



A QUICK GUIDE TO DRY EYE

Dry eye may not blind your patients, but moderate or severe disease is making some of them miserable. Spot and treat this overlooked condition in its early stages, and make a difference for your patients.

As a cornea fellow some 30 years ago, Robert S. Feder, MD, was shown a cartoon of an elf holding a watering can. “That was the model for treating dry eye disease. Water the cornea,” said Dr. Feder, at Northwestern University in Chicago.

Fifteen years later, not much had changed. “Doctors said, ‘Take these tears and go home,’” said Giacomina Massaro-Giordano, MD, now at Penn Dry Eye and Ocular Surface Center, Philadelphia. “Dry eye was ignored.” Or, worse, these patients were dismissed as crazy. Indeed, this was the case with Dr. Massaro-Giordano’s mother when she complained about her eyes.

But patients who say they have foreign body sensations in their eyes—or burning, dryness, or exquisite sensitivity to wind or air conditioning drafts—suffer from a very real condition. Today doctors better understand dry eye disease (DED), a multifactorial condition associated with ocular surface inflammation

and tear film hyperosmolarity. There are even centers, such as Dr. Massaro-Giordano’s, dedicated to its treatment.

Growing prevalence. As the population ages, doctors will be diagnosing DED with greater frequency. Though the condition is not associated exclusively with aging, its prevalence increases with every decade of life over 40. It is also associated with contact lens use, cigarette smoking, diabetes, prolonged video display viewing, and low-humidity environments.

Twenty percent of the U.S. population is diagnosed with dry eye, said Dr. Massaro-Giordano. Still, the disease is very underdiagnosed, Dr. Feder noted. “It is also underappreciated in that you don’t see frank pathology as you do in macular degeneration or cataract, so it may be easy to ignore,” said Penny A. Asbell, MD, FACS, at Icahn School of Medicine in New York.

Unhappy patients. The more severe forms of DED have been ranked equivalent to unstable

MIRIAM KARMEL, CONTRIBUTING WRITER

angina in quality-of-life utility assessments.¹ “You may not go blind from it, but it does affect your whole persona,” said Dr. Massaro-Giordano. Dr. Asbell added that patients who have significant dry eye “are not too happy.” It’s a chronic pain syndrome, she said. “These can be challenging patients to care for.”

Frustrating for physicians. Dr. Asbell noted that DED can be challenging to diagnose. For instance, when a dry eye patient reads the chart, she may have 20/20 vision because she blinked before reading, yet she still says, “But I don’t see well,” said Dr. Asbell. She likens this to a car with a dirty windshield. Clean it off (or blink) and you can see through it. However, many of these patients are not blinking often enough to maintain good vision throughout the day.

A few years ago, Dr. Asbell surveyed ophthalmologists on their perceptions about treatment of dry eye, and they reported being frustrated, saying that patients with moderate to severe DED were difficult to treat. Ophthalmologists wanted more treatment options.²

Multifactorial misery. DED is also challenging to diagnose and manage because it is multifactorial. To better handle patients with DED, the Penn Dry Eye Center, for example, has a team of experts to address the range of conditions that might be associated with DED: a rheumatologist for autoimmune disease; a dermatologist for underlying rosacea; an oculoplastic specialist for malpositioned eyelids, which can affect the tear film; an endocrinologist for the hormonal component; and a contact lens specialist.

Most ophthalmologists don’t have the extensive support of a dry eye center to deal with advanced disease. But even mild DED poses challenges. What’s the best management strategy? Yes, watering the eyes with artificial tears may provide symptomatic relief. But before you reach into the sample drawer and say, “Try this tear supplement,” consider what the experts are saying about DED.

CAUSES OF DRY EYE

The two major types of DED are aqueous tear deficiency (ATD) and evaporative dry eye. In the latter, which is linked to meibomian gland dysfunction, lipid insufficiency may result in increased evaporation and tear film instability, among other sequelae.³

It’s important to try to differentiate between the two underlying causes. In many—but not all—cases, the treatments are the same, said Robert W. Weisenthal, MD, at SUNY Upstate Medical University, Syracuse. Dr. Asbell added that some patients may have a little of both types. “The reality is that it’s pretty hard to tell. There’s no surefire test.” Still, you want to think about findings that point more toward ATD or evaporative DED because that may alter your treatment, she said.



Either way, DED will progress. Chronic inflammation of the lids from meibomian gland dysfunction and evaporative dry eye, coupled with tears that contain inflammatory components, can further damage the meibomian glands, said Dr. Massaro-Giordano. Tear insufficiency dry eye, on the other hand, may point to an underlying autoimmune disorder. “Over time, that can destroy the lacrimal glands,” she said.

