

2nd Annual Dry Eye Report

Dry Eye Management

for the

New Century

The latest on causes and treatments.

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Treatment of ocular surface disease, including dry eye, has become an important part of optometric practice. And, when you consider that 35% of the U.S. population has symptoms related to dry eyes—for example, 9.3 million patients were diagnosed with keratoconjunctivitis sicca alone in 1999—this condition will likely be an expanding segment of our practices.¹

An individual who complains of dry eye symptoms is not simply the patient with a routine “nuisance” complaint. Rather, this patient may have significant ocular or systemic disease. Left untreated, this can result in sight-threatening sequelae such as bacterial keratitis and sterile corneal melts.

We must stay abreast of new developments, findings and tools for diagnosing

and treating dry eye and its related conditions. We’ll review some of them here.

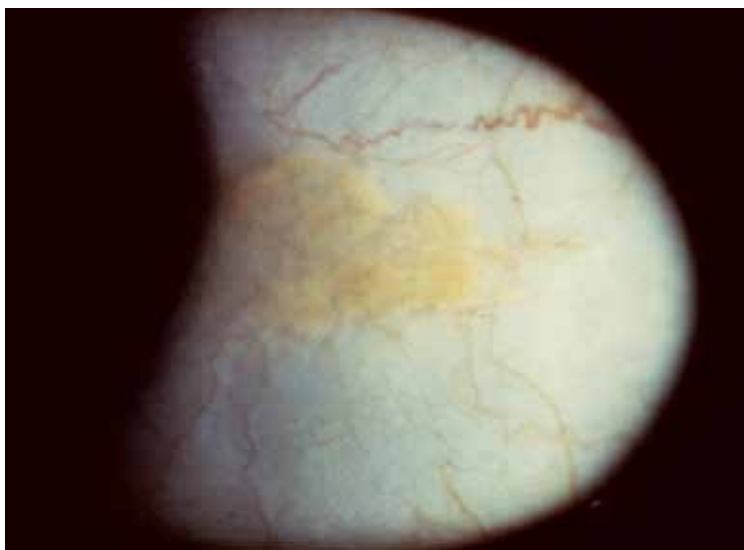
Pre-Disposing Factors

Treatment of dry eye begins with an understanding of the factors that predispose the patient to this problem. Among them:

- Age and sex. Studies show that androgen hormones regulate homeostasis of many structures, including the lacrimal and mei-

bomian glands.² Experimental evidence indicates that androgen hormones (primarily estrogen, but also progesterone and testosterone) improve lacrimal gland secretory function and help maintain the anti-inflammatory state for the ocular structures.³ Hormonal deficit, as with menopause, may remove this protection; so as patients grow older, deficiencies in these circulating hormones can more easily initiate inflammation of the ocular surface and lacrimal glands.⁴⁻⁶

- Environment. Air conditioners, heaters and ceiling fans all remove moisture from the air. Patients who work in drier environments—for example, pilots and flight attendants—may be more prone to dry eyes. So are patients who spend significant time working at computers. Researchers



Poor ocular surface wetting in marginal dry eye patient.

Courtesy: Joseph P. Shovlin, O.D.

have found a correlation between smoking and significant caffeine intake and dry eye, and now consider these the top two environmental or intake sources, though they have not determined the cause.⁷

- Anterior segment disease

(primarily blepharitis and posterior meibomianitis). Patients with blepharitis are approximately twice as likely to experience dry eye symptoms than patients without blepharitis.⁸ Blepharitis and meibomianitis



Inferior SPK may indicate lagophthalmos, trichiasis, blepharitis, meibomianitis or other lid conditions.

may also indicate a systemic problem such as acne rosacea.⁹

• Systemic disease. This is a strong contributing factor to dry eye, especially among patients with diabetes and rheumatoid arthritis.^{7,10} Also, due to slow and/or abnormal healing in many diabetics, this condition poses a risk of significant sequelae such as bacterial keratitis and persistent corneal erosion or epithelial defects.

