and eyelash hygiene[A:III]
- Atopy[A:III]
- Menopause[A:III]
- Systemic inflammatory diseases:[A:III] e.g., Sjögren syndrome, GVHD, rheumatoid arthritis, systemic lupus erythematosus, scleroderma
- Other systemic conditions:[A:III] e.g., lymphoma, sarcoidosis
- Systemic medications:[A:III] e.g., antihistamines, diuretics, hormones and hormonal antagonists, antidepressants, cardiac antiarrhythmic drugs, isotretinoin, diphenoxylate/atropine, beta-adrenergic antagonists, chemotherapy agents, any other drug with anticholinergic effects
- Trauma:[B:III] e.g., chemical
- Chronic viral infections: [B:III] e.g., hepatitis C, HIV
- Nonocular surgery:[B:III] e.g., bone marrow transplant, head and neck surgery, trigeminal neuralgia surgery
- Radiation of orbit[B:III]
- Neurological conditions:[B:III] e.g., Parkinson disease, Bell palsy, Riley-Day syndrome, trigeminal neuralgia
- Dry mouth, dental cavities, oral ulcers[B:III]

Examination

The physical examination includes a visual acuity measurement,[A:III] an external examination,[A:III] and slit-lamp biomicroscopy.[A:III] The purpose of the external examination and the slit-lamp biomicroscopy is to do the following:

- Document the signs of dry eye
- Assess the presence and severity of deficient aqueous tear production and/or increased evaporative loss
- Determine other causes of ocular irritation

The external examination should pay particular attention to the following:

- Skin:[A:III] e.g., scleroderma, facial changes consistent with rosacea
- Eyelids:[A:III] incomplete closure/malposition, incomplete or infrequent blink, eyelid lag, erythema of eyelid margins, abnormal deposits or secretions, entropion, ectropion
- Adnexa:[A:III] enlargement of the lacrimal glands
- Proptosis[B:III]
- Cranial nerve function:[A:III] e.g., cranial nerve V (trigeminal), cranial nerve VII (facial)
- Hands:[B:III] joint deformities characteristic of rheumatoid arthritis

The slit-lamp biomicroscopy should focus on the following:

- Tear film:[A:III] height of the meniscus, debris, increased viscosity, mucus strands, and foam
- Eyelashes:[A:III] trichiasis, distichiasis, deposits
- Anterior and posterior eyelid margins:[A:III] abnormalities of meibomian glands (e.g., orifice metaplasia, reduced expressible meibum, atrophy), character of meibomian gland secretions (e.g., turbid, thickened, foamy, deficient), vascularization crossing the mucocutaneous junction, keratinization, scarring
- Puncta:[A:III] patency, position, presence, and position of plugs

- Conjunctiva:
  - Inferior fornix and tarsal conjunctiva:[A:III] e.g., mucous threads, scarring, erythema, papillary reaction, follicle enlargement, keratinization, foreshortening, symblepharon
  - Bulbar conjunctiva:[A:III] e.g., punctate staining with rose bengal or fluorescein dyes; hyperemia; localized drying; keratinization
- Cornea:[A:III] localized interpalpebral drying, punctate epithelial erosions, punctate staining with rose bengal or fluorescein dyes, filaments, epithelial defects, mucous plaques, keratinization, pannus formation, thinning, infiltrates, ulceration, scarring, neovascularization, evidence of corneal or refractive surgery

Diagnostic Tests

For patients with mild irritation symptoms, a rapid tear break-up time may indicate an unstable tear film with normal aqueous tear production, and there may be minimal or no dye staining of the ocular surface.[49]

For patients with moderate to severe aqueous tear deficiency, the diagnosis can be made by using one or more of the following tests: tear break-up time test, ocular surface dye staining (rose bengal, fluorescein, or lissamine green), and the Schirmer test. These tests should be performed in this sequence because the Schirmer test can disrupt tear film stability and cause false-positive ocular-surface dye staining. (See Appendix 4 for detailed descriptions of these tests.) Corneal sensation should be assessed when trigeminal nerve dysfunction is suspected.[50] [A:III] A laboratory and clinical evaluation for autoimmune disorders should be considered for patients with significant dry eye, other signs and symptoms of an autoimmune disorder (e.g., dry mouth), or a family history of an autoimmune disorder.[A:III]

CLASSIFICATION OF DRY EYE SYNDROME

Specific systems to classify dry eye severity have been developed (see Appendix 5); however, these are primarily for research purposes and have not been widely used in clinical care.

Dry eye is generally classified according to a combination of symptoms and signs. In this PPP, dry eye has been classified as mild, moderate, and severe based on both symptoms and signs, but with an emphasis on symptoms over signs.[51] Due to the nature of dry eye disease, this classification is imprecise because characteristics at each level overlap.

Patients with mild dry eye syndrome may have symptoms of irritation, itching, soreness, burning, or intermittent blurred vision. It is often difficult to diagnose dry eye definitively in its mild form because of the inconsistent correlation between reported symptoms and clinical signs[52] as well as the relatively poor specificity and/or sensitivity of clinical tests.[53,54] Because most dry eye conditions have a chronic course, repeated observation and reporting of symptoms over time will allow clinical diagnosis of dry eye in most cases.