Consider systemic conditions. A number of inflammatory autoimmune conditions can cause dry eye. One of the most important objectives of the dry eye evaluation is ruling out Sjögren syndrome, said Esen K. Akpek, MD, at Wilmer Eye Institute, Baltimore. One in 10 patients with clinically significant dry eye will have Sjögren’s, which puts the patient at risk for systemic conditions such as lymphoma and major organ involvement, including the lungs, kidneys, and liver, she said. These patients often complain of dry mouth, fatigue, and joint pain. The clinician should always inquire about these symptoms in assessing dry eye patients.

Symptoms of concern. Dr. Feder said to beware of potential underlying conditions when dry eye is accompanied by the following symptoms:

- Fullness and/or tenderness in the superotemporal eyelid—the area of the lacrimal gland—should trigger consideration of dacryoadenitis, either postviral or associated with inflammatory disorders such as sarcoidosis. If a conjunctival granuloma is present, it can be biopsied.
- Proptosis and/or eyelid swelling may indicate thyroid disease.
- Subepithelial fibrosis in the conjunctiva of an elderly patient should be evaluated for ocular mucous membrane pemphigoid, with conjunctival biopsy for immunopathology looking for antibodies to the basement membrane.

DIAGNOSE DRY EYE

Because dry eye disease is hard to diagnose, “What we need is a metric that says, ‘Yes, you have it. Or don’t,’” Dr. Asbell said. Ideally, that metric also could distinguish severe from mild cases. She compared it with HIV, where a blood test confirms that you either do or don’t have the disease. It can measure viral load

DIAGNOSTICS & TESTS

Several diagnostic tests for dry eye are available, but expert opinion about their use is mixed.

Dr. Feder pointed out that ophthalmologists are still learning about the utility of these products for everyday practice. But, he said, “if the goal of therapy is to reduce symptoms, improve function, and prevent damage, and if you can do that in the vast majority of patients for the cost of a fluorescein or Schirmer strip, you have to ask, ‘Is it worth the extra expense to buy equipment and administer a sophisticated test?’” Dr. Weisenthal noted that even though these tests quantify what you see, they don’t alter his treatment approach.

Here are a few devices and tests on the market:

Keratograph 5M (Oculus) and **Tear Stability Analysis System** (Tomey).

If the tear film isn’t thick enough or doesn’t last long enough between blinks, holes appear in the tear film, causing irregularity of the surface.

“These two devices assess the irregularity or regularity of the surface between blinks,”

Dr. Akpek said, adding that they’re essentially topographers that can be very useful for dry eye specialists. She recommended their incorporation into LASIK and premium lens implant practices because they are topography-based



KERATOGRAPH 5M

and give good information on TBUT, in addition to corneal power, which affects refraction.

Dr. Asbell called the Keratograph one of the promising newer devices. “That machine has a lot of potential for putting us in the realm of what we want: minimally invasive objective metrics.”

LipiView Ocular Surface Interferometer (TearScience). This device measures TBUT by taking a photo of the tear film and looking for areas of desiccation.

It’s used to diagnose evaporative dry eye, Dr. Akpek said. “Whenever we see a dry eye, we apply gentle digital pressure on the lid margins to get meibum secretion out of the glands. We look at its

appearance. An experienced ophthalmologist can distinguish good quality from bad quality. Although LipiView does not evaluate the quality of meibum, it gives good information about whether there are adequate amounts of meibum in the tear film,” she said.

RPS InflammDry Detector (Rapid Pathogen Screening). In 10 minutes, this device delivers a reading on levels of MMP-9 (matrix metalloproteinase-9), an inflammatory marker shown to be elevated in the tears of DED patients. Increased MMP-9 activity may contribute to deranged



LIPIVIEW



RPS INFLAMMADRY DETECTOR

corneal epithelial barrier function, increased corneal desquamation, and corneal surface irregularity. However, the device doesn’t distinguish dry eye from other inflammatory disorders, Dr. Akpek said. Still, objective MMP measures may guide treatment decisions. “It tells me the surface is not healthy and that the patient needs to be aggressively treated.” The device may correlate to fluorescein punctate staining of the cornea, she said.

Sjö (Nicox). This in-office finger-stick blood test, which is sent out to Immco labs, is designed to check for novel antibodies that may be positive earlier than the traditional antibody tests. Because Sjö is very new, it is not clear whether all insurance companies will cover it, said Dr. Massaro-Giordano.



SJÖ

TearLab Osmolarity System (TearLab). This device measures tear osmolarity, which if too high may damage the cornea and conjunctiva. Dr. Akpek said the osmolarity system would be a good addition to the armamentarium. “It’s quicker and less invasive than Schirmer testing. It can be done by a technician. It is reimbursed.”



