Improve the Diagnosis, Management and Treatment of Inflammatory Dry Eye

USING INFLAMMADRY® TO IDENTIFY INFLAMMATION IN DRY EYE PATIENTS FACILITATES TARGETED TREATMENT AND BETTER OUTCOMES.

TO VIEW THE ENTIRE PRESENTATION VISIT
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Dry eye is a multifactorial disease of the tears and the ocular surface that results in discomfort, visual disturbance and tear film instability. It may be evaporative, as in meibomian gland dysfunction, or aqueous deficient, as in Sjögren’s syndrome, and is characterized by increased osmolarity of the tear film and inflammation of the ocular surface.1

Understanding the cycle of inflammation, which is a chronic process in dry eye disease, is important for effective management and treatment (Figure 1). When the epithelial cells of the conjunctiva, the cornea and the lacrimal system are stressed or unhealthy, they release pro-inflammatory markers, cytokines and proteolytic enzymes, specifically, matrix metalloproteinase (MMP-9).2 Elevated MMP-9 causes epithelial cell disruption that leads to corneal staining and a cascade of common dry eye symptoms.2,3

Patients report their eyes feel sandy or scratchy, and they experience excessive tearing, photophobia and fluctuating vision that requires the need to constantly blink to focus. These symptoms worsen over time, as the inflammation becomes chronic. Environmental factors — such as low humidity, wind and proximity to air conditioning ducts or fans — exacerbate symptoms. Patients struggle to see their smartphones, e-readers and computer monitors clearly. Their reading speed decreases, as does their work productivity, and driving at night becomes more difficult.

Timely and targeted treatment is vital to alleviate the symptoms of ocular surface disease, avoid...
long-term damage and improve quality of life measures for your dry eye patients. Diagnosis is the all-important first step toward implementing a treatment regimen customized for each patient.

**IDENTIFYING INFLAMMATION HELPS GUIDE TREATMENT**

Of the various tests available for dry eye diagnosis, I rely mostly on fluorescein and lissamine green staining to evaluate ocular epithelial health. I also measure tear osmolarity to assess tear health and perform the InflammaDry test to detect the presence of a clinically significant level of ocular surface inflammation. These tests provide objective data for my diagnosis, and patients appreciate having objective results to confirm or rule out the presence of disease.

The InflammaDry test, which has high sensitivity and specificity for inflammatory dry eye (Figure 2), helps me choose the appropriate therapy for each patient. For example, about 50% of patients who are symptomatic may have a negative InflammaDry test. Those patients may be symptomatic only in the presence of significant environmental stresses and not chronic enough to lead to persistent inflammation, or they may have underlying neuropathic mechanisms that may create a symptomatic response to a noninflammatory type of dry eye.

When inflammation is present, artificial tears alone will not reduce MMP-9 levels or help the clinical management; however, cyclosporine is an excellent first-line treatment for patients whose InflammaDry test is positive. In fact, researchers studying patients with thyroid-related dry eye disease found that those who had positive InflammaDry tests had significantly reduced MMP-9 levels after 2 months of treatment with cyclosporine (Figure 3). This strongly suggests we should be looking at cyclosporine to control inflammation in patients who test positive with InflammaDry.

Punctal occlusion (Figure 4) may be helpful for some patients, but only after the clinically significant inflammation has been ruled out or addressed. The best method for detecting inflammation is to perform the InflammaDry test. A positive test contraindicates the use of punctal plugs, because plugging the puncta would exacerbate the condition by increasing the contact time of the pro-inflammatory mediators in the tear film against the ocular surface. You must first treat the inflammation with your preferred modalities, such as oral omega-3s, cyclosporine or a short course of steroids. Once the patient is re-tested with InflammaDry, and the test results are negative, punctal plugs can be used.

The presence or absence of MMP-9, or inflammation,
on the ocular surface drives therapeutic decision-making, and the InflammaDry test is the only FDA-cleared test to identify MMP-9 (Figure 5). A positive result can give you the confidence and data necessary to customize treatment for each patient.