Patients with moderate dry eye syndrome have increased discomfort and frequency of symptoms, and the negative effect on visual function may become more consistent.

Patients with severe dry eye syndrome have increasing frequency of symptoms which may become constant, as well as potentially disabling visual symptoms.

Dry eye syndrome is also loosely categorized into one of two forms, aqueous tear deficiency and evaporative tear deficiency, and both of these conditions may be present in patients with the disease. Table 2 lists characteristic findings for each diagnostic test for each condition.

TREATMENT

Patients with dry eye symptoms often have many contributory factors. It is imperative to treat any causative factors that are amenable to treatment. Tear replacement is frequently unsuccessful when used as the sole treatment if additional causative factors are not concomitantly addressed.

For patients with irreversible tear deficiency or evaporative increase associated with chronic conditions such as blepharitis, the ophthalmologist should educate the patient about the natural history and chronic nature of dry eye.[A:III] Realistic expectations for therapeutic goals should be set and discussed with the patient. Patient education is an important aspect of successful management of this condition.

Table 3 lists treatments of dry eye syndrome according to the type of therapy used. Of these treatments, those particularly effective for evaporative tear deficiency include environmental modifications, eyelid therapy for conditions such as blepharitis or meibomianitis, artificial tear substitutes, moisture chamber spectacles, and/or surgery such as tarsorrhaphy.

TABLE 2 **CHARACTERISTIC FINDINGS FOR DRY EYE SYNDROME DIAGNOSTIC TESTING**

	Test	Characteristic Findings
Aqueous Tear Deficiency	Tear break-up time	Less than 10 seconds considered abnormal
	Ocular surface dye staining	Pattern of exposure zone (interpalpebral) corneal and bulbar conjunctival staining typical
	Aqueous tear production and clearance (Schirmer test)	5 mm or less for Schirmer test with anesthesia considered abnormal
	Fluorescein clearance test/tear function index	Test result is compared with a standard color scale
	Lacrimal gland function	Decreased tear lactoferrin concentrations
	Tear osmolarity	Increased
Evaporative Tear Deficiency	Tear break-up time	Less than 10 seconds considered abnormal
	Ocular surface dye staining	Staining of inferior cornea and bulbar conjunctiva typical
	Tear osmolarity	Increased

TABLE 3 **CATEGORIES OF DRY EYE TREATMENTS**

Type of Therapy	Treatment
Environmental/Exogenous	• Education and environmental modifications* • Elimination of offending topical or systemic medications
Medication	
Topical medication	• Artificial tear substitutes, gels/ointments* • Anti-inflammatory agents (topical cyclosporine and corticosteroids) • Mucolytic agents • Autologous serum tears
Systemic medication	• Omega-3 fatty acids* • Tetracyclines* (for meibomianitis, rosacea) • Systemic anti-inflammatory agents
Surgical	• Punctal plugs • Permanent punctal occlusion • Tarsorrhaphy* • Repair of eyelid malpositions or exposure}* • Mucous membrane, salivary gland, amniotic membrane transplantation*
Other	• Eyelid therapy (warm compresses and eyelid hygiene)* • Contact lenses • Moisture chamber spectacles*

* Particularly helpful for increased evaporative loss

Data from Pflugfelder SC (Chair). Management and Therapy Subcommittee of the International Dry Eye Workshop. Management and therapy of dry eye disease: report of the Management and Therapy Subcommittee of the International Dry Eye Workshop (2007). Ocul Surf 2007;5:163-78.

Specific treatment recommendations depend on the severity and source of the dry eye. The sequence and combination of therapies should be determined on the basis of the patient's needs and preferences and the treating ophthalmologist's medical judgment.[A:III] Table 4 lists treatments for dry eye syndrome based on the severity level of the disease. Specific therapies may be chosen from any category regardless of the level of disease severity, depending on physician experience and patient preference.

TABLE 4 TREATMENT RECOMMENDATIONS FOR DRY EYE SYNDROME BY DISEASE SEVERITY LEVEL

Mild	• Education and environmental modifications[A:III] • Elimination of offending topical or systemic medications[A:III] • Aqueous enhancement using artificial tear substitutes, gels/ointments[A:III] • Eyelid therapy (warm compresses and eyelid hygiene)[A:III] • Treatment of contributing ocular factors such as blepharitis or meibomianitis[A:III] (see Blepharitis PPP[55])
Moderate	*In addition to above treatments:* • Anti-inflammatory agents (topical cyclosporine[56,57] [A:I] and corticosteroids[58-61] [A:II]), systemic omega-3 fatty acids supplements[62,63] [A:II] • Punctal plugs[A:III] • Spectacle side shields and moisture chambers[A:III]
Severe	*In addition to above treatments:* • Systemic cholinergic agonists[64-66] [A:I] • Systemic anti-inflammatory agents[A:III] • Mucolytic agents[A:III] • Autologous serum tears[67,68] [A:III] • Contact lenses[A:III] • Correction of eyelid abnormalities[A:III] • Permanent punctal occlusion[A:III] • Tarsorrhaphy[A:III]

Adapted with permission from Pflugfelder SC (Chair). Management and Therapy Subcommittee of the International Dry Eye Workshop. Management and therapy of dry eye disease: report of the Management and Therapy Subcommittee of the International Dry Eye Workshop (2007). Ocul Surf 2007;5:174.