Sjögren's syndrome, an autoimmune and arthritis-type condition, involves a triad of dry mouth, dry eye and systemic immune dysfunction, such as polyarteritis. Recent research into Sjögren's syndrome suggests a lymphocytic infiltration of the lacrimal and salivary glands. Sjögren's has a prevalence of 4 in 1,000, and 95-98% of patients with Sjögren's are women.^{11,12} Again, lower androgen counts, especially in post-menopausal women, may contribute to a breakdown of the salivary and lacrimal glands. One study found that patients with Sjögren's are 46.3 times more likely to develop a non-Hodgkin's lymphoma. Sjögren's patients should

have regular exams for this type of malignancy.¹³

Another systemic disease, acne rosacea, is perhaps one of the most misdiagnosed causes of dry eye. Rosacea also involves meibomian gland dysfunction, blepharitis and dry eyes, and can lead to rosacea keratitis.¹⁴

- Medications. Antihistamines, anti-hypertensives, anticholinergics, antidepressants and even oral contraceptives can all contribute to dry eye. So, too, can topical ophthalmic

medications and their preservatives. These include glaucoma medications and any chronic medication with preservatives.

• Contact lens wear. Because the pre-lens tear film is thinner than the pre-ocular tear film, contact lens wear is likely to exacerbate dry eye symptoms.^{15,16} The Canada Dry Eye Epidemiology study found that half of contact lens wearers reported dry eye symptoms vs. less than one-fourth of non-wearers (see "The CLIDE Files," page 59).¹⁷

• LASIK. Refractive surgery has also been shown to contribute to dry eye, primarily in the first 3-6 months post-op.^{18,19} There are three theories on this: the neurotrophic theory, which suggests that a severing of nerves in the corneal stroma, which takes some 3 months to regenerate, may contribute to lack

of sensory input back to the lacrimal and accessory lacrimal glands; that the suction ring used during LASIK disrupts the high concentration of goblet cells at the limbus, decreasing mucin production; and tear flow alteration, which results from the alteration of the corneal surface—a temporary condition because the iron deposits that appear centrally in long-term LASIK patients support tear flow.¹⁹

Patient Workup

We can probably diagnose many dry eye cases by the initial presenting symptoms: burning, stinging, transient blur, photophobia, injection and foreign body sensation. Even so, you must thoroughly examine the patient to arrive at a proper diagnosis, especially in determining the underlying cause. Include the following in your workup:

- Eyelids, lid margins and eyelashes. Look for anterior segment disease such as blepharitis and posterior meibomian gland dysfunction. Also look for ectropion, entropion and trichiasis.



Significant meibomian gland dysfunction causes dry eye symptoms.

Courtesy: Joseph P. Showlin, O.D.

Dermatochalasis may also contribute significantly to dry eye-type symptoms. In fact, one study shows that this condition existed in more than 86% of cases following a blepharoplasty.²⁰

• The cornea and conjunctiva. Evaluate the quality and size of the tear film on every patient.²¹ This can be noted by looking at the size of the tear meniscus as well as the quality based on debris in the tear film.

Look for staining. Using Lis-

samine Green dye, the conjunctiva will stain at 3 and 9 o'clock in dry eye patients. Using fluorescein dye, it is the cornea that is examined for staining. Its location helps you determine how to proceed with treatment. Inferior superficial punctate keratitis clearly indicates incomplete blink, lagophthalmos, or blepharitis and posterior meibomian gland dysfunction.

- Cranial nerve function. Problems in this area, especially a seventh nerve palsy, may result in an incomplete blink and/or chronic exposure.

- Skin. Check for erythema, telangiectasia, pustules, prominent sebaceous glands and rhinophyma—the characteristic findings of rosacea. Systemic rosacea usually presents in the cheek region in women, and on the nose and forehead in men.

- Hands. Be sure to look at the patient's hands to determine if ar-

thritis is the contributing cause (see "Case Report: Octogenarian with Keratoconjunctivitis Sicca," below).

Making Changes

The first step in your treatment: Educate these patients that their condition is chronic and that there is no current cure available. If they understand this, they're more likely to comply with treatment.

Next, try to reduce or eliminate any underlying, exacerbating factors. Encourage patients to consume less caffeine and quit smoking, increase their water intake (at least 6-8 cups a day) and use a humidifier.