**SURGICAL PATIENTS**

Diagnosing ocular surface inflammation prior to surgery is critically important. Studies have shown the effects of ocular surface inflammation on surgical outcomes. The more inflammation there is, the less reliable the preoperative data — such as keratometry, aberrometry, and biometry — will be. For example, if a cataract surgeon bases his or her implant calculations on unreliable data, there’s a higher probability that the outcome may be a refractive surprise. No patient and no surgeon will be happy with that. The same is true with LASIK. If a patient has ocular surface inflammation, postsurgical complications are more likely to develop.

The best course is to inform the patient that he has a preexisting condition that requires treatment before surgery. I like to engage patients in that process, so they understand they have a chronic condition that will require long-term treatment. Once the ocular surface is optimized, the surgeon can proceed with the preoperative measurements and feel confident that the refractive outcomes have a higher possibility of achieving the set target.

There is also evidence that perioperative management of elevated MMP-9 may not only accelerate visual recovery and reduce dry eye symptoms, but a recent study by Shetty and colleagues suggests that this strategy may also protect against potential ectasia in forme fruste keratoconus.

Thus, knowing the InflammaDry test results can help surgeons decide which peri-surgical treatment plan will be most effective for their patients.

**CONTACT LENS PATIENTS**

Dry eye is a leading cause of contact lens intolerance and fitting challenges. Contact lens wearers who report discomfort and reduced wearing times are excellent candidates for the InflammaDry test. If the test is positive, I recommend the following:

- Switch the patient to daily disposable contact lenses.
- Start treatment with cyclosporine to help fight the inflammation.
- Initiate oral omega-3 treatment, which is an excellent anti-inflammatory option.
- Reserve punctal occlusion until after the inflammation has resolved.

If the InflammaDry test is negative, you can use punctal plugs immediately and initiate omega-3 treatment. Cyclosporine isn’t indicated if the test is negative. By avoiding the unnecessary use of cyclosporine, you’ll save patients the expense of the drug and possible frustration if they don’t see an improvement in their symptoms with the use of a prescription medication.

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**InflammaDry** is the only test for MMP-9.

**Elevated MMP-9** may predict which patients will respond to anti-inflammatory therapy.

Figure 5. InflammaDry is the only test that is FDA-cleared to identify MMP-9.
GLAUCOMA PATIENTS

The InflammaDry test is also beneficial to evaluate patients who are being treated for glaucoma. Most glaucoma patients have to use anti-glaucoma medications day in and day out for the rest of their lives, and sometimes they’re using more than one topical medication to control their intraocular pressures. Most of these medications contain preservatives, and sometimes the pH of these medications must be at a certain level to enhance the penetration of the drug into the eye. Consequently, many patients who use topical anti-glaucoma drops have serious ocular surface issues. These patients may benefit from the concomitant use of cyclosporine.

A positive InflammaDry test will help you decide which path to select for these patients. For example, you may want to recommend earlier Selective Laser Trabeculoplasty (SLT) to avoid additional topical therapeutics, or you may be able to switch patients to preservative-free glaucoma drops. The InflammaDry test will help you identify patients who may benefit from a drainage device, such as the iStent (Glaukos) at the time of cataract surgery, to reduce the probability of needing a second glaucoma medication. Finally, if the InflammaDry test identifies significant ocular surface disease in a patient who is scheduled to undergo trabeculectomy surgery, the ocular surface disease must be pretreated to ensure a more successful outcome with less chance of a bleb failure.

The corollary to that is, if the InflammaDry test is negative, patients with glaucoma can continue using their current medications; there’s no need to consider the more expensive, preservative-free options.

INFLAMMADRY BENEFITS

The following features make the InflammaDry test simple to incorporate into your practice:

• **CLIA-waived.** The Centers for Medicare and Medicaid Services designates laboratory tests as one of three options: waived, intermediate and complex. A waived test, such as the InflammaDry test, can be performed in physicians’ offices, often by technicians, whereas intermediate and complex tests must be performed in certified laboratory settings.