Mild Dry Eye

Because of the inconsistent correlation between reported symptoms and clinical signs[52] as well as the relatively poor specificity and/or sensitivity of clinical tests,[53,54] patients with suggestive symptoms without signs should be placed on trial treatments with artificial tears when other potential causes of ocular irritation have been eliminated.[A:III] For patients with a clinical diagnosis of mild dry eye, potentially exacerbating exogenous factors such as antihistamine or diuretic use, cigarette smoking and exposure to second-hand smoke, and environmental factors such as air drafts (e.g., use of ceiling fans), and low-humidity environments should be addressed.[A:III] Exacerbating medications should be eliminated when possible. Cigarette smoking has been found to be associated with dry eye because of the adverse effects on the lipid layer of the precorneal tear film and tear proteins.[69,70] Humidifying ambient air and avoiding air drafts by using shields and by changing the characteristics of airflow at work, at home, and in the car may be helpful. Measures such as lowering the computer screen to below eye level to decrease lid aperture,[71] scheduling regular breaks, and increasing blink frequency may decrease the discomfort associated with computer and reading activities.

As the severity of the dry eye increases, aqueous enhancement of the eye using topical agents is appropriate. Emulsions, gels, and ointments can be used. The use of artificial tears may be increased, but the practicality of frequent tear instillation depends on the lifestyle or manual dexterity of the patient. Nonpreserved tear substitutes are generally preferable; however, tears with preservatives may be sufficient for patients with mild dry eye and an otherwise healthy ocular surface. When tear substitutes are used frequently, (e.g., more than four times a day), nonpreserved tears are generally recommended.

Contributing ocular factors such as blepharitis or meibomianitis should also be treated (see Blepharitis PPP[55]).

Moderate Dry Eye

In addition to the treatments for mild dry eye, the following medications, surgical procedures, and other treatments may be helpful for moderate dry eye.

Anti-inflammatory therapies may be considered in addition to aqueous enhancement therapies. Cyclosporine is a fungus-derived peptide that prevents activation and nuclear translocation of cytoplasmic transcription factors that are required for T-cell activation and inflammatory cytokine production. It also inhibits mitochondrial pathways of apoptosis. In clinical trials submitted for Food and Drug Administration (FDA) approval, topical cyclosporine 0.05% demonstrated a statistically significant 10 mm increase in Schirmer wetting compared with vehicle at 6 months in those patients whose tear production was presumed to be decreased because of ocular inflammation. This effect was noted in 15% of cyclosporine-treated patients compared with 5% of vehicle-treated patients. While the drop is typically well tolerated, ocular burning was reported in 17% of the patients.[56] The small number of patients in this study with punctal plugs or who were using topical anti-inflammatory drugs did not have increased tear production. A subsequent small study demonstrated the efficacy of cyclosporine 0.05% in the treatment of dry eye in patients who had undergone punctal occlusion.[72] A recent study evaluated the efficacy of topical cyclosporine 0.05% in patients with mild, moderate, and severe dry eyes. They demonstrated success in 74%, 72%, and 67% of patients, respectively. The study had a minimum follow-up time of 3 months, because the authors believe it typically takes 3 months for the medication to take effect.[73]

Corticosteroids have been reported to decrease ocular irritation symptoms, decrease corneal fluorescein staining, and improve filamentary keratitis.[58-60] In one study, a 2-week pretreatment of patients with a topical nonpreserved corticosteroid before punctal occlusion was reported to reduce ocular irritation symptoms and corneal fluorescein staining.[61] Loteprednol etabonate 0.5% has been found to be beneficial in patients with KCS with at least a moderate inflammatory component.[58] Low-dose corticosteroid therapy can be used at infrequent intervals for short-term (2-week) suppression of irritation secondary to inflammation. Patients prescribed corticosteroids for dry eye should be monitored for adverse effects such as increased intraocular pressure, corneal melting, and cataract formation.[A:III]

Use of systemic omega-3 fatty acid supplements for dry eye treatment has been reported[74] to be potentially beneficial, but there have been few studies analyzing their efficacy. A double-masked study of 71 patients with mild to moderate dry eye syndrome demonstrated a nonstatistically significant improvement in the Schirmer test, tear break-up time test, and fluorescein and lissamine green staining with the oral administration of polyunsaturated fatty acids.[62] Another study suggested that higher dietary intake of omega-3 fatty acids is associated with a decreased risk of dry eye syndrome in women.[63]

For patients with aqueous tear deficiency, punctal occlusion is considered when the medical means of aqueous enhancement are ineffective or impractical.[75] Punctal occlusion can be accomplished surgically with silicone or thermal labile polymer plugs that are lodged at the punctal orifice. Silicone plugs placed in the punctum and both silicone and collagen plugs placed in the canaliculus have been shown to improve dry eye signs and symptoms.[75-78] Punctal plugs have the advantage of being removable if the patient develops symptoms of epiphora, and they may be retained for many years without complications, provided they are appropriately sized. One study found that 56% of silicone plugs were retained after 2 years; but in those patients whose plugs were spontaneously lost, 34% were reported to have canalicular stenosis at 2 years.[79] Patients who benefit from having punctal plugs in place but spontaneously lose them may have the lost plug(s) replaced or undergo permanent closure of their punctum by cautery or alternative means. Punctal plugs that are displaced into the lacrimal system may pass through the entire system, but blockage with secondary infection has been reported.[80,81] Rarely, surgical removal is necessary.