Also, the patient may need to reduce the dosage or switch certain medications such as antihistamines. Involve other doctors who are treating the patient in this decision.

Medications

Your first target of treatment: blepharitis, meibomianitis or sys-

temic causes. Otherwise, the signs and symptoms of dry eye and ocular surface disease usually will not clear.

Treatment of blepharitis depends upon severity. Patients can treat mild, non-symptomatic conditions with hot compresses for 10 minutes a day and lid hygiene. Diluted baby shampoo application may be effective for acute cases and short-term treatment, although longer-term use results in chafing and chronic dryness of the lids, causing irritation.²² Fortunately, there are now commercial lid scrubs available that appear to be effective.

More advanced cases of blepharitis and meibomianitis warrant the use of medications, including:

- Anti-infectives such as bacitracin and ofloxacin. Bacitracin is a good ointment in mild, inflammatory cases of blepharitis because of its effectiveness against gram-positive bacteria such as Staphylococcus, the primary pathogen of blepharitis and meibomianitis. Secondly, bacitracin is topical, so bacterial resistance to this drug is fairly limited.

- Antibiotic/steroid combinations. Patients who experience significant inflammation with erythema and edema of the lid margins may require a combination such as Blephamide (sulfacetamide/prednisolone) or Tobradex (tobramycin/dexamethasone). Blephamide had fallen out of favor because of the relatively high bacterial resistance (60-70%) to sulfacetamide and the high level of allergic response.²³ Although only anecdotal evidence exists, since so many eye doctors have avoided it, bacteria may be increasingly susceptible to this medication. The steroid combination will certainly regress the inflammation and edema and

Case Report: Octogenarian with Keratoconjunctivitis Sicca

An 82-year-old white female with a longstanding history of keratoconjunctivitis sicca presented to her primary eye-care provider about 2 months before we saw her. She said her symptoms had become more severe. The clinician diagnosed severe dry eye and prescribed numerous lubricants and artificial tears.

Four weeks later, the patient showed no improvement, so the doctor referred her to our center. We noted significant corneal thinning on examination.

When we looked at the patient's hands, we realized that arthritis was an underlying systemic cause of her dry eye. The patient said she was aware of her arthritic condition but had never seen a rheumatologist or internist; rather, she simply took ibuprofen daily.

This patient eventually experienced a neurotrophic or arthritic corneal melt with uveal prolapse, and lost her eye. Earlier referral to a rheumatologist and treatment with systemic immunosuppressants may have saved the patient's eye; without oral immunosuppressants, her condition advanced to a complete corneal perforation.³⁹

This patient demonstrates why we must consider systemic causes of dry eye and, in patients such as this one, look at their hands when they present with dry eye symptoms.—P.M.K.



This 82-year-old female with a history of rheumatoid arthritis eventually experienced a corneal melt.

relieve symptoms much faster than a non-steroid.

- Oral tetracyclines. These are especially effective in severe or chronic cases of blepharitis and meibomi- an gland dysfunction because they accumulate in oil glands and limit lipase enzyme activity.²⁴ Also, tetracyclines help reduce inflammation resulting from anterior segment disease and systemic inflammatory conditions such as arthritis.^{24,25} For these patients, consider Doxycycline 100mg bid for 4 weeks, then taper to qd as a maintenance dose.

Doxycycline is also recommended for treating acne rosacea. The recommended dosage is 100mg bid for 4-6 weeks, then qd until fully resolved. Other effective treatments for rosacea include MetroGel (metronidazole) or MetroCream (metronidazole) in the involved regions.²⁶ Also educate the patient on common triggers of rosacea such as spicy foods, alcohol and, in some cases, heat.

Of course, you must use caution when prescribing tetracyclines. Don't forget the usual warnings: the risk of phototoxic reactions (patients should wear sunscreen or protective clothing); chelation with dairy products and antacids, which may render them ineffective; and the risk of gastric inflammation.²⁷ Patients who use Minocycline may experience vertigo or

dizziness. Of course, Doxycycline is contraindicated in children, pregnant women and nursing women due to possible teratogenic effects and the possibility of tooth and bone deformities in children.²⁷ Pseudotumor cerebri is a rare but possible ocular side effect, so monitor patients for this condition.²⁸

Tears and Lubricants

The artificial tear supplement you choose should depend, in part, on the severity of the patient's

condition, location of staining, systemic involvement and the cause of symptoms (e.g., lagophthalmos). You may need to experiment to determine which brand works best.