• **Rapid.** InflammaDry test results are available in as soon as 10 minutes.

• **Easy to use.** The InflammaDry test is performed in four simple steps, as illustrated by Figure 6, and can be performed by a nurse or technician during the initial workup with no change to patient flow.

• **Performed in office.** This point-of-care immunoassay test aids in dry eye diagnosis during the office visit.

• **Low cost.** No expensive or accessory equipment required.

TIPS FOR SUCCESS

• **Use a questionnaire.** In addition to assessing signs and symptoms, clinicians are encouraged to use a questionnaire designed to elicit dry eye-related information from patients. In our practice, we incorporated questions related to the most common dry eye symptoms into our electronic medical records under the “history of present illness” section. If a patient answers yes to any of these symptoms, our technicians are empowered to perform tear osmolarity and InflammaDry testing. Remember

Figure 6. The InflammaDry test is performed in 4 simple steps.
that you must document these symptoms to meet insurance requirements for the test.

- **Do not instill drops of any kind before performing the InflammaDry test.** This test cannot be performed if drops of any kind have been instilled. This is why we educate and empower our technicians to perform this test at the time of the screening portion of the office visit, before mydriatic agents or anesthetic drops have been placed in the eye.

- **Wait a full 10 minutes for results.** We use timers; when the buzzer sounds, we know the test is ready to be read.

- **Read any form of a red line as a positive result.** Even if the red line is faint or broken, consider it a positive result. The brightness of the red line is directly proportional to the amount of MMP-9 in the tears.

- **Collect a sufficient tear sample.** The sampling fleece should glisten, as shown in Figure 7. First, let the patient know that a tear test will be performed that takes about 30 seconds and may feel a little scratchy. Then, have the patient look up, pull the lid down, dab and press the tarsal conjunctiva several times (do not scrape), and then release the lid. Let the patient blink once or twice, then repeat for 5 seconds and then remove. Reflex tearing does not affect the test results.

In conclusion, I believe that the InflammaDry test provides reliable data regarding MMP-9 pro-inflammatory biomarkers on the ocular surface to allow the eye care provider to customize the treatment for each patient, which ultimately results in improved patient outcomes.

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**REFERENCES**


8. FDA Section 510(k) number k083184 for TearLab™ Osmolarity System; May 5, 2009.


Cynthia Matossian, MD, is founder and CEO of Matossian Eye Associates, an integrated ophthalmology and optometry private practice with locations in Mercer County, NJ, and Bucks County, PA. She is a clinical assistant professor of ophthalmology at Temple University School of Medicine in Philadelphia. She has published extensively in peer-reviewed journals and has participated in numerous clinical trials. She was the only physician to be named one of the top 25 leading women entrepreneurs in New Jersey, one of U.S. News and World Report’s Top Docs, one of New Jersey’s Best 50 Women in Business, one of Pennsylvania’s Best 50 Women in Business, and an Outstanding Female Ophthalmic Leader.
InflammaDry Q&A

During a recent webinar, Dr. Matossian fielded a variety of questions from listeners. Below are some highlights from the Q&A session.

Q: DO YOU TEST BOTH EYES WITH INFLAMMADRY? IF SO, CAN YOU BILL FOR BOTH EYES?
A: I test both eyes. Sometimes, surprisingly, one eye is positive while the other eye is not. Or you may see a faint red line, which indicates less inflammation, for one eye, and a brilliant red line, indicating more MMP-9 markers are present in the other eye. Knowing this, you can titrate the treatment for each eye. Often, when one eye is positive, I assume both eyes have inflammation and design a treatment regimen for both eyes. And yes, you can bill for both eyes.