Intracanalicular plugs may offer ease of insertion and a decreased chance of extrusion, but they have been associated with the occurrence of epiphora, canaliculitis, and dacryocystitis.[80]

Spectacle side shields and moisture chambers are noninvasive therapies that can be used, but they may be poorly tolerated because of the negative cosmetic effect. Moisture inserts (hydroxypropyl cellulose, Lacrisert, Aton Pharma, Inc., Lawrenceville, NJ) are occasionally helpful for patients who are unable to use frequent artificial tears.[82,83]

Severe Dry Eye

In addition to the treatments for mild and moderate dry eye, the following treatments may be considered for severe dry eye.

Oral medications are also available to treat severe dry eyes, especially in patients with combined dry eye and dry mouth (Sjögren syndrome).[64,65,84] Cholinergic agonists, pilocarpine and cevimeline, have been approved by the FDA to treat the symptoms of dry mouth in patients with Sjögren syndrome. These medications bind to muscarinic receptors, which stimulate secretion of the salivary and sweat glands, and they appear to improve tear production. Most clinical studies demonstrate greater improvement in dry mouth than dry eye.[64,66] Patients treated with pilocarpine at a dose of 5 mg orally four times a day experienced a significantly greater overall improvement in the ability to focus their eyes during reading and in symptoms of blurred vision compared with placebo-treated patients.[64] The most common side effect from this medication was excessive sweating, which occurred in over 40% of patients. Two percent of the patients taking oral pilocarpine withdrew from the study because of this and other drug-related side effects. Cevimeline is another oral cholinergic agonist that has been found to improve ocular irritation symptoms and aqueous tear production.[65] This agent may have fewer adverse systemic side effects than oral pilocarpine.

For patients with systemic disease such as rheumatoid arthritis, systemic anti-inflammatory/ immunosuppressive therapy may be appropriate. Autologous serum drops have been reported to improve ocular irritation symptoms as well as conjunctival and corneal dye staining in patients with Sjögren syndrome[67] and GVHD.[68]

Filamentary keratopathy can be treated with debridement of the filaments or application of topical mucolytic agents, such as acetylcysteine 10% four times a day. Filaments can be debrided with a cotton-tip applicator, dry cellulose sponge, or jewelers' forceps. Soft contact lenses are effective in preventing recurrence of filamentary keratopathy but are poorly tolerated if the patient has severe dry eye. If the patient has associated neurotrophic keratopathy, contact lenses should be avoided.[A:III]

Correcting eyelid abnormalities resulting from blepharitis,[55] trichiasis, or lid malposition (e.g., lagophthalmos, entropion/ectropion) may be considered prior to permanent punctal occlusion.

Permanent punctal occlusion can also be accomplished by means of thermal or laser cautery. The main disadvantage of punctal cautery is that it is not readily reversible. If occlusion with cautery is planned, a trial occlusion with nonpermanent implants generally should be performed first to screen for the potential development of epiphora.[A:III] Collagen implants usually block tear flow long enough (a few days) to allow judgment as to whether the patient is at risk for epiphora after permanent occlusion, but they may not persist long enough to predict whether the patient's symptoms will be relieved. Silicone punctal plugs are more useful for this purpose. A stepwise approach to cautery occlusion is generally recommended so that no more than one punctum is cauterized in each eye at a treatment session.[A:III] In general, laser cautery is not as effective as thermal cautery in achieving permanent, complete occlusion, and it is more expensive.

A limited tarsorrhaphy can be performed to decrease tear evaporation in patients with severe dry eye who have not responded to other therapies.[85]

FOLLOW-UP

The purpose of the follow-up evaluation is to assess the response to therapy as a basis for altering or adjusting treatment as necessary, to monitor for structural ocular damage, and to provide reassurance. The frequency and extent of the follow-up evaluation will depend on the severity of disease, the therapeutic approach, and the response to the therapy. For example, patients with sterile corneal ulceration associated with dry eye may require daily follow-up.[A:III]

PROVIDER AND SETTING

Because dry eye can be associated with systemic immunological disorders and the use of systemic medications, broad medical skills and training are important for appropriate diagnosis and management. Patients with dry eye who are evaluated by nonophthalmologist health care providers should be referred promptly to the ophthalmologist if any of the following occurs:[A:III]

- Visual loss
- Moderate or severe pain
- Lack of response to the therapy
- Corneal infiltration or ulceration

COUNSELING/REFERRAL

The most important aspects of caring for patients with dry eye are to educate them about the chronic nature of the disease process and to provide specific instructions for therapeutic regimens. It is helpful to reassess periodically the patient's compliance and understanding of the disease, the risks for associated structural changes, and to reinform the patient as necessary.[A:III] The patient and physician together can establish realistic expectations for effective management.