TEARLAB

over time. “There’s no equivalent for dry eye disease,” she said. But there are ways to make a diagnosis.

Listen. You can get a pretty good idea by listening to the patient and taking a careful history, Dr. Asbell said. Dr. Massaro-Giordano added, “What sets some people off doesn’t set off others. It takes a lot of chair time with patients trying to figure out what makes their eyes feel better.”

Dr. Weisenthal suggests that physicians ask the

following questions:

- Is your dry eye worst upon awakening? Or does it get worse as the day goes on? The former suggests aqueous tear deficiency; the latter, meibomian gland dysfunction.
- What activities make it better or worse?
- Are you using diuretics or antihistamines? (These exacerbate symptoms of dry eye and are known to make dry eye worse, said Dr. Massaro-Giordano.)



Dr. Massaro-Giordano squeezes a patient's meibomian glands.

• Do you have dry mouth? Gum disease? These symptoms may be associated with systemic disease like Sjögren's.

Look. Though tests will confirm the diagnosis, Dr. Weisenthal said he often knows the results before doing them. "You can tell by looking at the patient." He advises checking for the following:

- **Rosacea in the face and eyelids.** Rosacea is associated with meibomianitis and evaporative dry eye.
- **Look at the lids.** Are they floppy? Floppy eyelid syndrome can cause symptoms of dry eye.
- **Red lid margins.** This suggests meibomian gland dysfunction. Press on the lids. If there's a toothpaste-like secretion or no secretion, the glands are blocked.
- **Watch how often the patient blinks.** The norm is 12 blinks per minute. The patient who doesn't blink for 30 seconds has a problem.
- **Is there an incomplete blink?** This is often seen after blepharoplasty.
- **Malpositioned lids.** Eyelids that are turned in or out may evert the lacrimal punctum.
- **Swelling of the conjunctiva.** This may indicate conjunctivochalasis.

Test. Dr. Feder said that by performing the following, "you would miss very few cases of dry eye."

- **Slit-lamp exam** to evaluate the tear film. "A tear meniscus on the inferior lid should be a certain thickness and the fluid should be clear. Some patients have cellular debris or mucus within that tear film that just is not healthy," Dr. Weisenthal said.
- **Schirmer test with anesthetic** to measure basal tear production.
- **Fluorescein staining** to test for tear film breakup time (TBUT), which is defined as the interval between the last complete blink and the first appearance of a dry spot or disruption in the tear film. Once in the tear film, fluorescein should stay intact for at least 10 seconds. This test provides evidence of tear film stability, which suggests how well the meibomian glands are



Schirmer's test.

functioning. It is the first-line stain to use in evaluating the ocular surface.

- **Lissamine green or rose bengal staining** to reveal devitalized epithelium. Use these stains to evaluate the ocular surface, not just the cornea, Dr. Weisenthal said. "If fluorescein doesn't confirm my suspicion, I do one of these." Dr. Akpek said you won't see much staining in early stages of DED. By the time these stains highlight unhealthy areas of the cornea or the conjunctiva, the disease is moderate to advanced.

TREATMENT

Treatment for both mild evaporative and aqueous deficient dry eye is relatively straightforward, but it's worth keeping a few things in mind.

For evaporative dry eye, the experts recommend the following.

- **Warm compresses.** Warm compresses and eyelid hygiene improve meibomian gland function. Moist compresses are better than dry heat, Dr. Massaro-Giordano said. Hygiene entails removing any make-up, then gently scrubbing eyelashes and eyelids with a commercially available premoistened pad. (Diluted baby shampoo or gentle face wash also works.) Apply mild pressure along the rims of the eyelids



in order to express some "oil" from the meibomian glands. Then rinse off and pat dry, she said.

Preservative-free glaucoma drops are advised for dry eye patients.

- **Manage the environment.** "Recognition of the environment as a cause of dry eye can make a huge difference for the patient," Dr. Feder said. Prolonged visual effort—reading, watching TV, computer work—reduces the blink rate, causing desiccation of the ocular surface. Other environmental causes of drying are fans, car vents, circulating airplane air, and drafts from air conditioners. Patients may improve in summer and get worse in winter.

"Desktop humidifiers are becoming increasingly popular," said Dr. Feder. He added that if the patient can't change the environment, eye protection such as moisture chamber glasses—which have side shields to keep the eyes' moisture in—may be helpful.

- **Beware of eyedrops.** Preservatives in glaucoma medications can destabilize the tear film. Dr. Massaro-Giordano advises working with the glaucoma specialist for a preservative-free option. If that's not possible, she suggests considering surgery that

reduces the need for glaucoma medications.