For patients with severe dry eye and little or no tear production (less than 5mm over 5 minutes on Schirmer test), a preservative-free artificial tear is warranted to reduce the risk of preservative toxicity.²⁹ Preservatives will exacerbate symptoms in patients with conditions such as rheumatoid arthritis, in

which they have little to no tear production.²⁹

The same may happen with the "disappearing" preservative found in many brands of artificial tears. The disappearing preservative, often borate or hydrogen peroxide, dissolves from H₂O₂ to H₂O when it comes in contact with tears, but many patients lack sufficient tears to dissolve the preservative. H₂O₂ can be toxic to an already compromised cornea.

However, tears with the disappearing preservative are ideal for patients without significant keratoconjunctivitis sicca and who have moderate tear production sufficient to dissolve the preservative. These brands combine convenience and cost-savings, two factors that usually increase compliance. Clinically, they appear to be a better choice than preserved tears in regards to preservative build-up and toxicity, so long as the patient

Diagnostic Testing

Many diagnostic tests that aid us in positively diagnosing dry eye have been developed over the years. Most clinicians rely on traditional tests, such as tear breakup time, Schirmer's and ocular surface staining for proper diagnosis of dry eye disease.

However, using several diagnostic aides is better for identifying a patient's dry eye condition than a single test alone.⁴⁰ For example, patient questionnaires about symptoms and risk factors give some credibility to the diagnosis; however, many patients experience many of the common symptoms related to dry eye.⁴¹

Some additional tests:

- Tear break-up time. This is an effective test, but proper testing and proper administration of the dye is important. This includes instilling an ample amount of sodium fluorescein dye, performing the test prior to instillation of other drops, and waiting 1 full minute for fluorescein and tears to become uniform.

Tests such as the Dry Eye Test (DET) and Zone-Quick cotton thread tests provide quicker, repeatable ways to assess tear film-breakup time. Schirmer's tear testing is also of value.

- Staining. Both sodium fluorescein or lissamine green are good indicators of this condition.

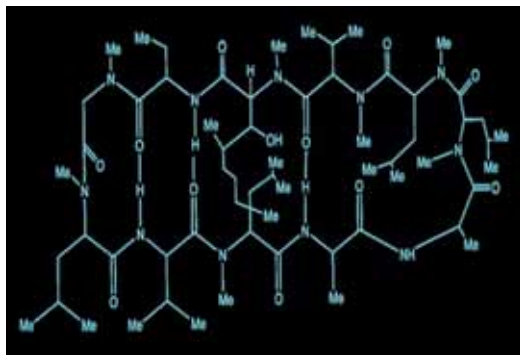
Lissamine green has at least three advantages over rose Bengal: it's less toxic to the cells, does not last as long in cosmetically conscious patients and does not sting as much.⁴² As with rose Bengal, lissamine green stains devitalized cells, but is not as effective in staining cells unprotected by a deficient mucin layer.⁴³ When examining a patient with lissamine green dye, first look at the conjunctiva, not the cornea, as dry eye signs will be most evident in the exposure areas of 3 and 9 o'clock. If the cornea stains with lissamine green, you probably have a significantly dry eye.

The location of the corneal staining can vastly affect treatment for dry eye patients. Significant inferior staining alone would suggest lagophthalmos or blepharitis and posterior meibomianitis. Superior staining alone might suggest superior limbic keratoconjunctivitis.

There are numerous other tests—lactoferrin microassay and impression cytology among them—although you might be able to make a proper diagnosis with those mentioned earlier. They're most appropriate for an optometric practice.⁴⁴—P.M.K., J.J.T.

has sufficient tears to dissolve the preservative.

Any patient who uses more than 8-10 drops a day should switch to true preservative-free tears or consider punctal occlusion. (Punctal occlusion is an excellent option for



Cyclosporin inhibits inflammatory cytokine production and may one day allow longer-term use without the potential side effects of steroids.

elderly, arthritic patients who lack the dexterity to instill artificial tears regularly.)