Patients with severe dry eye are at greater risk for contact lens intolerance and associated complications. Patients with pre-existing dry eye should be cautioned that refractive surgery, particularly LASIK, may worsen their dry eye condition.[86] [A:III] Patients who have dry eye and are considering refractive surgery should have the dry eye treated before surgery.[87]

Referral of a patient with dry eye may be necessary, depending on the severity of the condition and its responsiveness to treatment. In moderate to severe cases that are unresponsive to treatment or when systemic disease is suspected, timely referral to an ophthalmologist who is knowledgeable and experienced in the management of these entities is recommended.[A:III] Referral to an internist or rheumatologist can be considered for patients with systemic immune dysfunction or for those who require immunosuppressive therapy. Patients with systemic disease such as primary Sjögren syndrome, secondary Sjögren (associated with a connective-tissue disease), or connective tissue disease such as rheumatoid arthritis should be managed by an appropriate medical specialist.[A:III] Patient support groups such as the Sjögren's Syndrome Foundation (www.sjogrens.com) may help patients adjust to their condition. Some patients may benefit from professional counseling as an aid in coping with the chronic disease state.

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. SUMMARY OF MAJOR RECOMMENDATIONS FOR CARE

DIAGNOSIS

The initial evaluation of a patient who presents with symptoms suggestive of dry eye should include the features of the comprehensive adult medical eye evaluation relevant to dry eye.[48] [A:III]

Patient History

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

- Symptoms and signs:[A:III] e.g., irritation, tearing, burning, stinging, dry or foreign body sensation, mild itching, photophobia, blurry vision, contact lens intolerance, redness, mucous discharge, increased frequency of blinking, eye fatigue, diurnal fluctuation, symptoms that worsen later in the day
- Exacerbating conditions:[B:III] e.g., wind, air travel, decreased humidity, prolonged visual efforts associated with decreased blink rate such as reading and computer use
- Duration of symptoms[A:III]
- Topical medications used, their frequency, and their effect on symptoms:[A:III] e.g., artificial tears, "eyewash," antihistamines, glaucoma medications, vasoconstrictors, corticosteroids
- Contact lens wear, schedule, and care[A:III]
- Allergic conjunctivitis[B:III]
- Ocular surgical history:[A:III] e.g., prior keratoplasty, cataract surgery, keratorefractive surgery
- Ocular surface disease:[A:III] e.g., herpes simplex virus, varicella zoster virus, ocular mucous membrane pemphigoid, Stevens-Johnson syndrome, aniridia, GVHD
- Punctal surgery[A:III]
- Eyelid surgery:[A:III] e.g., prior ptosis repair, blepharoplasty, entropion/ectropion repair
- Bell palsy[A:III]
- Smoking or exposure to second-hand smoke[A:III]
- Dermatological diseases:[A:III] e.g., rosacea
- Technique and frequency of facial washing including eyelid and eyelash hygiene[A:III]
- Atopy[A:III]
- Menopause[A:III]
- Systemic inflammatory diseases:[A:III] e.g., Sjögren syndrome, GVHD, rheumatoid arthritis, systemic lupus erythematosus, scleroderma
- Other systemic conditions:[A:III] e.g., lymphoma, sarcoidosis
- Systemic medications:[A:III] e.g., antihistamines, diuretics, hormones and hormonal antagonists, antidepressants, cardiac antiarrhythmic drugs, isotretinoin, diphenoxylate/atropine, beta-adrenergic antagonists, chemotherapy agents, any other drug with anticholinergic effects
- Trauma:[B:III] e.g., chemical
- Chronic viral infections: [B:III] e.g., hepatitis C, HIV
- Nonocular surgery:[B:III] e.g., bone marrow transplant, head and neck surgery, trigeminal neuralgia surgery
- Radiation of orbit[B:III]
- Neurological conditions:[B:III] e.g., Parkinson disease, Bell palsy, Riley-Day syndrome, trigeminal neuralgia
- Dry mouth, dental cavities, oral ulcers[B:III]

Examination

The physical examination includes a visual acuity measurement,[A:III] an external examination,[A:III] and slit-lamp biomicroscopy.[A:III]

The external examination should pay particular attention to the following:

- Skin:[A:III] e.g., scleroderma, facial changes consistent with rosacea

- Eyelids:[A:III] incomplete closure/malposition, incomplete or infrequent blink, eyelid lag, erythema of eyelid margins, abnormal deposits or secretions, entropion, ectropion
- Adnexa:[A:III] enlargement of the lacrimal glands
- Proptosis[B:III]
- Cranial nerve function:[A:III] e.g., cranial nerve V (trigeminal), cranial nerve VII (facial)
- Hands:[B:III] joint deformities characteristic of rheumatoid arthritis

The slit-lamp biomicroscopy should focus on the following:

- Tear film:[A:III] height of the meniscus, debris, increased viscosity, mucus strands, and foam
- Eyelashes:[A:III] trichiasis, distichiasis, deposits
- Anterior and posterior eyelid margins:[A:III] abnormalities of meibomian glands (e.g., orifice metaplasia, reduced expressible meibum, atrophy), character of meibomian gland secretions (e.g., turbid, thickened, foamy, deficient), vascularization crossing the mucocutaneous junction, keratinization, scarring
- Puncta:[A:III] patency, position, presence, and position of plugs
- Conjunctiva
  - Inferior fornix and tarsal conjunctiva:[A:III] e.g., mucous threads, scarring, erythema, papillary reaction, follicle enlargement, keratinization, foreshortening, symblepharon
  - Bulbar conjunctiva:[A:III] e.g., punctate staining with rose bengal or fluorescein dyes; hyperemia; localized drying; keratinization
- Cornea:[A:III] localized interpalpebral drying, punctate epithelial erosions, punctate staining with rose bengal or fluorescein dyes, filaments, epithelial defects, mucous plaques, keratinization, pannus formation, thinning, infiltrates, ulceration, scarring, neovascularization, evidence of corneal or refractive surgery

Diagnostic Tests

Corneal sensation should be assessed when trigeminal nerve dysfunction is suspected.[50] [A:III] A laboratory and clinical evaluation for autoimmune disorders should be considered for patients with significant dry eye, other signs and symptoms of an autoimmune disorder (e.g., dry mouth), or a family history of an autoimmune disorder.[A:III]

TREATMENT

Specific treatment recommendations depend on the severity and source of the dry eye. The sequence and combination of therapies should be determined on the basis of the patient's needs and preferences and the treating ophthalmologist's medical judgment.[A:III] Table 4 in the main body of the text lists treatments for dry eye syndrome based on the severity level of the disease. Specific therapies may be chosen from any category regardless of the level of disease severity, depending on physician experience and patient preference.

FOLLOW-UP

The frequency and extent of the follow-up evaluation will depend on the severity of disease, the therapeutic approach, and the response to the therapy. For example, patients with sterile corneal ulceration associated with dry eye may require daily follow-up.[A:III]

PROVIDER AND SETTING

Patients with dry eye who are evaluated by nonophthalmologist health care providers should be referred promptly to the ophthalmologist if any of the following occurs:[A:III]

- Visual loss
- Moderate or severe pain
- Lack of response to the therapy
- Corneal infiltration or ulceration

COUNSELING/REFERRAL

The most important aspects of caring for patients with dry eye are to educate them about the chronic nature of the disease process and to provide specific instructions for therapeutic regimens. It is helpful to reassess periodically the patient's compliance and understanding of the disease, the risks for associated structural changes, and to reinform the patient as necessary.[A:III] The patient and physician together can establish realistic expectations for effective management.

Patients with pre-existing dry eye should be cautioned that refractive surgery, particularly LASIK, may worsen their dry eye condition.[86] [A:III] Patients who have dry eye and are considering refractive surgery should have the dry eye treated before surgery.[87]

APPENDIX 3. ASSOCIATED DISEASES

SJÖGREN SYNDROME

Sjögren syndrome is defined as dry eye and dry mouth associated with systemic immune dysfunction. It is characterized by infiltration of the lacrimal and salivary glands with lymphocytes with secondary compromise of gland function. Patients with primary Sjögren syndrome have nonclassifiable systemic disease and symptoms that may include arthralgia, myalgia, or fatigue. Patients with primary Sjögren syndrome may also have associated thyroid dysfunction, especially autoimmune thyroid disease and autoimmune thyroiditis.[88] Patients with secondary Sjögren syndrome have a distinct autoimmune disease such as rheumatoid arthritis, scleroderma, or systemic lupus erythematosus. An epidemiologic study performed in Sweden reported that the prevalence of Sjögren syndrome is approximately 0.4%.[89] A Greek epidemiologic study reported the annual incidence of Sjögren syndrome as 5.3 per 100,000 and a prevalence of 92.8 cases per 100,000, with a female-to-male ratio of 20:1.[90] A study in Slovenia estimated the annual incidence of primary Sjögren syndrome as 3.9 per 100,000.[91] Women are much more commonly diagnosed with Sjögren syndrome than men.[92,93] Sjögren syndrome should be suspected if intrinsic tear-production deficiency is detected in nonelderly women, especially if it is rapid in onset and/or marked in severity. Diagnosis and treatment of underlying systemic immune disorders may decrease morbidity and may even be life saving. Patients with dry eye syndrome associated with Sjögren syndrome may develop other ocular manifestations of immune dysfunction, including scleritis, keratitis, and uveitis. Patients are also at increased risk for potentially life-threatening vasculitic lymphoproliferative disorders. Studies have shown that patients with decreased C4 levels at the time of diagnosis of Sjögren syndrome had a higher risk of developing lymphoma.[94,95]

Defined, objective criteria for diagnosing and classifying Sjögren syndrome have been proposed. The revised U.S.-European criteria are the most comprehensive and include the following elements:[96]

- Ocular irritation symptoms
- Symptoms of a dry mouth
- Objective evidence of dry eyes
- Objective evidence of salivary gland involvement
- Laboratory abnormality (anti-Ro [SS-A] or anti-La [SS-B], ANA or rheumatoid factor)

A diagnosis of definite Sjögren syndrome is made when three criteria plus either a positive SS-A antibody or a positive minor salivary gland biopsy are present.