Q: DO YOU USE THE INFLAMMADRY TEST FOR PATIENTS WHO ARE USING CYCLOSPORINE?
A: Yes, for several reasons. Sometimes, a patient’s inflammation is so severe that cyclosporine alone may not be adequate to treat it, or a patient may have had an exacerbation of his ocular surface disease, requiring a short course of a steroid. First, however, I want to establish that the patient has been adhering to the cyclosporine regimen. If he admits to missing doses, I emphasize the importance of using the cyclosporine twice a day. If the patient has been using the cyclosporine as prescribed and the InflammaDry test is positive, I know an additional treatment is needed to address the level of ocular surface inflammation.

Q: A RECENT STUDY1 FOUND THAT ELEVATED MMP-9 WAS ASSOCIATED WITH KERATOCONUS AND ITS PROGRESSION. DO YOU THINK PREOPERATIVELY TREATING PATIENTS WHO HAVE ELEVATED MMP-9 WITH CYCLOSPORINE MIGHT HELP REDUCE THE RISK OF POST-LASIK ECTASIA?
A: The study showed that patients with keratoconus had elevated MMP-9 markers and that treating them with cyclosporine helped stabilize the progression of keratoconus and helped flatten their corneas. Additional studies are needed in this area, but the use of cyclosporine is showing positive results in patients with keratoconus. It would be beneficial to use InflammaDry to identify patients who should undergo targeted dry eye treatment before scheduling LASIK.

Q: DO YOU USE INFLAMMADRY ONLY IF THE OSMOLARITY READING IS ABOVE 308?
A: I use InflammaDry as an independent tool, not related to a specific tear osmolarity reading. If a patient is symptomatic but his tear osmolarity is in the normal range, I still perform the InflammaDry test. I recently had a patient whose tear osmolarity readings were 285 and 287, yet his InflammaDry test was strongly positive.

Q: HAS USING INFLAMMADRY HAD ANY EFFECT ON YOUR CHAIR TIME?
A: Yes, it has — a positive effect, because I now have an objective test result to share with patients while they’re in my examination chair. The InflammaDry test confirms the existence of ocular surface inflammation. Patients love getting a yes-or-no answer right away. When we have confirmation that inflammation is present, we focus on how we’re going to treat it.

Q: DOES THE TEST HURT? DO YOU USE ANESTHETIC BEFORE PERFORMING THE TEST?
A: The test doesn’t hurt at all. You gently pull down the lid and dab the sampling fleece along the tarsal conjunctival surface, starting laterally and moving nasally toward the inner canthus. In fact, do not use an anesthetic drop before performing the test, because it will invalidate the result.

Q: WHEN TREATING TO STABILIZE TEAR FILM PRIOR TO SURGERY DO YOU RETEST WITH INFLAMMADRY BEFORE PERFORMING KERATOMETRY AGAIN? ALSO, PLEASE COMMENT ON YOUR STEROID PROTOCOL FOR THAT SITUATION.
A: I’m very particular with my preoperative testing. If a patient’s keratometry and topography readings don’t show consistency among four or five different pieces of equipment, there’s a reason; so I stop. If the InflammaDry test is positive, I start the patient on re-esterified oral omega-3 (Physician Recommended Nutriceuticals®, PRN), a microwaveable hot mask, and cyclosporine. If the InflammaDry test isn’t positive, but the patient has signs of ocular surface disease, I start loteprednol etabonate ophthalmic gel (LOTEMAX®, Bausch + Lomb) twice a day for a short course, about 2 weeks instead of starting cyclosporine. I then bring the patient back to repeat the measurements. If the InflammaDry test is negative at this visit, I am confident my data will be reliable. I look at the patient’s keratometry and topography readings, and make sure they’re consistent, that there’s less than 0.50D change between the different measurements in the magnitude of the astigmatism, and that the axis is no more than 10 degrees apart.

REFERENCE
Diagnose with Confidence

Identify Ocular Surface Inflammation

InflammaDry is the first and only, rapid, in-office test that detects MMP-9, an inflammatory marker that is consistently elevated in the tears of patients with dry eye disease.¹

Reimbursable with CPT® Code 83516

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