Patients who use less than 4 drops a day or experience occasional dryness in their eyes should probably use preserved tears because these patients are more likely to leave the bottle around for long periods of time.

Ointments are better suited as a nighttime lubricant or for patients with significant vision loss. Of course, because ointments compromise vision, their daytime use is limited.

Gels offer greater contact time than drops without the visual compromise of ointments. However, they also don't have the contact time of an ointment. Again, we caution their use in patients with severe dry eye because the disappearing preservative has the rare chance to cause mild toxicity in this type of patient, particularly one atopic in nature.²⁹

Punctal Occlusion

Many patients report much greater comfort when using these devices. Collagen plugs that last 3-7 days are certainly easier to insert, but usually yield little change in symptoms over a 3-day period. The advent of new 2-week dissolving

plugs may be a significant improvement and a great consideration for post-LASIK patients. Silicone plugs appear to be the most effective punctal occlusion device because they block a greater amount of outflow tears and do not dissolve.³⁰

Some clinicians recommend upper punctal occlusion in patients with chronic blepharitis or significant inflammation, such as with rheumatoid arthritis. These clinicians

postulate that patients with blepharitis, upper occlusion allows the Staphylo coccus to accumulate in the lower lid margin to wash away more easily through an open lower punctum.

Alternative Treatments

Besides some of these traditional dry eye treatments, many alternative therapies are in the pipeline. Among them:

- Corticosteroids. Many clinicians are starting to consider corticosteroids effective treatments for dry eye because corticosteroids can inhibit most inflammatory pathways, including cytokine production, cell adhesion molecules and vascular permeability. In fact a study by P. Prabhasawat and S.C. Tseng showed an 83% subjective improvement in symptoms and an 80% improvement in certain clinical observations with a 2-week regimen of prednisolone 1% qid.³¹

While steroids are generally good for short-term use, dry eye is a chronic condition. Remember, long-

term use of steroids carries with it potential risks such as posterior subcapsular cataracts, IOP rise and possible glaucoma, and secondary infections such as bacterial or HSV keratitis.³²

- Cyclosporin A. Although now under investigation, cyclosporin A may eventually allow longer-term use without the potential side effects of steroids. Studies have shown topical cyclosporin to significantly improve signs of keratoconjunctivitis sicca in dogs, and it has been approved by the Food and Drug Administration for treatment of veterinary dry eye disease.³³

Cyclosporin inhibits inflammatory cytokine production. Cytokines lead to tissue damage, activation of more T lymphocytes and production of additional inflammatory substances that result in breakdown of the lacrimal and ocular surface.³⁴ Studies show a significant increase of cytokines and T-lymphocytes of the conjunctiva and lacrimal gland in individuals with keratoconjunctivitis sicca.³⁵



Silicone punctal occlusion of the upper puncta may be an effective treatment in some cases.

So, we are now starting to see a shift in thinking; dry eye is not only a disease of evaporation or insufficient tear production, but rather a localized, immune-mediated inflammatory response affecting the lacrimal gland and ocular surface. Clinical trials involving cyclosporine ophthalmic emulsion 0.05%

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- Which one of the following is a predisposing factor to keratoconjunctivitis sicca?
 - Race.
 - Anterior segment disease.
 - Excess hormones.

d. Premenstrual syndrome in women.

- What may alleviate the type of dry eye that is caused by environmental factors?
 - Antihistamines.
 - Antibiotics.
 - Lid scrubs.
 - Humidifiers.
- Which one statement is true regarding the treatment of blepharitis?
 - It depends on the patient's age and gender.
 - It depends on the severity of the patient's condition.
 - It can't be accomplished with warm compresses and lid scrubs alone.
 - Doxycycline is always indicated.
- Oral tetracyclines are contraindicated in patients with :
 - Inflammation from anterior segment disease.
 - Inflammation from arthritis.
 - Mild blepharitis or meibomianitis.
 - Severe blepharitis or meibomianitis.