Table A3-1 gives a summary of the evidence supporting different treatment options for dry eye associated with Sjögren syndrome.[97]

TABLE A3-1 SUMMARY OF EVIDENCE FOR THE TREATMENT OF SJÖGREN'S SYNDROME ASSOCIATED-DRY EYE

Treatment Modality	Strength of Evidence	Clinical Recommendation
Topical lubricants	II	A
Systemic secretagogues	II	B
Topical steroids	III	B
Topical cyclosporine	II	A
Topical nonsteroidal antiinflammatories	Insufficient	Not recommended
Punctal occlusion	II	B
Serum tears	II	B
Systemic dietary supplements	Insufficient	Not recommended
Systemic immunomodulatory treatments	Insufficient	Not recommended

Reproduced with permission from Akpek EK, Lindsley KB, Adyanthaya RS, et al. Treatment of Sjogren's syndrome-associated dry eye. An evidence-based review. Ophthalmology 2011;118:1242-52.

OCULAR ROSACEA

Rosacea is a disease of the skin and eye that is observed more frequently in fair-skinned individuals,[98] but it can occur in people of all ethnic origins. Characteristic facial skin findings include erythema, telangiectasia, papules, pustules, prominent sebaceous glands, and rhinophyma. Rosacea may be difficult to diagnose in patients with darker skin tones because of the difficulty in visualizing telangiectasia or facial flushing.[98] While rosacea is more prevalent in women, it can be more severe when it occurs in men.[99,100] Because many patients exhibit only mild signs, such as telangiectasia and a history of easy facial flushing, the diagnosis of rosacea is often overlooked, especially in children who may present with chronic recurrent keratoconjunctivitis, punctate erosions, keratitis, meibomian gland disease, or recurrent chalazia and have subtle signs of rosacea.[101] Children with ocular rosacea often present with corneal involvement, asymmetry of ocular disease, and the potential for sight-threatening visual impairment. Cutaneous rosacea is less frequent in children and associated atopy is common.[102,103] Children with a history of styes have an increased risk of developing adult rosacea.[104]

APPENDIX 4. DIAGNOSTIC TESTS

This appendix summarizes the applicability of currently utilized tests to diagnose tear film and ocular surface disorders. These tests include the tear break-up time test to evaluate tear-film stability; ocular surface dye staining to evaluate ocular surface disease (KCS); the Schirmer test and fluorescein clearance test to evaluate aqueous tear production and clearance; the lacrimal gland function text to evaluate lacrimal gland function; and tear osmolarity testing .

TEAR BREAK-UP TIME TEST

Tear break-up time is determined by instilling fluorescein dye in the inferior cul-de-sac and then evaluating the stability of the precorneal tear film.[49] The test is performed by moistening a fluorescein strip with sterile nonpreserved saline and applying it to the inferior tarsal conjunctiva. Fluorescein-anesthetic combination drops are not ideal for this purpose, as the anesthetic may affect the result of the test. After several blinks, the tear film is examined using a broad beam of the slit-lamp biomicroscope with a cobalt blue filter. The time lapse between the last blink and the appearance of the first randomly distributed dark discontinuity in the fluorescein-stained tear film is the tear break-up time. The tear break-up time should be evaluated before the instillation of any eye drops and before the eyelids are manipulated in any way.

Recurrent tear break-up in the same area may indicate localized anterior basement-membrane abnormalities. Break-up times less than 10 seconds are considered abnormal.[49] A rapid tear break-up time is observed in both aqueous tear deficiency and meibomian gland disease.[49]

OCULAR SURFACE DYE STAINING

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

Fluorescein dye stains areas of the corneal and conjunctival epithelia where there is sufficient disruption of intercellular junctions to allow the dye to permeate into the tissue.[105] Saline-moistened fluorescein strips or 1% to 2% sodium fluorescein solution is used to stain the tear film. After instilling the dye, the ocular surface is examined through a biomicroscope using a cobalt blue filter. Staining may become more apparent after 1 to 2 minutes. Staining is more intense when it is observed with a yellow filter. Mild fluorescein staining can be observed in normal eyes and may be more prominent in the morning. Exposure-zone punctate or blotchy fluorescein staining is observed in dry eye, and staining is more easily visualized on the cornea than on the conjunctiva.

Rose bengal staining of the tear film may be performed using a saline-moistened strip or 1% solution. (Patients should be informed that the drop might irritate the eye.) The saline drop used to moisten the strip should remain in contact with the strip for at least a minute to achieve an adequate concentration of rose bengal to stain the ocular surface. Rose bengal staining is more intense on the conjunctiva than the cornea. The dye stains ocular surface cells that lack a mucous coating as well as debris in the tear film[105]; the staining may be easier to observe with a red-free filter.

Lissamine green dye has a staining profile similar to that of rose bengal,[106-108] but causes less ocular irritation.[107,108] It is not recommended for evaluating corneal epithelial disease.