- **Recognize systemic medication effects.** Anticholinergics, antidepressants, or oral allergy and decongestant medications designed to dry up mucous membranes all can dry the surface of the eye, Dr. Feder said. Dr. Massaro-Giordano noted that a lot of patients have itchy lids resulting from advanced anterior blepharitis. “They get an over-the-counter allergy drug, which in turn dries them out further.”

For aqueous tear deficiency, the experts recommend the following.

- **Artificial tears.** For mild cases, Dr. Weisenthal gives patients two or three samples to try. “People seem to have their favorite.” The experts agreed that anyone using tear supplements more than four times a day should use preservative-free varieties.
- **Anti-inflammatory agents.** For moderate to severe cases of dry eye, a mild topical steroid may help. Dr. Weisenthal starts with steroids four times a day for two weeks and tapers to twice a day for two weeks. No more than two to four weeks of treatment is recommended, Dr. Weisenthal warned.

Topical cyclosporine (Restasis) has anti-inflammatory properties without the side effects associated with steroids. But it can take time for increased tear production to kick in. For immediate relief, Dr. Weisenthal prescribes a steroid (as above) for four weeks. By then the cyclosporine kicks in, and he stops the steroids.

Restasis benefits many, but not all, patients. “It’s not particularly helpful for evaporative dry eye,” Dr. Feder said. “Its greatest utility is for patients with connective tissue disease who have inflammation of the lacrimal glands.”

- **Punctal plugs.** For moderate to severe cases of dry eye, Dr. Feder prefers punctal plugs to cautery because they’re reversible. But in cases of severe dry eye associated with a chronic systemic disease, such as rheumatoid arthritis, he’ll consider cautery. “If you’re going to use punctal plugs, put in the largest plug possible because it’s more likely to stay in.”

Dr. Weisenthal considers plugs as an alternative to long-term Restasis for patients with ATD. He warned that using plugs in cases of meibomian gland dysfunction will sometimes make the condition worse.



Silicone punctal plug.

- **Omega-3.** When she heard reports that omega-3 “works great” for dry eye disease, Dr. Asbell went to the literature. The data were limited to a few small trials, all using different types and amounts of omega-3s and different endpoints, she said. “We needed a real trial.”

That trial is now under way. DREAM (Dry Eye Evaluation and Management) is the first clinical trial for dry eye funded by the NEI. Six hundred patients at 21 sites across the United States will be randomized into two groups to determine whether oral supplementation with omega-3s is an effective treatment for dry eye disease compared with placebo. DREAM will also assess potential biomarkers for inflammation.

When to refer. All of the experts agreed that some cases require specialized care. Dr. Massaro-Giordano recommended referral to an academic center with an interest in DED or to a doctor who deals in surface

PEARLS FROM THE EXPERTS

ACADEMY GUIDELINES. “Review the Academy’s Dry Eye Syndrome *Preferred Practice Patterns*. The evidence-based information has been carefully reviewed by a panel of experts. It’s a great resource. It’s easily accessible. And it’s free.” —*Dr. Feder*

Find the guidelines at www.aao.org/ppp and scroll to Dry Eye Syndrome PPP - 2013.

ARTIFICIAL TEARS. “Not all artificial tears are the same. They have different consistencies. Although there can be some trial and error, it’s worth taking a look at some of the newer artificial tears. Some drops are geared more toward lipid abnormality, others toward mild lubrication. And some are more long-lasting.”

—*Dr. Asbell*

EXAMINING THE EYELIDS. “Look at those lids! Put pressure up against the eyelid with a fingertip or cotton swab. See what’s coming out. Is it granular? Opaque?”

If it’s tough to get out, you know you have a problem.”

—*Dr. Massaro-Giordano*

PATIENT EXPECTATIONS.

“Dry eye is not something you can treat for two months and it will go away. It can be controlled, but it’s not something that disappears.

So it’s important to set up expectations so the patient understands this is something they need to pay attention to and will have to continue to manage.”

—*Dr. Weisenthal*

SJÖGREN SYNDROME. “One main objective in seeing any dry eye patient is to ask: Is this the 1 in 10 that has Sjögren’s? Dry eye doesn’t kill anyone, but Sjögren’s can.” —*Dr. Akpek*



disease. Because of the multifactorial nature of the disease, a team approach can be very helpful.

Bottom line. Our understanding of DED has advanced since the days of the watering can. Now it's up to the ophthalmologist to apply what's been learned. Success with these patients, said Dr. Feder, "really starts with your curiosity, a careful evaluation, and

then going beyond treating all dry eye symptoms the same way." ■

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- 2 Asbell PA, Spiegel S. *Eye Contact Lens*. 2010;36(1):33-38.
- 3 Nichols KK et al. *Invest Ophthalmol Vis Sci*. 2011;52(4):1922-1929.

MEET THE EXPERTS

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