OSC QUIZ

- tis.
- Medications likely to result in dry eye include:
 - Antidepressants and antihistamines.
 - Antihistamines and insulin.
 - Antidepressants and insulin.
 - Beta-blockers and oral tetracyclines.
 - Which systemic disease is likely to cause decreased tear secretion?
 - Hypertension.
 - HIV.
 - Heart disease.
 - Rheumatoid arthritis.
 - The triad for Sjögren's syndrome includes:
 - Dry eye, dry mouth and dry skin.
 - Dry eye, dry skin and arthritis (or similar systemic immune dysfunction).
 - Dry eye, dry mouth and arthritis (or similar systemic immune dysfunction).
 - Dry eye, dry mouth and irregular heartbeat.
 - Treatment for acne rosacea may involve:
 - Beta-blockers.
 - Topical antibiotics.
 - Antihistamines.
 - Metronidazole or doxycycline.
 - Which one combination of symptoms is likely to present with dry eye?
 - Flashes and floaters.
 - Dry mouth and dry scalp.
 - Transient blur and stinging.
 - Pain and elevated IOP.
 - When examining a patient with dry eye, you look at the patient's hands for what reason?
 - To gauge the severity of dry skin present.
 - To determine if the patient may have arthritis.
 - To look for any unusual discoloration.
 - To look for the presence of scleroderma.
 - What one statement is true about lissamine green staining?
 - More toxic to the epithelial cells than rose Bengal.
 - Longer-lasting than rose Bengal.
 - More effective than rose Bengal at staining cells unprotected by a mucin layer.
 - Similar to rose Bengal in the way it stains devitalized epithelial cells.
 - Circulating hormones, particularly estrogen, help:
 - Maintain a non-inflamed state in the tissues.
 - Create an inflammatory state that can cause a breakdown of the lacrimal glands and ocular surface.
 - Heal meibomian gland dysfunction without resorting to drugs.
 - Lead to the development of keratoconjunctivitis sicca in post-menopausal females.
 - Sjögren's syndrome increases the patient's chance of developing:
 - Hormone deficiency.
 - Non-Hodgkin's lymphoma.
 - Diabetes mellitus.
 - Blepharitis or meibomianitis.
 - Which are leading dietary contributors to dry eye?
 - Unsaturated fats and cholesterol.
 - Sugars and carbohydrates.
 - Smoking and caffeine.
 - Carbonated beverages.
 - Which lid disease will not lead to an increase in dry eye-type symptoms?
 - Dermatochalasis.
 - Blepharitis.
 - Distichiasis.
 - Ectropion.
 - The neurotrophic theory of post-LASIK dry eye suggests that:
 - The suction ring used during LASIK disrupts the high concentration of goblet cells at the limbus.
 - The severing of nerves in the corneal stroma may decrease mucin production.
 - The severing of nerves in the corneal stroma may contribute to lack of sensory input to the lacrimal and accessory lacrimal glands.
 - Increased pressure on the optic nerve disrupts tear flow.
 - Which treatment would you recommend for acne rosacea in a 45-year-old male?
 - Oral doxycycline 100mg bid for 4 weeks, then taper.
 - Oral azithromycin 1,000mg once.
 - Oral erythromycin 250mg qid for 10 days.
 - Oral Augmentin (amoxicillin, clavulanate potassium) qid for 10 days.
 - Inferior staining alone may indicate:
 - Lagophthalmos, blepharitis or superior limbic keratoconjunctivitis.
 - Superior limbic keratoconjunctivitis, meibomianitis or blepharitis.
 - Superior limbic keratoconjunctivitis, Sjögren's syndrome or post-LASIK dry eye.
 - Lagophthalmos, blepharitis or posterior meibomianitis.
 - Which type of tear supplement is best for a patient with severe dry eye, filamentary keratitis and Schirmer tear test measuring 2mm?
 - Preservative-free artificial tears.
 - Preserved artificial tears.
 - Artificial tears with a "disappearing" preservative.
 - No tear supplements.
 - Treatment of a corneal melt in a patient with rheumatoid arthritis must involve which of the following?
 - Artificial tears.
 - Steroid drops.
 - Immunosuppressives prescribed by a rheumatologist.
 - Doxycycline.