Diffuse corneal and conjunctival staining is commonly seen in viral keratoconjunctivitis and medicamentosa. Staining of the inferior cornea and bulbar conjunctiva is typically observed in patients with staphylococcal blepharitis, meibomian gland dysfunction, lagophthalmos, and exposure, while staining of the superior bulbar conjunctiva is typically seen in superior limbic keratoconjunctivitis. A pattern of exposure zone (interpalpebral) corneal and bulbar conjunctival staining is typically seen with aqueous tear deficiency.[109,110]

AQUEOUS TEAR PRODUCTION (SCHIRMER TEST)

The Schirmer test is frequently performed to evaluate aqueous tear production, but it is well recognized to give variable results and should not be used as the sole criterion for diagnosing dry eye.[A:III] It is performed by placing a narrow filter-paper strip in the inferior cul-de-sac. Aqueous tear production is measured by the length in millimeters that the strip wets during the test period, generally 3 or 5 minutes.[110] Schirmer testing may be performed with or without the use of topical anesthesia. The Schirmer test with anesthesia, also referred to as a basic secretion test, has been reported to give more variable results than the Schirmer test done without anesthesia.[54] Results of 5 mm or less for the Schirmer test with anesthesia are generally considered abnormal.[52] If topical anesthesia is applied, excess fluid should be gently removed from the cul-de-sac prior to insertion of the filter paper. Although no absolute cutoff has been established for this test, less than 10 mm of strip wetting in 5 minutes is suggestive of abnormality in patients tested without anesthesia.[49] While an isolated abnormal result can be nonspecific, serially consistent low results are highly suggestive of aqueous tear deficiency.

FLUORESCEIN CLEARANCE TEST/TEAR FUNCTION INDEX

The clearance or turnover of tears on the ocular surface can be assessed using a number of tests, including the fluorescein clearance test and tear function index.[111,112] These tests are performed by instilling a measured amount of fluorescein dye on to the ocular surface, then assessing clearance of the dye by visually comparing the residual dye in the inferior tear meniscus of the Schirmer strip placed onto the ocular surface with a standard color scale.[111,112] This test assesses aqueous tear production, tear volume, and tear drainage. It has been found to show better correlation with the severity of ocular irritation symptoms and corneal fluorescein staining than the Schirmer test.[113,114]

LACRIMAL GLAND FUNCTION TEST

Lactoferrin is the most abundant tear protein that is secreted by the lacrimal gland.[49] Tear lactoferrin concentrations have been reported to decrease in Sjögren syndrome and other causes of lacrimal gland dysfunction,[115] and they have been found to correlate with the severity of ocular surface rose bengal staining.[116] The Touch Tear analyzer (Touch Scientific, Inc., Raleigh, NC) is a commercially available tear immunoassay for lactoferrin that has been approved by the FDA.

TEAR OSMOLARITY TEST

Tear osmolarity has been shown to be a more sensitive method of diagnosing and grading the severity of dry eye compared to corneal and conjunctival staining, tear break-up time, Schirmer test, and meibomian gland grading.[117] Tear Lab Osmolarity System, a lab-on-a-chip test that requires 50 nL of tears, is commercially available (TearLab Corp., San Diego, CA).

APPENDIX 5. DRY EYE SEVERITY SCALES

Table A5-1 outlines the grading scheme devised by an expert group to classify dry eye severity.[118]

TABLE A5-1 DRY EYE SEVERITY GRADING SCHEME

Dry Eye Severity Level	1	2	3	4*
Discomfort, severity & frequency	Mild and/or episodic; occurs under environmental stress	Moderate episodic or chronic, stress or no stress	Severe frequent or constant without stress	Severe and/or disabling and constant
Visual symptoms	None or episodic mild fatigue	Annoying and/or activity limiting, episodic	Annoying, chronic and/or constant, limiting activity	Constant and/or possibly disabling
Conjunctival injection	None to mild	None to mild	+/-	+/++
Conjunctival staining	None to mild	Variable	Moderate to marked	Marked
Corneal staining (severity/location)	None to mild	Variable	Marked central	Severe punctate erosions
Corneal/tear signs	None to mild	Mild debris, ↓ meniscus	Filamentary keratitis, mucus clumping, ↑ tear debris	Filamentary keratitis, mucus clumping, ↑ tear debris, ulceration
Lid/meibomian glands	MGD variably present	MGD variably present	Frequent	Trichiasis, keratinization, symblepharon
TFBUT (sec)	Variable	≤10	≤5	Immediate
Schirmer score (mm/5 min)	Variable	≤10	≤5	≤2

TFBUT = fluorescein tear break-up time; MGD = meibomian gland disease

* Must have signs AND symptoms.

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The Ocular Surface Disease Index (OSDI; Allergan, Inc., Irvine, CA) was developed to grade dry eye severity by assessing the discomfort and interference with quality of life of patients with dry eye syndrome. Patients answer 12 questions about their symptoms and grade the frequency of occurrence over the last week. In calculating the OSDI, the denominator is the number of questions answered by the patient. The numerator is the sum of the scores from the patient questionnaire multiplied by 25. The OSDI is assessed on a scale of 0 to 100, with higher scores representing greater disability. A value of 25 or more signifies presence of dry eye disease.[119]

RELATED ACADEMY MATERIALS

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Dry Eye (2011)

Dry Eye (Spanish – Ojo Seco) (2011)

Preferred Practice Pattern

Comprehensive Adult Medical Eye Evaluation (2010)

To order any of these materials, please call the Academy's Customer Service number, 866.561.8558 (U.S. only) or 415.561.8540 or visit www.aao.org/store.

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